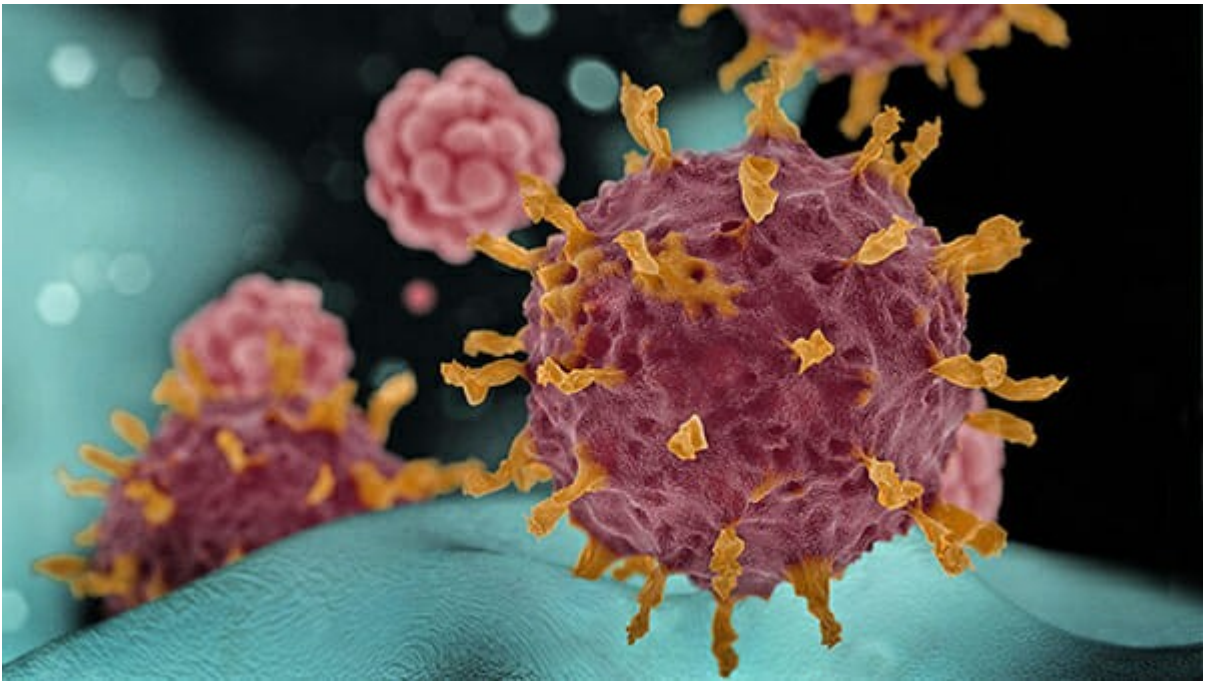


Coronavirus 2019, Covid19, SARS CoV2-19.



H. Robert Silverstein, MD, FACC for the Preventive Medicine Center

First principles. Simplicity.

Clyde W. Yancy, MD, Vice Dean for Diversity and Inclusion Chief of Cardiology in the Department of Medicine, Feinberg School of Medicine at Northwestern University in Chicago

Clyde W. Yancy, MD: *“I’m exhausted by the stress; disheartened by the toll on human life; concerned deeply about the exposure to healthcare workers- BUT, I am emboldened by the display of courage, selflessness, compassion, and sacrifice that I see in physicians, nurses and health care workers across the country.”*

This 2019 corona virus CoV2-19 is an entirely new RNA virus (as opposed to a DNA virus) with 30 proteins. The word “VIRUS” means “poison.” A human cell has 20,000 different proteins. Being an RNA virus, it is similar to hepatitis C; it is

not a DNA virus like hepatitis B. There are 200 viruses that can cause the common cold and several of these are corona viruses. “Corona” is Latin for “crown” which is how the virus looks in the microscope as if it has an encircling crown. The specific CoV2-19 genetic RNA fact and its “SPIKE” projections will affect anti-viral treatment design and decisions. That virus spike binds to and fuses with host cells. “The SARS-CoV-2 spike protein trimer is only ~10nm in size (1/100,000 of a millimeter) and there are approximately 100 of these on the surface of a single viral particle, which itself is about 100nm in diameter.” CoV2-19 was detected by it having a new genetic sequence as recognized by GenBank—it may have been around for a thousand years, but it is just now discovered. The Chinese symbol for it is pronounced “wayGee” and means both “crisis” and “opportunity”: two sides of the same coin. The first known novel and important coronavirus was called SARS = Severe Acute Respiratory syndrome. There are only 2 known previous serious corona virus outbreaks: SARS and Middle East respiratory syndrome = MERS, the latter epidemic was smaller, but with a 1/3 (33%!) death rate!

This Covid-19/CoV2-19 corona virus was originally named for its site of ORIGIN (Wuhan, China) as was the Ebola (a river in Zaire) virus, German measles, Rocky Mount spotted fever, Norovirus (Norwalk, Connecticut), and Spanish flu, etc. Corona virus-19/CoV2-19 was first documented mid-November, 2019, in China. Although the Chinese government is currently stating that the virus originated in the United States, almost certainly it originated in either what is called a live or “wet” market where wild animals are sold for food in Wuhan, China, or the virus escaped the research Wuhan National Biosafety Laboratory close to Wuhan, China: the latter is considered a reasonable possibility.

The fascinating sequence of VIRAL ESCAPE resulting in HUMAN INFECTION is that corona virus infected bat meat whether from the research labs in Wuhan, China, or just wild living bats may have gone through intermediate hosts such as snakes, pangolins, and now dogs are also recognized as a possible vector. Ed Yong in the 4/29/20 *The Atlantic* (magazine) “...scientists have also identified about 500 other coronaviruses among China’s many bat species. “There will be many more—I think it’s safe to say tens of thousands,” says Peter Daszak of the EcoHealth Alliance, who has led that work. Laboratory experiments show that some of these new viruses could potentially infect humans. SARS-CoV-2 likely came from a bat, too.

It seems unlikely that a random bat virus should somehow jump into a susceptible human. But when you consider millions of people, in regular contact with millions of bats, which carry tens of thousands of new viruses, vanishingly improbable events become probable ones. In 2015, Daszak’s team found that 3 percent of people from four Chinese villages that are close to bat caves had antibodies that indicated a previous encounter with SARS-like coronaviruses.*he Atlantic Magazine*: “... scientists have identified 500 other [corona viruses](#) among China’s many

bat species. ‘There will be many more—I think it’s safe to say tens of thousands,’ says Peter Daszak of the EcoHealth Alliance. It seems unlikely that a random bat virus should somehow jump into a susceptible human. But when you consider millions of people, in regular contact with millions of bats, which carry tens of thousands of new viruses, **vanishingly improbable events become probable ones**. In 2015, Daszak’s team found that [3 percent of people](#) from four Chinese villages that are close to bat caves had antibodies that indicated a previous encounter with SARS-like coronaviruses....”

Human invasion by the corona virus is favored by its **low “CpG”** content. CpG is recognized by the human immune system as a foreign invader, thereby activating the ZAP neutralizing protein. Low CpG levels will escape ZAP immune attack. Thus, the virus is able to invade the human body via its ACE2 protein which is in highest concentration in the intestinal tract. **More information:** *Molecular Biology And Evolution* (2020). DOI: [10.1093/molbev/msaa094](https://doi.org/10.1093/molbev/msaa094) *Molecular Biology and Evolution* The corona virus CoV2-19 entry into [human cells](#) is aided by an enzyme called TMPRSS2. INTERFERON is a virus-induced virus-attacking cytokine (a cytokine is made in many locations throughout the body, but is not made in a single area like thyroid hormone which is just made in the thyroid gland). Interferon turns on the ACE2 gene allowing more sites for CoV2-19 entry into the human body.

Jon Barron on LUNG INVASION: “COVID-19 appears to have a preference for two specific types of lung cells: goblet cells and ciliated cells. Goblet cells produce the mucus that both keeps your lungs moist and also captures particles, bacteria, and even viruses that you might inhale. Ciliated cells, on the other hand, have little hairs on them that move in a wavelike manner pushing the mucus (and anything it captured) up and out of the lungs into the back of the throat, where you can cough it out.” M Wadman et al. in 4/17/20 *Science* “Front-line white blood cells release inflammatory molecules called CHEMOKINES, which in turn SUMMON more immune cells that target and kill virus-infected cells, leaving a STEW OF FLUID AND DEAD CELLS-PUS behind in the alveoli (air sacs). This is the UNDERLYING PATHOLOGY of the CoV2-19 PNEUMONIA, with its corresponding symptoms: coughing; fever; and rapid, shallow respiration.” Severe cases have multiorgan dysfunction, and hemodynamic instability (unstable circulation), as well as cardiovascular complications including myocardial injury, myocarditis, acute myocardial infarction (heart attack), heart failure, dysrhythmias (irregular heart beat), and venous thromboembolic events (clots).

See the comment of world-famous virologist David Ho below.

KEY DATES IN COV2-19 THE DAILY TELEGRAPH NEWSPAPER

11/9/15: Wuhan Institute of Virology publish a study revealing they created a new virus in the lab from SARS-CoV.

12/6/19: Five days after a man linked to Wuhan's seafood market presented pneumonia-like symptoms, his wife contracts it, suggesting human to human transmission.

12/27/19: China's health authorities told a novel disease, then affecting some 180 patients, was caused by a new coronavirus.

12/26-30/19: Evidence of new virus emerges from Wuhan patient data.

12/31/19: Chinese internet authorities begin censoring terms from social media such as Wuhan Unknown Pneumonia.

1/1/20: Eight Wuhan doctors who warned about new virus are detained and condemned.

1/3/20: China's top health authority issues a gag order.

1/5/20: Wuhan Municipal Health Commission stops releasing daily updates on new cases. Continues until January 18.

1/10/20: PRC official Wang Guangfa says outbreak "under control" and mostly a "mild condition".

