

THE ALCIVAX

Alcimed analyzes the impact of superspreaders and redefining the definition of COVID on the healthcare system.

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COVID: Do we understand the problem?

"If you define the problem correctly, you almost have the solution," Steve Jobs. This has perhaps been one of the prevailing problems in our response to COVID-19, which has racked up 100K new cases a day globally for the past two weeks. After cataloging odd symptoms, questions have been raised if labeling COVID-19 as a respiratory disease may be focusing efforts in the wrong direction.



SARS-CoV-2: One of a Kind

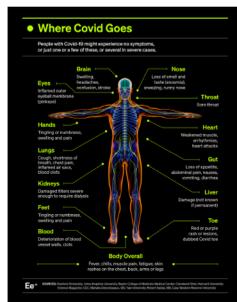


It may seem like a basic question, but there is a current debate as to whether COVID-19 should be classified as a predominately respiratory or vascular disease. In the beginning of the pandemic, we stuck to what we know. Coronaviruses cause respiratory infections. Yet over the course of the pandemic, data demonstrates that 40% of people die from cardiac complications. Autopsies show that COVID patients have 9 times more

blood clots in their lungs than someone who died of H1N1 flu. The new theory suggests that SARS-CoV-2 while replicating in the lungs gains access to the blood vessels and causes direct and indirect damage to the walls of the vessels.

This damage would cause three things, vascular leakage, blood clots, and inflammation, leading to a deadly second non-respiratory phase of the disease. The inflammation would lead to acute respiratory distress syndrome (ARDS) which many patients die of, the Kawasaki like disease seen in children, and the higher number of heart attacks. The blood clots would also explain the neurological symptoms including stroke recorded. Damage to endothelial cells that line blood vessels would also damage the liver, kidneys, and intestines.

This respiratory to vascular transition certainly makes SARS-CoV-2 unique.



InfoGraphic by Elemental



The Permanent Damage

There are a growing number of patients who have survived severe Covid-19 but have not yet recovered. Many are younger and previously healthy, but are now debilitated after days of deep sedation and mechanical ventilation. Some need to learn how to walk again—and others—to dress themselves. About 15% of COVID patients develop acute kidney injuries that can lead to dialysis and permanent loss of kidney function.

Some patients may even be facing long-term disability. Reports of damage to lungs, kidneys and heart are joined by symptoms of ongoing/crushing fatigue, muscle pain and even cognitive problems. As Covid-19 is a new disease, there are limited to no studies about its long-term trajectory for those with more severe symptoms, including lung scarring, heart damage, and neurological and mental health effects. On CT scans, Covid-19 patients' lungs frequently have lighter gray patches, which may not heal and can occur in up to 77% of patients. Covid-19 also seems to affect the central nervous system, with potentially long-lasting consequences. In studies from China and France, many people hospitalized with confirmed Covid-19 had neurological symptoms, including dizziness, headaches, impaired consciousness, vision, taste/smell impairment, and nerve pain.

Is the healthcare system ready to deal with the long-term consequences?



Superspreaders

Having a grasp on the high rate of potentially life-long complications from COVID-19, it is even more important to consider how to prevent the potentially devastating 2nd wave of infection that is predicted for the fall. Recent analysis suggests that this may come down to being able to control the superspreader.

What is a superspreader? A superspreader is a person that manages to give COVID-19 to a larger number of people that predicted by the average attack rate. A growing database at the London School of Hygiene and Tropical Medicine is beginning to analyze superspreader events to identify elements that they have in common.

How many people can get infected at a single event? Studies from London combined with studies from Tel Aviv University and the Institute for Disease Modeling suggest 10% of cases may cause up to 80% of new infections.

While research shows that some people do shed more virus than others, but it may also come down to how a person speaks. Shouting and singing, for example produce more respiratory droplets than normal speaking, but the effects can be mitigated through the use of a mask. This higher volume of respiratory droplets spreads best in crowded indoor environments, explaining how a single choir practice contain 61 people infected 53 people in under 2.5 hours. Similar superspreader events have been seen worldwide, and explain why such large numbers of new cases can spring up as a result of re-opening activities.

What is clear is there are unlikely to be any "Typhoid Marys" that arise from the COVID-19 crisis, as biology is less to blame than conditions, but this should allow us to configure reopening procedures that limit superspreader events and thus contain the spread more effectively. Waste water testing is even being implemented to track the re-emergence of COVID hotspots after re-opening in Finland, Germany, and the Netherlands.

How do you avoid superspreaders? Stay out of large indoor crowds talking or singing at loud volumes.



COVID Treatments

With roughly 40% of COVID deaths due to cardiovascular complications, and a growing body of evidence that coronavirus can infect blood vessels, it may also be time to rethink what we need to treat COVID-19. To prevent the endothelial cell damage that leads to the break down of blood vessels, currently approve drugs such as statins, which improve endothelial cell function and reduce inflammation, may blunt the deadly vascular side of COVID. In addition, the FDA has given emergency approval to treat COVID patients with severe cardiac symptoms with the Abiomed heart pump.