1/12/20: Professor Zhang Yongzhen's lab in Shanghai is closed by authorities for "rectification", one day after it shares genomic sequence data with the world for the first time.

1/14/20: PRC National Health Commission chief Ma Xiaowei privately warns colleagues the virus is likely to develop into a major public health event.

1/24/20: Officials in Beijing prevent the Wuhan Institute of Virology from sharing sample isolates with the University of Texas.

2/6/20: China's internet watchdog tightens controls on social media platforms.

2/9/20: Citizen-journalist and local businessman Fang Bin disappears.

4/17/20: Wuhan belatedly raises its official fatalities by 1290.

China notified the World Health Organization of this infection 12/31/19 saying "the (corona virus 19) disease is preventable and controllable" incorrectly at that time. 7 million people had been in, and then left, Wuhan to go else(every)where outside of China beginning December, 2019. Flights were

completely stopped from Wuhan to the rest of China, but not elsewhere, during that period of time. As noted, in contrast to the rest of the world where every large city has been affected by the corona virus CoV2-19, ALL other large Chinese cities were REPORTED to have had virtually no incidence of the corona virus because of that policy. January, 21, 2020, China stated, and the World Health Organization (WHO)'s Dr. Tedros repeated, that this corona virus could not be transmitted from person to person: that, too, was wrong. The first overseas CoV2-19 case was documented 1/15/20. The first USA case was found 1/21/20. The city of Wuhan, China, (not the whole country) lockdown began 1/31/20. The shutdown of immigration to the USA for non-Americans began 1/31/20. The virus is now in 185 of 203 countries in the world.

In 1348, the BLACK PLAGUE killed 1/3 to 1/2 (50%!) of the WORLD's population. That was due to the bacteria *Pasteurella* or *Yersinia pestis* carried by the rat flea. The quite recent MERS = Middle Eastern Severe Respiratory disease was 33% lethal! For a more recent perspective, the HONG KONG 1968-1969 FLU ravaged the world; it killed more than one million (1,000,000) worldwide, over 100,00 in the USA with no lockdown nor closure of businesses, but with social distancing: this memory may seem unbelievable, yet it is true and in contrast with now.

The 2009-2010 SWINE FLU H1N1 virus originated in Mexico when there was an open Southern USA border. The WHO declared the H1N1 virus an **imminent** threat on 4/29/09, however, the WHO waited until 6/11/2009 to declare it a world pandemic. The Swine Flu virus was in the United States 7 months before the government called it a national emergency and that was several months after it was named a pandemic by the World Health Organization (WHO). Learning from the past, the current national emergency was so named 2 months after the virus was first here 1/21/20 and several days after the WHO called it a pandemic. As for the seasonal flu, the CDC website for 2019-2020 now projects there will be 48,000,000 illnesses, 22,000,000 medical visits, 550,000 hospitalizations and 43,000 deaths: less now than the current CoV2-19 (78,000), but the latter in a much shorter time frame. In harsher flu years, 60-80,000 Americans are lost. During the current CoV2-19 the number of deaths is 77,000 deaths likely headed to 100,000 total, that is overall 1.5 in 10,000 for the total USA population.

As further perspective, in 2015, Ian Goldin, an Oxford University professor, in his book *The Butterfly Defect*, warned of the risks of a "global pandemic in a modern, interdependent world": no one in the USA federal/state/local governments and other governments, listened or prepared for the future thus affecting our ability to appropriately respond now. These are historical facts.

The FLU vs CoV2-19: the latter is more serious. See this comparison link.

https://www.nola.com/news/coronavirus/article_e33c0cf0-7090-11ea-b3da-53f5ab31dd4b.html

There is no prior experience with this current CoV2-19 virus; it spreads relatively easily. That spread has slowed significantly in China. 95+% of the Chinese population did not contract the virus. In China, infectivity has decreased from 2 to 3 other people per infected case to 1.5 per case. In the beginning, the infection rate doubles every five days as has been documented with increased testing. Newer information from the USA's Los Alamos National Laboratory states that 5 people are infected per case. Influenza (the flu) spreads to 1.7 people per original case. A wide screen in San Diego, Calif, implies that there may be 10 million in the USA who are already infected. Social distancing to break the chain of viral transmission is said to continue until at least 5/1/20, but individual states are starting to return to normal as of 4/17/20. Sweden only shut down minimally: scia distance + protection of the elderly. Multiple tests MAY be necessary to prove if a patient is infected. On 3/30/20 there was a report from Wuhan, China, of CoV2-19 corona virus re-infection. This is now also true of Singapore and South Korea, even as returnees also increase the number of cases.

As reported by Anthony Fauci, MD, Chief of the National Institutes of Health (NIH) Infectious Disease section, the current influenza virus is 0.1% lethal and this CoV2-19 virus is 3.4% lethal, although in Germany it was found to be **0.37%** lethal; although not 3.4% lethal, still it is **4 times more lethal** than the <https://www.thepmc.org/lib/corona-virus-4-28-20-and-forward2019> seasonal flu. Jon Barron offers this information: "the mortality rate is as low is 2.1% in Turkey and 2.5% in Germany. But it's as high as 12.8% in Belgium and Italy. The US mortality rate is 4.1%, and the global average is disturbingly high at 6%." 90% of those admitted have underlying chronic health conditions. ONLY 5% will need the ICU. Michael Greger, MD: statistics "from South Korea: of confirmed cases, about 1 in 1,000 died in their 30-40s, 1 in 150 of those in their 50s, 1 in 50 in their 60s, 1 in 15 in their 70s, and 1 in 5 in their 80s. Harlan Krumholz of Yale University said "Its ferocity is breathtaking and humbling."

It has recently been estimated that only 6% of cases have been identified (*Lancet Infectious Diseases* 2020. DOI: [10.1016/S1473-3099\(20\)30243-7](https://doi.org/10.1016/S1473-3099(20)30243-7)). This means there are 10 million infected in the USA. The true death rate is unknown because the actual number of infected is based on those tested and MANY more who have this infection but are not yet identified as they have not been tested and found. In 80% of the infected it will be a mild cold or flu. 25% may be asymptomatic carriers. While it can affect the young, it is most severe in those over 65, those with high blood pressure, overweight, diabetes, high population density living, asthma, heart disease, exposed to

air pollution, the immune immobilized, etc. These are risk factors more identifiable in the Black and Latino communities. The IMHE (Institute for Health Metrics and Evaluation) model that advises the Federal government on the coronavirus has been remarkably incorrect. This model predicted that over 121,000 Americans would be hospitalized by 4/1/20: the actual number was 31,142. The scariest predictions of lethality have NOT come to pass which is in part to social distancing and quarantining + effective treatment.

From *Wired* online *Magazine* by G M Graff : “An Oral History of the Day Everything Changed, 3/11/20” “... History will record that Wednesday, March 11, the 71st day of 2020, proved to be unlike any other in American history—the pivot point on which weeks of winter unease about the looming novel coronavirus turned in a matter of hours into a sudden, wrenching, nation-altering halt to daily life and routine. Just a day earlier, Americans across much of the country were still going into the office, meeting friends for drinks, and shaking hands in meetings. That morning, the number of coronavirus cases in the US crossed the 1,000 mark, up 10-fold from the prior week. Only 29 Americans had died.

But on that Wednesday, the World Health Organization, which had only begun referring to the virus as Covid-19 a month earlier, declared the disease a global pandemic. Every hour seemed to bring major new developments: On Wall Street, after days of huge up-and-down gyrations, the Dow Jones Industrial Average fell 1,465 points and officially entered bear territory; Capitol Hill faced its first confirmed Covid-19 case; the NCAA announced it would play its basketball tournament without fans; and then, in rapid-fire succession that evening, President Trump gave an Oval Office address, announcing a travel ban from Europe, the NBA suspended its season after player Rudy Gobert tested positive for the virus, and Tom Hanks and his wife, Rita, posted on Instagram that they too had been diagnosed while in Australia and were recuperating....”

TRENDING: "This is the Beginning of the End of the Pandemic" - Dr. Stephen Smith Announces Hydroxy-Chloroquine Study that is "Game Changer" in Battle Against Coronavirus (VIDEO)

See also the more optimistic 3/25/20 *Wall Street Journal* article by Bendavid and Bhattacharya.

B. Hume: ““I think it’s time to consider the possibility... that this lockdown, as opposed to the more moderate mitigation efforts... is a colossal public policy calamity.” Economist Scott Grannis observed 4/12/2020: “Almost overnight, we have wiped out all the net job gains of the past 14 years.” Grannis bluntly concluded that, “The shutdown of the U.S. economy will prove to be the most expensive self-inflicted injury in the history of mankind.”

N J Kaster 4/25/20: “Despite their air of authority, the experts never had enough knowledge about this virus to make reliable calculations about the future. But the real problem with the models weren’t that they proved to be false, but rather that they were promoted with false certitude. “I confess that I prefer true but imperfect

knowledge,” economist Friedrich Hayek once said, “to a pretense of exact knowledge that is likely (proved later to be) to be false.”

Hayek’s remark, given as he was accepting the Nobel Prize in 1974, was that thinking of economics as a “science” might lead to “a pretense of knowledge,” the idea that any one person might know enough to engineer society successfully, unmindful of unintended consequences.

“There is danger in the exuberant feeling of ever growing power which the advance of the physical sciences has engendered and which tempts man to try, ‘dizzy with success’... to subject not only our natural but also our human environment to the control of a human will. The recognition of the insuperable limits to his knowledge ought indeed to teach the student of society a lesson of humility which should guard him against becoming an accomplice in men’s fatal striving to control society--a striving which makes him not only a tyrant over his fellows, but which may well make him the destroyer of a civilization which no brain has designed but which has grown from the free efforts of millions of individuals.”

In contrast to the USA, this is essentially the approach Sweden has chosen. In an article in the UK *Spectator*, Fredrik Erixon, the director of the European Centre for International Political Economy in Brussel, explained that about Covid-19. Many people work from home. Restaurants are open, but not bustling. Keeping two metres apart at bus stops is something Swedes were pretty good at before the crisis: we don’t need much encouragement now. We’re careful. But our approach to fighting the pandemic starts from something more fundamental: in a liberal democracy you have to convince and not command people into action. If you lose that principle, you will lose your soul.”

So far, the Swedish strategy of allowing some exposure to the virus in order to build immunity among the general population while protecting high-risk groups like the elderly appears to be paying off. The country’s chief epidemiologist reported “herd immunity” could be reached in the capital of Stockholm in a matter of weeks. Moreover, Sweden has achieved this while taking a less economic hit than other countries in Europe. Sweden’s approach was a mixture of epidemiology and principle. Erixon noted that the concept of a national lockdown is “deeply illiberal -- and, until now, untested.” He allowed that Sweden may change if facts warrant. “But,” he wrote, “the vast majority, for now, want Sweden to keep its cool. We don’t want to remember 2020 as the time when we caused irreparable harm to our liberties -- or lost them entirely” Kaster finished.

Top Israeli Mathematician Claims COVID-19 Peaks After 40 Days With or Without Economic Lockdown: leading doctor dismisses his claims

By Times of Israel 4/14/2020

A prominent Israeli mathematician, analyst and former general claims simple statistical analysis, Isaac Ben-Israel, demonstrates that the spread of COVID-19 peaks after about 40 days and declines to almost zero after 70 days — no matter where it strikes, and no matter what measures governments impose to try to thwart it. Prof [Isaac Ben-Israel \(I B-I\)](#), head of the Security Studies program in Tel Aviv University and the chairman of the National Council for Research and Development said that research he conducted with a fellow professor, analyzing the growth and decline of new cases in countries around the world, showed repeatedly that **“there’s a set pattern” and “the numbers speak for themselves.”**

While he said he **supports social distancing, the widespread shuttering of economies worldwide constitutes a demonstrable error** in light of those statistics. In Israel's case, he noted, about 140 people normally die every day. To have shuttered much of the economy because of a virus that is killing one or two a day is a radical error that is unnecessarily costing Israel 20% of its GDP, he charged. I B-I stated that the closure policies of the quarantine countries can be replaced by more moderate social distancing policies. "The numbers simply do not support quarantine or economic closure."

On the reasonableness of Israel's unprecedented quarantine and closure, he commented to the news agency, "I think it's mass hysteria. I have no other way to describe it." Prof. Gabi Barbash, a hospital director and the former Health Ministry director general, insisted in an exchange that Ben-Israel is mistaken, and that the death tolls would have been far higher if Israel and other countries had not taken the steps they did.

But Ben-Israel said the figures — notably from countries, such as Singapore, Taiwan, and Sweden, which did not take such radical measures to shutter their economies — proved his point. (He [posted](#) an Hebrew paper to this effect on Facebook, with [graphs](#) showing the trajectories). When Barbash cited New York as ostensible proof that Ben-Israel was mistaken, I B-I noted the latest indications from New York were precisely in line with his statistics that indicate daily new cases figures peaking and starting to fall after about 40 days.

Asked to explain the phenomenon, I B-I, who also heads Israel's Space Agency, later said: "I have no explanation. There are all kinds of speculations. Maybe it's related to climate, or the virus has a life-span of its own." He said the policy of lockdowns and closures was a case of "mass hysteria." Simple social distancing would be sufficient, he said.

If the lockdowns instituted in Israel and elsewhere were not causing such immense economic havoc, there wouldn't be a problem with them, he said. "But you shouldn't be closing down the entire country when most of the population is not at high risk." Asked to explain why the virus had caused such a high death toll in countries such as Italy, he said the Italian health service was already overwhelmed. "It collapsed in 2017 because of the flu," he said. Barbash, speaking after Ben-Israel had left the studio, insisted that "we're going to be living with the coronavirus for the next year."

"Close to 60% of ALL infections in the US are within a 350 mile radius of NYC. The majority of the remaining US infections are also concentrated in urban metro areas like Detroit, New Orleans, Philadelphia, Atlanta etc. In New Jersey, its seven "commuter" counties closest to NYC contain 75% of the state's positive infections. The majority of deaths are people with: pre-existing medical conditions and/or who are over 65 and/or who are living in nursing, dementia care, or assisted living facilities and/or are addicted to drugs/alcohol. The county infection data confirms this is primarily an urban/metro area pandemic: very few healthy addiction-free people under 65 are dying from Covid-19 infection."

REOPENING in GERMANY, NORWAY, the CZECH Republic and DENMARK all lifted some restrictions 4/20/20: figures published by German disease control agency Robert Koch Institute 4/16/20 stated that the person-to-person infection rate has dropped to 0.7. Shops up to 800 square meters (8,600 square feet) will be allowed to reopen if they uphold hygiene rules, Chancellor Merkel said 4/15/20. Schools are set to reopen 5/4/20 in Germany with priority given to pupils taking exams soon. Rules will remain in force preventing groups of more than two people from gathering in public, other than family groups who live together, while large public events remain banned until 8/31/20.

HONG KONG (HK)MODEL: “**testing, contact tracing, and population behavioral change** were far less disruptive socially and economically than total lockdown. HK averted a major COVID-19 outbreak up to 3/31/20, by adopting far less drastic control measures than most other countries using a combination of border entry restrictions, quarantine and isolation of cases and contacts, together with some degree of social distancing, as reported in *The Lancet Public Health* journal. As of 3/31/20, HK had 715 confirmed COVID-19 cases including 94 asymptomatic infections, and 4 deaths in a population of about 7.5 million.”

Advance Care Planning and “The Love Song of J. Alfred Prufrock”

[Daniel P. Sulmasy, MD, PhD](#) JAMA Intern Med. Online April 13, 2020

doi:10.1001/jamainternmed.2020.0796 “...T. S. Eliot’s poem, “The Love Song of J. Alfred Prufrock”⁷ (eAppendix in the [Supplement](#)), first published in 1915, **considers the need to act under uncertainty and in the face of our certain mortality.** The poem can help us to understand why personal and cultural transformation are more important than legal documents, planning, scripted conversations, or AI....”

ENTRANCE of the virus is gained to the human body via a protrusion on the virus’s outside called a “SPIKE” by using the receptor binding domain (RBD)—which is responsible for this binding action attaches to an enzyme called ACE2 in the human body. ACE is expressed in 2 isotypes: a short and long form, with the convertase activity of the former being substantially faster than the latter, resulting in higher pathogenicity of the short form. Interestingly that is an enzyme that is blocked by certain medications used in the treatment of high blood pressure; it has been reported that patients who are on related blockers called “ARBs”, such as losartan and olmesartan, are resistant to the CoV2-19 virus infection by replenishing the low levels of ACE2 in CoV2-19 infection. But there is also debate about the safety of the use of ACE inhibitors and ARBs as being either protective versus harmful for CoV2-19 infection. <https://www.thepmc.org/lib/corona-virus-4-10-20-and-forward/>

CoV2-19 Attacks the 1-Beta Chain of Hemoglobin and Captures the Porphyrin to Inhibit Human Heme Metabolism: slightly edited

Posted 3/3/20 by [liu wenzhong](#) Li hualan In this study, **conserved domain analysis, homology modeling, and molecular docking** were used to compare the biological roles of certain proteins of this virus. Its **ORF8 and surface glycoprotein** bind to the porphyrin. At the same time, orf1ab, ORF10, and ORF3a proteins coordinate the **attack of the heme** on the 1-beta chain of hemoglobin to dissociate the iron to form the **porphyrin**. This attack will cause less and less hemoglobin availability. The lung cells have extremely intense poisoning and inflammation likely due in part to the **inability to exchange carbon dioxide and oxygen**. This results in the ground-glass-like lung images. These traits also interfere with the normal heme **anabolic** pathway. Chloroquine could prevent orf1ab, ORF3a, and ORF10 from attacking heme to form the porphyrin, and inhibit the binding of ORF8 and surface glycoproteins to porphyrins to a certain extent, effectively relieving the symptoms of respiratory distress. FAVIPRAMIR could inhibit the envelope protein and ORF7, a protein that binds to porphyrin, prevent the virus from entering host cells, and catching free porphyrins.

SYMPTOMS initially are fever (50% in the beginning and later 90%), dry cough, mild shortness of breath, malaise, headache, reddish eyes (conjunctivitis), 30% will have loss of the sense of SMELL and TASTE, but much less of runny nose, diarrhea, or vomiting. X-Ray/thin slice CT SCAN findings show “ground glass” bilaterally in both lungs, no pneumothorax, effusions or lymphadenopathy. 80% of non-severe cases have normal chest X-rays or CT scans. Chest ULTRAOUND can also visualize and follow the course of the CoV2-19 pneumonia. Incubation is 2 to 11 days, for an average of five days; that is, symptoms develop on average 5 days after exposure. Reports of NEUROMUSCULAR complications are an axonal peripheral neuropathy (nerve toxicity) or a myopathy (muscle toxicity) with elevated blood creatinine kinase muscle enzyme. Pathology showed widespread VASCULITIS and disseminated clotting in many organs, including striated muscle. These clinical features might be part of the corona virus infection more than just nonspecific complications of any severe illness. There was a report of a patient with olfactory neuropathy (disorder of smell).

Five of 206 patients in Singapore developed large-vessel strokes. Four of these patients had their strokes in the setting of critical illness and 3 were associated with hypotension/low blood pressure. The elevated cardiac blood test **troponin strongly predicted mortality**.