There have also been some further treatment disappointments. Protease inhibitors for HIV treatment, lopinavir and darunavir, show no efficacy against COVID-19. Additionally, hydroxychloroquine has no preventative benefits, based on a recent major trial hopefully putting to bed the anti-malarial hype. Gilead's remdesivir, however, does show improvement for patients even with moderate COVID pneumonia.



The Antibody Race

Eli Lilly and Company has started the first human trial of an antibody therapy to treat the novel coronavirus. The antibody therapy was created through a partnership with AbCellera, a Canada-based biotech company and the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases. If the trial is successful, the therapy could be available by the fall. Merck has also promised that all of their COVID assets (2 vaccine candidates and 1 antiviral) will be "broadly accessible and affordable globally." "Operation Warp Speed" in the US includes the Merck vaccine in their announced group of 5 vaccines most likely to succeed, which also included Moderna, AstraZeneca, J&J, and Pfizer. Makes you wonder what happened to Sanofi and GSK's candidate that has BARDA funding.



The Testing Quagmire

From the beginning of the outbreak, the WHO has been at the forefront of testing guidelines and recommendations. However, with the US announcing its official decision to withdraw from the WHO, after 72 years, while still owing the WHO \$200 M, the ability of the WHO to drive testing as the pandemic continues is at stake. It will also further isolate the US to attempt to deal with the pandemic on its own.

Controlling the pandemic is not likely to be successful without testing data that can be reliably interpreted. The intense demand for testing has led more than 200 COVID antibody tests flooding the market in the last few weeks. Only 15 of those tests have actually received approval from a regulatory body. The uncertainty generated from faulty test data has made the exit from lock down even more confusing. The disarray seems worse in the US than in other countries, as the FDA has removed 30 tests from the market last week.

But not all the testing news is bad, several important advancements have also been made. More at home test kits have received approval (LabCorp & Quest), and real advancement has been made in developing testing that will actually predict the outcome for the patient once infected. Genetic testing research has begun to help predict which COVID patients will get the worst disease.

Roche has developed a test for monitoring patients IL6 levels. By monitoring the inflammatory cytokine, doctors can more readily predict which patients may develop respiratory distress and need a ventilator. The test is also used in Europe to predict whether non-COVID patients likely to develop sepsis. CLEW Medical's remote data monitoring system can also use remote monitoring AI to predict respiratory failure and insufficient blood flow in ICU COVID patients. Academic researchers are also now working on rapid tests (10 min) with visual readouts for active infection, increasing our ability for point of care testing under many different scenarios as nasal and saliva samples can both be used.



Approval & Profiteering

US FDA director Hahn signaled this week that the changes to drug approval processes during the pandemic that have accelerated drug approval processes may be here to stay, as regulatory bodies gain more confidence in real world evidence.

If accelerated approval are going to become the norm, then a large discussion needs to take place on the need for real transparency in the how the accelerated data is collected and what it really means. In recent weeks, eyebrows have been raised as to how much money biopharma companies have raised on potentially misleading information. The concern is in response to the \$57 B raised in market capitalization this year by just 5 companies, all with COVID vaccine or therapeutic assets. Moderna's executives \$89 M cash out is a prime example of what looks from the outside like profiteering.

While no laws have been broken, the time for deciding how real-world evidence transparency and accelerated approval communications are regulated is now.



All Joking Aside

5 Hawaiians caught 220 lbs tuna and donated it to healthcare workers after being converted into 300 poke bowls. Keep in mind they only caught one fish.



A retired healthcare worker in Derby, England is claiming that she beat Coronavirus at 104 in only 10 days by drinking champagne, but it is unclear if you can claim that on your medical bills.

The warmer weather has had mixed results for public figures of late. On the upside, the Queen of England has made her first public appearance riding her horse on the grounds of Windsor Castle. But the Armenian Prime Minister is now isolating after testing positive for COVID, as has the Belgian Prince Joachim. Little sympathy has been solicited for the Prince how contracted the virus while partying in Spain. The Prince has issued a public apology.

Hugs are Back! At least if you follow a few simple guidelines

These positions are bad.

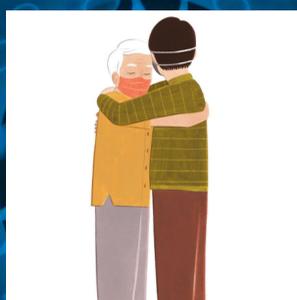
The positions are preferred and don't increase risk.



No face to face hugs



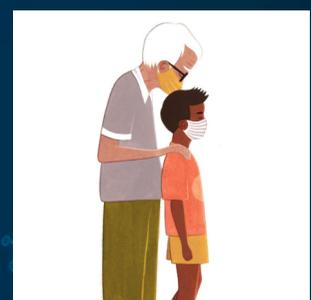
No cheek to cheek hugs



Yes to facing opposite



Yes to waist hugging



Yes to kisses on the head