- Onset to recovery is 12-32 days. Patients at high RISK are over age 65, have high blood pressure, a d-dimer blood test greater than 1 ug/mL implying the now documented diffuse intravascular & pulmonary clotting, and who have an adverse SOFA sepsis score. One is SAFE 3 days after having no fever + resolved respiratory symptoms + improved chest CT scan + 2 negative PCR tests for the virus separated by 1 day. Viral shedding can occur for up to 37 days after onset of symptoms. Viral RNA can persist in the blood for up to 29 days and does not correlate with symptoms. It is (medically) believed that an ALKALINE cellular chemistry impedes the virus: that is thought to be a mechanism for how HYDROXYCHLORQUINE (HCQ) & AZITHROMYCIN (AZITH) work: increasing alkalinity inside the cell. The corona virus attaches to its ACE2 receptor(s) and then is internalized by microphagic vesicles, which eventually fuse with lysosomes, strip the viral genome from its envelopes and set it free. HCQ inhibits the fusion of lysosomal and endosomal vacuoles which may be another mode of action of HCQ. See [Mechanism of action of antimalarial drugs: inhibition of antigen processing and presentation](#). Fox RI, Kang HI. *Lupus*. 1993 Feb;2 Suppl 1:S9-12. PMID: 8097945 Review. Zinc sulphate is a part of that treatment regimen.
-
- **Dr. Anthony Fauci** NIH director has known since 2005 that chloroquine is an effective inhibitor of coronaviruses. The NIH researched chloroquine and concluded that it was effective at stopping the SARS corona virus. COVID-19 is also a coronavirus, labeled SARS-CoV-2. While not exactly the same virus as SARS-CoV-1, it is genetically related and shares 79% of its genome, as the name SARS-CoV-2 implies. Both CoV1 and 2 use the same host cell receptor, which is what viruses use to gain entry to the human cell and infect the victim. The official publication of the NIH, the [Virology Journal](#), published 8/22/05 “**Chloroquine is a potent inhibitor of SARS coronavirus infection and spread.**” “We report...that chloroquine has strong antiviral effects on SARS-CoV infection of primate cells. These inhibitory effects are observed when the cells are treated with the drug either before or after exposure to the virus, suggesting both prophylactic and therapeutic advantage.”
-
- **HRS, this author**, states there is far too much concern and publicity about the very infrequent, “vanishingly low” frequency, although important irregular heartbeat potential (risk vs benefit) that should be observed for as opposed to the very high frequency disastrous effects of not treating corona virus infections with what has proven to be this very safe combination of medications. THE FDA guidelines that have come with hydroxychloroquine (HCQ) as in the treatment for lupus do not even recommend doing an EKG. From JAMA 4/24/20 regarding the safety of high dose HCQ:
-
- https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765270?utm_source=silverchair&utm_medium=email&utm_campaign=article_

alert-jamanetworkopen&utm_content=wklyforyou&utm_term=042420
“...high doses, such as HCQ 600 mg twice daily for 28 days, were already studied in patients with cancer, showing good safety even in phase I trials^{25-27...}” Here are the current Heart Rhythm Society recommendations:

- Electrocardiographic/QT interval monitoring:
- HCQ and AZITH should be withheld in patients with baseline QT prolongation or with known congenital long QT syndrome. HRS (c’est moi) states that QT prolongation is a very uncommon condition (“rare”) and unless known, in view of the seriousness of the need to treat a quite ill corona virus infected patient, this is very unlikely to need to be checked and seems an unreasonable request at this point in time.
- Cardiac rhythm and QT interval should be monitored; however, this may be difficult in critically ill patients as frequent contact may need to be minimized. HRS says this is absolutely correct and is as just stated above.
- If QTc exceeds a present threshold of 500 msec, the drugs should be discontinued. HRS again states this is unlikely to be as important as the need to treat a quite ill corona virus infected patient and unnecessarily exposes the EKG technician who will be required to do the EKG.
- Correcting hypokalemia and hypomagnesemia: HRS says this is routine and ALWAYS a good idea. So doing would likely reduce the complication rate reported in adverse studies.
 - Potassium levels > 4mEq/L
 - Magnesium levels > 2mg/dL
- Avoiding other QTc prolonging agents whenever feasible:
 - These may include quinolones, antifungals, atypical antipsychotics, antidepressants and opioids, among others.

See, also, alkaline and dietary suggestions in the Preventive Medicine Center Considerations below.

As of 5/4/20, the population of the USA is 330 million Americans with 1,300,000 known CASES of CoV2-19; 77,000 have died from this disease, and 174,000 have recovered. Some of these deaths labeled as due to corona virus are actually due to other causes but the patient ALSO had a corona virus infection and so are counted as a corona virus death, even though the virus was likely not the actual cause of death. An Australian study predicts that the maximum number of USA deaths from CoV2-19 will be 70,000. Worldwide there are 4,000,000 reported 2019 corona virus/CoV2-19 cases with 275,000 deaths and 1,300,000 recovered: 5% of cases are labelled as “SERIOUS”. Documented risk factors for developing CoV2-19 are obesity, diabetes, higher population density, air pollution, and asthma, ... which are more prevalent in the African American and Latino communities. Europe, which is about the same size and population as the USA, is now the world-wide epicenter of corona cases and deaths. As of 5/4/20 Europe/the

European Union has 1,225,000 corona virus cases with 150,000 deaths. On 5/3/20 the USA reported death rate is 3.4 % vs 1.5% in South Korea and 4% in China. On a per 100,000 population, the USA mortality is EIGHTH in the world, less than Italy, Spain, France, Switzerland, and the Netherlands. Sweden, with much less lockdown, has the same mortality rate as the USA and is EIGHTH in Europe for mortality. A German report based on ANTIBODIES, states that “One in Seven May Be Immune”: that reduces COVID lethality from 2% to **0.37%**, still nearly 4 times that of the current flu. Early on, most corona virus-19/CoV2-19 cases in the USA were elderly nursing home residents in Washington state. Now New York state leads, followed by New Jersey. Repeating, in the USA there are 500,000 FLU hospitalizations and 35,000 flu deaths per YEAR. In the 2019-2020 flu year there are 45,000,000 cases of the flu 43,000 deaths according to the CDC. Both the flu and CoV2-19 cause PNEUMONIA, “the old man’s friend”, and that is the usual cause of death for CoV2-19. It can affect the heart and elsewhere. 7,500 Americans die of all causes every DAY normally.

Here is an article that discusses the POSSIBLE need for 44 days of LOCKDOWN to DEFEAT CoV2-19. This below article does NOT TAKE INTO ACCOUNT the diagnosis and treatment developments that are rapidly happening in the USA: ANTIBIOTICS, CELLULAR ALKALINIZATION, IMMUNE ENHANCEMENT, TRANSFUSED ANTIBODIES, newly developed monoclonal antibodies (<file:///C:/Users/hrobe/AppData/Local/Temp/s41423-020-0426-7.pdf>) , VACCINES, and INTERFERING RNA, etc. Gerard J. Tellis et al. “How Long Should Social Distancing Last? Predicting Time to Moderation, Control, and Containment of COVID-19”, *SSRN Electronic Journal* (2020). DOI: [10.2139/ssrn.3562996](https://doi.org/10.2139/ssrn.3562996)

Here is the plan for how Germany plans to REOPEN the country after Covid-19. See also the plan outlined below with the associated table:
<https://www.ifo.de/en/publikationen/2020/monograph-authorship/making-fight-against-coronavirus-pandemicsustainable>

A COUGH can send infected droplets 15 feet. A strong SNEEZE can send infected droplets 25 feet. The virus can live in the air for three hours, on wet surfaces for three days, 24 hours on cardboard, and 3 days on plastic: after 45 minutes the viral count is reduced by half on copper. The half-life of the virus in infected droplets is 5 hours on stainless steel. The virus count decreases by half every 7 hours on plastic so that by day 2 there is only 1/100th of the original viral count on plastic.

In China, with its strong QUARANTINE and ISOLATION procedures, new cases have REPORTEDLY slowed to a trickle. This is exactly similar to the reaction of certain, but not all, USA cities during the 1918 SPANISH FLU that killed millions. This USA cities that most effectively “locked down” with what we now call “social isolation” had the best health and economic recoveries then. There is a major difference: once widespread testing, detection, isolation, and treatment begin, such isolation will be much less necessary in the USA. Presently,

South Korea has been the best and most effective country in dealing with this infection by using strong QUARANTINE and GPS TRACKING of contacts: “acceptance of (relevant public) surveillance” is the key. Their success occurred with high frequency testing of the public, tracing of contacts of those who are test-positive, and treating based on risk profile.

Covid-19 contact tracing system with roots in MERS

Reuters 4/15/20: What distinguishes the **Korean** model in controlling COVID-19 is its ability to trace individuals diagnosed with the disease who may have come into contact with the infected individuals. It’s known as the [COVID-19 Smart Management System \(SMS\)](#).

South Korea’s Centers for Disease Control and Prevention (KCDC) runs the contact tracing system that uses [data from 28 organizations](#) such as National Police Agency, The Credit Finance Association, three smartphone companies, and 22 credit card companies to trace the movement of individuals with COVID-19. This system takes 10 minutes to analyze the movement of the infected individuals. For people who come in contact with an infected person, the KCDC informs the local public health center near the infected citizen’s residence and [the health center sends the notification to them](#). If they test positive, they are hospitalized at the COVID-19 special facilities. Those without symptoms are asked to remain self-quarantined for 14 days.

The legal basis for accessing such personal information was prepared after the 2015 MERS outbreak when the government learned that tracing the movement of infected individuals and people who came in contact with them is crucial. As a safety measure, only epidemic investigators at KCDC can access the location information and once the COVID-19 outbreak is over, the personal information used for the contact tracing will be purged.

Israel has developed such a tracking app called Hamagen. 4/13/20 Apple and Alphabet’s Google will work together to create contact tracing technology in order to slow the spread of the coronavirus by allowing users to opt into a system that catalogs other phones they have been near. The 2 companies make the world’s dominant smartphone operating systems for iPhones and Android devices. This allows mobile devices to trade information via Bluetooth connections to alert people when they have been in close proximity with someone who has tested positive for COVID-19.

The technology will first be available in mid-May. Apple and Google also plan tracking technology directly into their underlying operating systems so that users do not have to download any apps.

The technology will not track location or identity, but instead will only capture data about when users’ phones have been near each other, with data being decrypted on the user’s phone rather than the companies’ servers. GPS location data is not part of the effort.

Prime Minister Jacinda Ardern said NEW ZEALAND will continue to pursue its goal of elimination with a strategy that differs from most other countries.

4/29/20 Newsletter Science X: Yale tacking method: 4/29/201 *Nature*, differs from existing epidemiological models by exploiting [real-time data](#) about [population](#) flows, such as phone use data and other "[big data](#)" sources that can accurately quantify the movement of people. ... "very accurately forecast the timing, intensity, and geographic distribution of the COVID-19 outbreak based on population movement alone," said Yale's professor N. A. Christakis. "..., by tracking population flows in real time, our model can provide policymakers and epidemiologists a powerful tool to limit an epidemic's impact and save lives." In developing the model, the researchers used nationwide mobile-phone geo-location data to track.

"Success doesn't mean zero COVID-19 cases. It means zero tolerance, which means that as soon as we know we have a case, we go in straight away, we're testing around that person, we're isolating them [...] we do our interviews and contact trace to find all the people who have been in contact with them while they may have passed it on, and we ask them to isolate. That's how we keep stamping out COVID cases." FLUTRACKER & Singaore's TRACE TOGETHER apps are being used for this purpose.

Dr. Hillel Kashtan, created the app MDHEALTHTRAK to track various illnesses & now Co V2-19. Not only does it monitor symptoms of the virus, he said, but using the app cuts down on person-to-person contact. For protection, "the physician can assess the patient at home, so others are protected." The app creates charts for all kinds of symptoms and tracks how those symptoms change over time. That information can then be sent to doctors to allow them to easily see the changes.

Oxford University's Professor Christopher Fraser developed a similar app that can also assist in reducing transmission and resurgence of CoV2-19 infections.

South Korea has drive-through testing which is ramping up in the USA. Unfortunately, South Korea, Hong Kong and Taiwan are seeing a SECOND WAVE of CoV2-19 infections as infected returnees come back to these areas from elsewhere. False negative testing and re-infection may be possibilities. Sweden is not doing our strong social distancing.

An excellent WEBSITE to follow the virus world-wide is by 17-year-old self-taught prodigy Avi Schiffman: <http://ncov2019.live/data> . Johns Hopkins University website is also excellent.

<https://coronavirus.jhu.edu/map.html> The website www.bing.com has excellent data. For optimism, check out the twitter of a garbage man whose handle I lost: it had 3 letters in caps at the end. Another fine source of information & perspective on CoV2-19 is Harvard's infectious disease specialist Dr. Lindsey R. Baden of Brigham and Women's Hospital.

Here is a link to what life was like in Wuhan, China during its lockdown:
<https://www.quora.com/What-is-it-like-inside-the-quarantine-zone-in-Wuhan-City>

A rather remarkable interview with world famous VIROLOGIST David Ho, MD

https://medicalxpress.com/news/2020-03-iceberg-virologist-discusses-covid-.html?utm_source=nwletter&utm_medium=email&utm_campaign=daily-nwletter

Here is a very MODERATE, EVENHANDED, optimistic yet sober STATISTICIAN's perspective on this corona CoV2-19 virus:

<https://www.powerlineblog.com/archives/2020/03/a-data-driven-look-at-the-wuhan-coronavirus.php>

A GENETICIST discusses what a virus is, what it does inside a cell, and what CoV2-19 is.

https://medicalxpress.com/news/2020-03-covid-virus.html?utm_source=nwletter&utm_medium=email&utm_campaign=daily-nwletter

Stanford University EPIDEMIOLOGIST John IOANNIDIS, MD, has published a profound article that says that the USA and all other countries simply lack reliable evidence to draw accurate conclusions regarding the seriousness of CoV2-19 infections. This is because the vast majority of cases are MISSED due to limited testing availability of the general public so far. He states that "short term lockdowns may be bearable" with the implication that long-term lockdowns likely will not be tolerable because of "profound financial and social consequences". I believe he is exactly correct. Douglas McKenzie described the current lockdown effects as "wholesale disruption of the American social fabric and its vibrant economy."

<https://www.statnews.com/2020/03/17/a-fiasco-in-the-making-as-the-coronavirus-pandemic-takes-hold-we-are-making-decisions-without-reliable-data/>

In the American population there are 950,000 HOSPITAL BEDS, 45,000 ICU beds and

150,000 available VENTILATORS. Ventilators have 150 parts and those new to that manufacturing will need to become expert in production of all. Continuous positive airway Pressure = CPAP is a halfway step developed by the Mercedes F1 racing team that can reduce

the need for ventilators. “...low sat’ “happy hypoxics” comfortably walking around did well with just high flow nasal cannulas and had no need for ventilators. Critical care physicians are questioning the widespread use of the breathing machines for Covid-19 patients, saying that large numbers of patients could instead be treated with less intensive respiratory support. Ventilators could be of little benefit to many and even harmful to some. Many patients have blood oxygen levels so low they should be dead. But they’re not gasping for air, their hearts aren’t racing, and their brains show no signs of blinking off from lack of oxygen.”

More patients could receive simpler, noninvasive respiratory support, such as the breathing masks used in sleep apnea. An oxygen saturation rate below 93% (normal is 95% to 100%) has long been taken as a sign of potential hypoxia and impending organ damage. Because some patients with Covid-19, blood-oxygen levels fall to hardly-ever-seen levels, into the 70s and even lower, physicians were intubating them sooner.

“Most hospitals, including ours, are now using simpler, noninvasive strategies first,” including the apnea devices and even nasal cannulas, “It doesn’t require sedation and the patient [remains conscious and] can participate in his care.”

As patients get worse, protocols developed for other respiratory conditions call for increasing the force with which a ventilator delivers oxygen, the amount of oxygen, or the rate of delivery. But if oxygen can’t cross into the blood from the lungs in the first place, those measures, especially greater force, may prove harmful. High levels of oxygen impair the lung’s air sacs, while high pressure to force in more oxygen damages the lungs.

Physicians in Germany and Italy said their Covid-19 patients were unlike any others with acute respiratory distress. Their lungs are relatively elastic (“compliant”), a sign of health “in sharp contrast to expectations for severe ARDS.” Their low blood oxygen might result from things that ventilators don’t fix. Such patients need “the lowest possible [air pressure] and gentle ventilation,” they said, arguing against increasing the pressure even if blood oxygen levels remain low. “We need to be patient.”

In the *Annals of Intensive Care*, physicians who treated Covid-19 patients in China found that the majority of patients needed no more than a nasal cannula. With BiPAP oxygen levels “significantly improved” after an hour or two. The researchers concluded that the more comfortable nasal cannula is just as good as BiPAP and that a middle ground is as safe for Covid-19 patients as quicker use of a ventilator.

Questioning the significance of oxygen saturation levels: those levels often “look beyond awful,” said Scott Weingart, MD, in New York/host of the “EMCrit” podcast. But many can speak in full sentences, don’t report SHORTNESS OF BREATH, and have no signs of the heart or other organ abnormalities that hypoxia can cause.

“The patients in front of me are unlike any I’ve ever seen,” Kyle-Sidell told Medscape about those he cared for in a hard-hit Brooklyn hospital. “They looked a lot more like they had altitude sickness than pneumonia.” Anecdotally, Weingart said, “we’ve had a number of people who

improved and got off CPAP or high flow [nasal cannulas] who would have been tubed 100 out of 100 times in the past.”

One reason Covid-19 patients can have near-hypoxic levels of blood oxygen without the usual gasping and other signs of impairment is that their blood levels of carbon dioxide, which diffuses into air in the lungs and is then exhaled, remain low. That suggests the lungs are still accomplishing the critical job of removing carbon dioxide even if they're struggling to absorb oxygen, REMISCENT OF ALTITUDE SICKNESS more than pneumonia.

Low cost compact ventilators designed by Southern Miss from hardware store parts now produced by Howard Industries can alleviate shortages and be used in various settings because of its size and ease of use. “This new bag-based ventilator could be produced very quickly,” said Dr. Joe Campbell, Forrest General's chief anesthesiologist.

Adapt sleep apnea machines: 4/8/20 scientists have developed a way to turn a sleep apnea machine into a ventilator to treat people with COVID-19. The modification of a Nippy3+ began at Leeds Teaching Hospitals at the University of Leeds. The modification is straightforward and involves changes to the device's settings and reconfiguring the supply of oxygen so it flows to the face mask worn by the patient. The machine operates in a mode called CPAP: constant positive airway pressure. That means the pressure inside the mask is slightly raised, keeping the patient's airway open and making it easier for them to breathe. It provides enriched oxygen of between 40 to 60 percent and because it is a modification to a device, it does not have to go through a full regulatory approval process. Last week, engineers at University College London and Mercedes announced that they had successfully reversed engineered a CPAP device that had widely been used in China. They said they have a device that has regulatory approval and can be rapidly manufactured. **More information:** A technical note written by the expert team has been submitted to MedRxiv, an online platform that allows researchers to rapidly disseminate important findings ahead of peer review. The technical note can be downloaded from AlphaGalileo: www.alphagalileo.org/DTControl...ntrol/Images/pdf.png

A PROFOUND article on RESPIRATORY MANAGEMENT from J J Marini of the U of Minn in JAMA Insight 4/24/20

https://jamanetwork.com/journals/jama/fullarticle/2765302?guestAccessKey=e0b408ba-3e6b-4d40-83bb-9e7dd9575c24&utm_source=silverchair&utm_campaign=jama_network&utm_content=covid_weekly_highlights&utm_medium=email

Based on a robust body of clinical evidence, including studies published in the [New England Journal of Medicine](#), a TIDAL VOLUME of around 6 cc per kilogram of patient body weight is the general standard of care for patients with Acute Respiratory Distress Syndrome/ARDS as part of "lung-protective" ventilation. SNORKLE/diving MASKS are being adapted as respirators. Prone positioning & inhaled nitric oxide are recommended, but not steroids. However, some are using 60 mg/day PREDNISON for 3 days, 40 mg for 2 days, and 20 mg for 1 day. MIT

created an inexpensive and simple respirator using Ambu bags. A very experienced respirator designer puts already FDA approved parts together to make a simple respirator that avoids VILI = Ventilator Induced Lung Injury—yet to be cleared by the FDA:

<https://www.facebook.com/brent.regan.370/videos/1333250890200601/>

COMING OFF THE VENTILATOR can be problematic. In 2017 FDA approved SUGAMMADEX which reverses the effect of muscle relaxants differently. In a new U of Michigan study, Kheterpal et al. compared the rates of serious lung complications in patients who received neostigmine vs sugammadex. The newer drug was associated with significantly reduced rates of complications.

"We saw a 37% decrease across all pulmonary (fibrosis, scarring, and jelly-filled lungs) complications and 55 % decrease in [respiratory failure](#)," says Kheterpal. "In many practices, neostigmine is no longer used in high risk patients or procedures," he says.

More information: Sugammadex versus Neostigmine for Reversal of Neuromuscular Blockade and Postoperative Pulmonary Complications (STRONGER): A Multicenter Matched Cohort Analysis. *Anesthesiology*. (2020) [DOI: 10.1097/ALN.0000000000003256](https://doi.org/10.1097/ALN.0000000000003256)

"Cough Sync" is a newly developed tool for aspirating thick lung secretions more effectively. 85% of medicines/pharmaceuticals are manufactured in China and India; all of USA's required rare earth metals for manufacturing come from China.

TRAVEL bans have been set up by Saudi Arabia, Russia, Poland, Kenya, Morocco, Argentina, Brazil, Canada, Denmark, the Netherlands, Germany, the European Union, and many other countries as well as quite appropriately, the USA beginning on 1/31/20. That quarantine was supported by the NIH's infectious disease chief Dr. A. Fauci.

At the present time almost all of us feel OFF BALANCE because of the inability to find out if we are (+) or (-) for the CoV2-19. There has been a general LOSS OF JOY across the United States. Being "shut-ins" has led to "cabin fever." The stock market is responding to FUD: fear, uncertainty, doubt—all of which translates as ANXIOUS UNCERTAINTY. And although I believe allowing oneself to panic is largely a personal responsibility, the nationwide information atmosphere seems responsible for predisposing the susceptible to panic. A psychiatrist trenchantly said this national stressor will make "those not well put together, go over the edge". In balance, it must also be asked what will be the psychological and economic cost of not returning to our more normal lives sooner than the various quarantines permit? Domestic violence, drug usage, worsening diet, and suicide will

increase. People will eventually adjust out of reason and/or necessity. It is important to be careful, but not to be paranoid. Humility and perseverance are the keys to dealing with these stressors.

Here is a perspective on how the economy could reasonably be opened based on being low risk

Very few Americans are dying to date from the coronavirus who had no pre-existing condition. 150 Americans to Date with NO Pre-existing conditions have died from the Corona Virus. [by Jim Hoft](#) 4/10/20

As of this morning, 4/10/20, there are now [16,697 Americans](#) who have died having the corona virus, 96,000 world-wide.

Country	Cases	Deaths	Recovered	Active	Tot/1M Pop	Deaths/1M Pop	Total Tests	Tests/1M Pop	Population	Active/1M Pop	Death/Cases
World	1,615,092	96,791	362,542	1,155,759	207	12.4	12,801,325	1,641	7,802	148	6.0%
USA	468,895	16,697	25,928	426,270	1,417	50	2,376,977	7,181	331	1,288	3.6%
Spain	157,022	15,843	55,668	85,511	3,358	339	355,000	7,593	47	1,829	10.1%
Italy	143,626	18,279	28,470	96,877	2,375	302	853,369	14,114	60	1,602	12.7%
Germany	118,235	2,607	52,407	63,221	1,411	31	1,317,887	15,730	84	754	2.2%
France	117,749	12,210	23,206	82,333	1,804	187	333,807	5,114	65	1,261	10.4%
China	81,907	3,336	77,455	1,116	57	2			1,437	1	4.1%
Iran	66,220	4,110	32,309	29,801	788	49	231,393	2,755	84	355	6.2%
UK	65,077	7,978	135	56,964	959	118	298,169	4,392	68	839	12.3%
Turkey	42,282	908	2,142	39,232	501	11	276,338	3,277	84	465	2.1%
Belgium	26,667	3,019	5,568	18,080	2,301	260	84,248	7,269	12	1,560	11.3%
Switzerland	24,172	958	10,600	12,614	2,793	111	178,500	20,625	9	1,458	4.0%
Netherlands	21,762	2,396	250	19,116	1,270	140	101,534	5,926	17	1,116	11.0%
Canada	20,765	509	5,311	14,945	550	13	370,315	9,812	38	396	2.5%
Brazil	18,176	957	173	17,046	86	5	62,985	296	211	81	5.3%
Portugal	13,956	409	205	13,342	1,369	40	140,368	13,766	10	1,309	2.9%
Austria	13,431	319	6,064	7,048	1,491	35	134,743	14,961	9	782	2.4%
Russia	11,917	94	795	11,028	82	0.6	1,090,000	7,469	145	76	0.8%
S. Korea	10,450	208	7,117	3,125	204	4	503,051	9,812	51	61	2.0%
Israel	10,095	92	1,061	8,942	1,166	11	117,339	13,557	9	1,033	0.9%
Sweden	9,141	793	205	8,143	905	79	54,700	5,416	10	806	8.7%
India	6,771	228	635	5,908	5	0.2	177,584	129	1,354	4	3.4%
Ireland	6,574	263	25	6,286	1,331	53	53,000	10,734	5	1,273	4.0%
Norway	6,219	108	32	6,079	1,147	20	121,034	22,326	5	1,121	1.7%
Australia	6,203	53	3,141	3,009	243	2	338,346	13,269	26	118	0.9%
Chile	5,972	57	1,274	4,641	312	3	68,353	3,576	19	242	1.0%
Poland	5,742	175	318	5,249	152	5	118,295	3,126	38	139	3.0%
Denmark	5,635	237	1,736	3,662	973	41	64,002	11,050	6	632	4.2%
Czechia	5,589	113	309	5,167	522	11	114,854	10,725	11	483	2.0%
Japan	5,530	99	685	4,746	44	0.8	64,387	509	126	38	1.8%

[The most recent data](#) shows that only 0.9% of deaths related to the corona virus are related to individuals with no comorbidity (i.e. any pre-existing condition):

COVID-19 Fatality Rate by COMORBIDITY:

*Death Rate = (number of deaths / number of cases) = probability of dying if infected by the virus (%). This probability differs depending on pre-existing condition. The percentage shown below does **NOT** represent in any way the share of deaths by pre-existing condition. Rather, it represents, for a patient with a given pre-existing condition, the risk of dying if infected by COVID-19.

PRE-EXISTING CONDITION	DEATH RATE confirmed cases	DEATH RATE all cases
Cardiovascular disease	13.2%	10.5%
Diabetes	9.2%	7.3%
Chronic respiratory disease	8.0%	6.3%
Hypertension	8.4%	6.0%
Cancer	7.6%	5.6%
<i>no pre-existing conditions</i>		0.9%

*Death Rate = (number of deaths / number of cases) = probability of dying if infected by the virus (%). The percentages **do not have to add up to 100%** as they do NOT represent share of deaths by condition

Based on this data, 150 Americans have died from the corona virus who had no pre-existing conditions out of 16,697.

In addition, of the top 29 countries in the world based on number of corona virus cases confirmed, eight of these countries have opened their countries up economically in some part or in full. (See countries highlighted above in yellow: China, Brazil, Austria, Sweden, Norway, Denmark Czechia and Japan.) The death rate per case identified for these countries is 4.1% which is less than the overall world average of 6% but the US death rate is slightly lower than both at 3.6%.

The US has shut down its economy because of the corona virus based on 17,000 deaths (less than this year's flu related deaths): 150 deaths of these deaths were individuals who had no pre-existing conditions. Those people could likely be allowed to safely return to work now.

https://www.thegatewaypundit.com/2020/04/numbers-150-americans-date-no-pre-existing-conditions-died-coronavirus-0-9/?fbclid=IwAR0ywZfZ8QEDiVPVtSdBWstsx_M78oSY16fAE9f-M6C6OeqWNib1Xml8Jk

Early on the CDC (Centers for Disease Control) did not allow TESTING development outside of its requirements. The recent CDC tests had a technical flaw and proved unreliable. Independent test development by D S Chugh, MD, of Washington state allowed the recognition of the first USA case of coronavirus 19/CoV2-19 on 1/21/20 which, remarkably, was in a teenager-- as it was felt then and afterwards that those of that age group were relatively immune to the serious consequences of corona 19/CoV2-19. Despite initially being held back by CDC regulations, she eventually decided on her own correctly to develop accurate testing by NOT adhering to the guidelines. The CDC & FDA are reported to still be slowing acceptance and release of new innovative testing kits and those for home testing. WHO test kits were made available to lower income countries without testing capability, not the USA. Better PREPARATION for this current viral pandemic after the much more dangerous 2003 SARS, 2007 Zika, 2014 Ebola, and 2012 MERS crises could have been accomplished. The federal Pandemic Office was not eliminated as some suggest, but was merged with other governmental groups.

A \$50 sensitive smartphone accessory was developed at U of Illinois at Urbana-Champaign by professors Brian Cunningham and Rashid Bashir was licensed to Reliant Immune Diagnostics and reported in the journal *Lab on a Chip*.

TESTING BREAKTHROUGH: 20 MILLION. Abbott's SARS-CoV-2 IgG test identifies the IgG antibody, which is a protein that the body produces in the late stages of infection and may remain for up to months and possibly years after a person has recovered. Abbott's IgG antibody test will initially be available on its ARCHITECT® i1000SR and i2000SR laboratory instruments*. More than 2,000 of these instruments are in use in U.S. laboratories. These instruments can run up to 100-200 tests per hour.

Abbott is significantly scaling up its manufacturing for antibody testing and is expecting to immediately ship close to 1 million tests this week to U.S. customers, and will ship a total of 4 million tests in total for April. **The company is ramping up to 20 million tests in the U.S. in June** and beyond as it expands the tests to run on its new Alinity™ i system. Abbott also will be expanding its laboratory antibody testing to the detection of the antibody, IgM, in the near future.

Lab-on-a-chip COVID-19 antibody test could offer rapid, portable, low cost, and accurate results.

From Newsletter X: Optofluidic Bioassay at the U of Michigan: a [microfluidic device](#) shrinks multiple lab functions onto a single chip just millimeters or centimeters in size: faster results with smaller sample sizes. It is "enzyme-linked immunosorbent assay," or ELISA. The U-M researchers have previously published results showing that their device can work as well as the slower, larger, standard ELISA set-up. Anyone working on COVID-19 antibody tests can use their reagents in this device.

ELISA tests are typically quantitative and accurate, showing the concentration of antibodies. That makes them more reliable and less prone to false positives than the [rapid diagnostic tests](#). But standard ELISA results take several hours, and the machines that provide them are the size of refrigerators. In addition, the sample needs to be sent to the test lab for analysis. But microfluidic ELISA can give a quantitative and accurate result in just 15 minutes, with a finger-prick's worth of blood.

This technique can monitor patients' immune response to infection, treatment, and vaccination. The estimated cost of testing is a few dollars per test of 2 to 3 different [antibodies](#). The machine can be the size of a microwave, and can [test](#) up multiple simultaneous samples of little more than a drop of blood from a fingertip in less than 20 minutes.

New COVID-19 test results in 45 minutes: 4/16/20 : The CRISPR-based [test](#), SARS-CoV-2 DETECTR, uses gene-targeting technology, requires no specialized equipment, and is published in 4/16/20 *Nature Biotechnology* by developer Dr. Charles Chiu of UCSF. The test targets any [genetic sequence](#), so test developers "programmed" it to find 2 sequences in the genome of SARS-CoV-2, the cause of COVID-19. One sequence is common to all SARS-like coronaviruses, while the other is unique to SARS-CoV-2. Checking both sequences ensures that the new test can distinguish between SARS-CoV-2 and related viruses. The test can detect coronavirus in samples from respiratory swabs, provides results in about 45 minutes, can be performed in virtually any lab using off-the-shelf chemical agents and common equipment, and it is easy to interpret. Much like a store-bought [pregnancy test](#), dark lines appear on test strips. PCR-based tests require specialized equipment, limiting them to well-equipped diagnostic labs. **More information:** CRISPR-Cas12-based detection of SARS-CoV-2, *Nature Biotechnology* (2020). [DOI: 10.1038/s41587-020-0513-4](https://doi.org/10.1038/s41587-020-0513-4) , <https://www.nature.com/articles/s41587-020-0513-4>

TINY IRON OXIDE NANOPARTICLES coated with SILICA have a strong affinity for the RNA genetic material inside the virus that causes COVID-19/CoV2-19. NORWEGIAN U of Science & Technology NTNU's & St. Olavs Hospital's [new test](#) uses the nanoparticles to extract RNA from a solution containing a sample from the patient. The solution contains substances that crack the virus open so that its RNA [genetic material](#) can be extracted.

"We can then identify the genetic code from the RNA and compare it to the coronavirus," Bjørås said. The researchers tested the accuracy of their method by running tests from patients in parallel with commercial tests. Bjørås said the new method is more sensitive than commercial tests. Bjørås said the lab at NTNU's Department of Chemical Engineering that is making the magnetic particles can make 30-40,000 tests a day, a rate that can be increased after Easter. The plan is to scale up to be able to produce a minimum of 150,000 tests per week.

BELGIAN ZenTech test rapidly detects antibodies against coronavirus infections. It has started making tens of thousands of the government-certified tests & can ramp up output to make up to 3 million per month. Diagnosis takes just 10-15 minutes and sensitivity is 100 percent: meaning it identifies all patients who have COVID-19 [antibodies](#).

POSITIVE RT-PCR Test Results in Patients RECOVERED From COVID-19. [Lan Lan, MD](#) JAMA. 2020;323(15):1502-1503. doi:10.1001/jama.2020.2783. This article shows the test can become NEGATIVE and then LATER POSITIVE with no new CoV2-19 exposure!

SOUTH KOREAN S D Biosensor is now making 350,000 test a day and ramping up to 1.5 million tests a day to be exported to the USA and other countries.

From *Trends-In-Medicine* 4/2/20: TESTING. The list of available/approved/cleared Covid-19 tests continues to grow. Most of the tests are laboratory or point-of-care tests for diagnosing Covid-19. The rapid 5-15 minute Abbott ID NOW test is starting to be used and even FDA Commissioner Stephen Hahn, MD, called it a game changer. It is a one-at-a-time test for individuals, not for larger populations. However, what is needed next is a serologic (ELISA) test that can detect who has been exposed to SARS-CoV-2 and developed antibodies – and therefore can't get sick and can't transmit the virus. Those are the people whose blood may be therapeutic and who could go back to work immediately. Dr. Deborah Birx said she has tasked researchers at the major universities in the country to develop a simple ELISA test, saying, "It is easy to do. In a day or two they could SCREEN AN ENTIRE HOSPITAL. I call on every university in every state to develop ElisAs. You can buy antigens and controls online. Get to work to test healthcare communities in your state... Our universities can do that by Friday [April 3]. I put that challenge out to them. We are not waiting. We are asking for help now. It could happen this month if the universities help us." She said this was done with HIV, and it is exactly the same concept and process for SARS-CoV-2.

Newsletter Science X 4/30/20: "...the most common tests rely on the reverse-transcriptase-polymerase chain reaction (RT-PCR), which amplifies a tiny amount of viral RNA collected from nasopharyngeal swabs. Because RT-PCR requires expensive instruments, trained personnel and often several days to generate results, researchers are avidly exploring other methods, such as isothermal nucleic acid amplification and transcription-mediated amplification, as well as CRISPR technologies...."

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

Clinical Infectious Diseases — Zhao J, Yuan Q, Wang H, et al. March 31, 2020

The antibody response in infected patient was tested by serial plasma samples (n = 535) from a total of 173 patients with SARS-CoV-2 infection during hospitalization for total antibodies (Ab), IgM and IgG against SARS-CoV-2. The seroconversion rate for Ab, IgM and IgG was 93.1%, 82.7% and 64.7%, respectively. For Ab, IgM and then IgG, the median seroconversion time was day11, day12 and day14, separately. The presence of antibodies was < 40% within 1 week since onset and increased rapidly to 100.0% (Ab), 94.3% (IgM) and 79.8% (IgG) as of day15 after onset. There was a decrease in viral RNA detectability from 66.7% (58/87) in samples collected before day 7 to 45.5% (25/55) during days 15-39. Significant improvement in the sensitivity for diagnosis of COVID-19 is when RNA and antibody detection are combined; this improvement was evident even in early phase of 1 week since onset. There was an independent association of a higher titer of Ab with a worse clinical condition.

Trends -In-Medicine 5/7/20 Coronavirus Page 8 Among the Covid-19 diagnostic tests that recently got an EUA from the FDA are:

- AIT Laboratories' SARS-CoV-2 Test
- Altona Diagnostics' RealStar SARS-CoV-2, real-time PCR kit for research use only
- Autobio Diagnostics' Anti-SARS-CoV-2 Rapid Test
- Biocerna's RT-PCR test, a modified version of Thermo Fisher Scientific's TaqPath Covid-19 test
- GenoSensor's GS Covid-19 RT-PCR kit
- Hologic's Aptima SARS-CoV-2 test, a molecular test that runs on its Panther system, was submitted for an EUA
- KorvaLabs' Curative-Korva SARS-CoV-2 Assay
- LabGenomics' LabGun Covid-19 RT-PCR Kit
- MicroGenDX' Covid-19 Key assay
- Nationwide Children's Hospital's SARS-CoV-2 assay
- Ortho Clinical Diagnostics' VITROS Immunodiagnosti

Trends-In-Medicine 5/7/20 Coronavirus

Antibody (serology) testing Demand for these tests has skyrocketed but so has the misunderstanding about what they can and cannot do. Basically, these tests can identify people who have antibodies to Covid-19, which means they were exposed to the virus, whether they got sick and recovered or were asymptomatic. Antibody positivity makes people potential donors for convalescent plasma, and it provides epidemiologists with a picture of the spread of the virus within the general population. The problem is there still is no evidence that a person with antibodies has any immunity to SARS-CoV-2 or, if there is immunity, how long it lasts. The FDA and NIH continue to remind people of this, but there remains a popular misconception about immunity related to a positive test. And the specificity and sensitivity of the tests are still unclear. The White House proposed that, in some circumstances, two antibody tests be administered to the same person. And the WHO warned against plans for proposed "immunity passports," which would allow people who have recovered from the coronavirus to resume unrestricted travel and work. Yet, there are a growing number of antibody tests getting either an EUA from the FDA or a CE Mark from the EMA, and there are more than 180 in development.

The latest antibody tests include:

- Abbott's SARS-CoV-2 IgG antibody test, which claims 99% sensitivity and specificity – EUA and CE Mark
- Erba Mannheim's ErbaLisa Covid-19 antibody Elisa detection kit – CE Mark
- Quest Diagnostics' Covid-19 antibody test, which consumers can buy online for \$119.
- Quotient's MosaiQ Covid-19 antibody microarray test, which claims 99.8% accuracy – CE Mark
- Roche's Elecsys Anti-SARS-CoV-2 antibody test, which claims specificity >99.8% and sensitivity of 100% – EUA and CE Mark
- Siemens Healthineers' fast total antibody test for SARS-CoV-2, which claims specificity and sensitivity of >99% – not yet approved

Among the tests still in development are: Cue Health got a \$13 million grant from the U.S. Biomedical Advanced Research and Development Authority (BARDA) to create, validate, and gain approval for a fast and portable SARS-CoV-2 point-of-care test. GenMark Diagnostics got a grant for up to \$749,000 from BARDA to develop and seek EUA for a diagnostic panel that combines a new SARS-CoV-2 viral target with the company's ePlex Respiratory Pathogen panel."

The current lack of preparedness was due to governmental and the wider society not having the necessary vision to understand the implications of what was happening then and then not preparing the appropriate response that could have been used now. CDC regulations are now updated. Now cities, states, and the private market are allowed independently to create their own testing. The Roche pharmaceutical company has developed a simplified and automated technology that will increase testing from 30 to 1,000 tests per day and Roche said it will be quickly able to upscale its production and distribution of this simpler and accurate CoV2-19 virus testing. AS ABOVE, ABBOTT has developed the ID NOW test that is a small, convenient, and easier to perform "point of care self-swab" that gives the answer in 5-15 minutes. Its disadvantage is that a one at-a-time test that cannot screen large populations effectively.

The PROPER SAMPLE culture areas are nasopharyngeal, oropharyngeal, and sputum samples, but not urine, blood, or stool. Companies that are making TEST KITS: ABBOT's ID NOW is the quickest and most convenient presently. However, it only tests 1 sample at a time, so an army of those machines will be necessary at any one location. Cepheid is a quick test providing positive or negative results for the virus in 45 minutes. S D Biosensor of Korea is ramping up making test kits. GeneMatrix, Chembiao Diagnostics, Hologic, GenMark, Integrated DNA, Pharma Mar, and Thermo Fisher are all developing tests. A new and quick results saliva test is being developed. It is ready for mass production and it will simplify collection, not requiring stringent protective (PPE) masks and gowns. Doing the test would still occur in a healthcare setting under the supervision of a qualified professional.

"SALIVA testing will help with the global shortage of swabs for sampling and increase testing of patients, and it will not require health care professionals to be put at risk to collect samples," Andrew Brooks, the chief operating officer of RUCDR Infinite Biologics, said. RUCDR is backed by Rutgers U. The saliva test builds on the existing TaqPath SARS-CoV-2 Assay used in

existing COVID-19 testing to identify RNA from the virus. In addition to identifying carriers of the virus, this form of testing could also make it easier to re-test people who have recovered so they can end their isolation.

3M is scaling up producing N95 face masks. Construction and other companies are donating their N95 mask and gown stockpiles while the federal government is shipping ventilators and other stockpiled necessities to infection hot spots. A safe and effective way to sterilize used N95 respirators to further conserve PPE (www.battelle.org/newsroom/news-details/battelle-cleared-to-sterilize-n95-masks-at-max-capacity-operate-in-other-states-to-fight-coronavirus-ppe-shortage. opens in new tab)

“Pipeline: Investigations therapies of COVID-19/CoV2-19

Diana Ernst, RPh of MPR wrote on 3/11/20:

“Currently, there are no antivirals licensed by the FDA to treat patients with COVID-19. While no specific treatment for corona 2019 (COVID-19/CoV2-19) is currently available, several therapies are being investigated globally.”

Antivirals

“A 5 day treatment with CHLOROQUINE or HYDROXYCHLOROQUINE (HCQ or Plaquenil) combined with AZITHROMYCIN (AZITH) seems quite EFFECTIVE for COV2-19. An open-label study investigated hydroxychloroquine in hospitalized patients with confirmed COVID-19 at The Méditerranée Infection University Hospital Institute in Marseille, France. (The study was run by epidemiologist Didier Raoult, MD.) Patients received oral HCQ 200 mg 3 times daily for 10 days (n = 20) vs control group (n=16). Patients were age 12 years and older, and had PCR documented SARS-CoV-2 in nasopharyngeal samples at admission. Treatment with the antibiotic AZITH was also provided. The end point was virological clearance at day 6. (There have been no cardiac complications due to the medicine combination in an experience now exceeding 1,000 patients.)

Results showed that by day 6 post-inclusion, 70% of HCQ-only treated patients were cured of the virus vs 12.5% in the control group ($p = .001$). At day 6, 100% of patients treated with HCQ + AZITH was cured of the virus compared with 57.1% of patients treated with hHCQ only, and 12.5% of the control group ($p < .001$). A significant difference between the HCQ and control groups was reported as early as day 3.” Similar results were found at the University of Minnesota.

While the results look promising, the researchers noted limitations to their study including small sample size, limited long-term outcome follow-up, and dropout of 6 patients from the study.” There is data that this combination is more effective in milder cases and less helpful in severe cases. A Brazilian study found no benefit and some cardiac down sides

High dose intravenous VITAMIN C 4-12,000 mg per day is already being used in New York hospitals.

TOCILIZUMAB (Actemra; Roche) and SARILUMAB (Kevzara, Regeneron and Sanofi) are INTERLEKIN (IL)-6 inhibitors. Both are being studied in patients for their ability to calm the cytokine storm in COVID-19 which is the overactive inflammatory response that occurs in the lungs causing acute respiratory distress syndrome. Tocilizumab is now being studied at Harvard's Massachusetts General Hospital.

TREATMENTS per *Trend In Medicine* 5/7/20

Treatments v Gilead Sciences' remdesivir, a direct-acting antiviral (an RNA polymerase inhibitor), was granted an EUA - not approval - for treating hospitalized Covid-19 patients. This is the first drug with an EUA for treating Covid-19 that has randomized trial data to back it up. Dr. Fauci called the results of that trial "quite good news," adding, "This is really quite important. What it has proven is that a drug can block this virus." He said remdesivir is now the "new standard of care" for all other trials. In preliminary results from the 1,063-patient ACTT trial (at 47 sites in the U.S and 21 in Europe and Asia) sponsored by NIAID, remdesivir was shown to shorten the time to recovery from 15 days to 11 days, on average, a significant improvement vs. placebo (p10 days after onset of symptoms. When data were pooled across treatment arms, by Day 14 62% of patients treated early were able to be discharged from the hospital vs. 49% of patients who were treated late.

- No new safety signals were identified.
- The most common adverse events with both regimens were nausea (10.0% vs. 8.6%), acute respiratory failure (6.0% vs. 10.7%). Grade ≥ 3 ALT elevations occurred in 7.3% of patients, with 3.0% discontinuing treatment as a result. v Convalescent plasma
 - There have been anecdotal reports of the efficacy of this therapy, but it has been used in 7,200 people in the past couple of months. Data on those patients are being analyzed, will be released in a couple of weeks, and should offer some useful insights, but it is not a randomized study.
 - The FDA issued guidance for healthcare providers and investigators on the administration and study of investigational convalescent plasma collected from people who have recovered from Covid-19, with recommendations on patient eligibility, donor eligibility/qualifications, labeling, recordkeeping, and more.
 - Johns Hopkins plans to start enrolling patients next week into two randomized clinical trials of convalescent plasma in the outpatient setting, with results expected in a couple of months: }A preventive study in nursing home patients to see if convalescent plasma will prevent them from catching Covid-19. }A treatment study in people with confirmed Covid-19 who are remaining at home to see if giving them convalescent plasma at home will prevent them from worsening to the point they need to be hospitalized. Asked how many recovered Covid-19 patients would qualify to donate plasma, Arturo Casadevall, MD, PhD, chair of the Department of Molecular Microbiology and Immunology at the Johns Hopkins Bloomberg School of Public Health, said, "The majority have high titers of antibodies...However, a small percentage have antibodies but not very high levels...And it depends on the antibody test used. They are not standardized very well. We are using an Elisa test

developed at Mount Sinai.” √ Hydroxychloroquine (HCQ). President Trump is one of the few people still speaking out positively about HCQ, though he isn’t pushing it as hard as he used to do. Some states are still stockpiling it. So, is it safe? Does it work? Two nondefinitive but positive trials were reported recently.

- A 568-patient retrospective Chinese study, available as a preprint on medRxiv.org, looked at critically ill Covid-19 patients who had severe acute respiratory distress syndrome (ARDS) despite antiviral + antibiotic therapy. Of the 568 patients, 48 also received **HCQ** (200 mg BID for 7-10 days). Mortality (the primary endpoint) was 18.8% with HCQ vs. 45.8% without it. Length of stay before death was 15 days with HCQ and 8 days without it. *Trends-In-Medicine* May 7, 2020 Coronavirus IL-6 levels were significantly lowered by the end of treatment with HCQ but not without it. The researchers concluded that HCQ significantly decreased mortality in critically ill patients through attenuation of inflammatory cytokine storm and should be prescribed for treatment of critically ill Covid-19 patients.

- A 1,061-patient retrospective analysis of **HCQ** in Marseille, France, in preprint, in which HCQ was combined with azithromycin, found that: 91.7% had a good clinical outcome and virological cure within 10 days. 4.3% of patients had a poor clinical outcome, and 8 died (0.75%). All the deaths were from respiratory failure, not cardiac toxicity. Poor clinical outcome was associated with older age, severity at admission, and low HCQ serum concentration. The researchers concluded that the combination of HCQ + azithromycin is safe and associated with a very low fatality rate.

- The negative news. A report on 90 Covid-19 patients treated at a Boston hospital, published in *JAMA Cardiology*, found a potential for serious cardiac arrhythmias – significant QTc prolongation (>500 ms). One patient developed torsade de pointe when given HCQ + azithromycin.

Roche’s Actemra (**tocilizumab**). This anti-IL-6R met the primary endpoint in the 129-patient French CORIMUNO-19 trial in hospitalized patients with moderate-to-severe Covid-19, with significantly fewer patients needing ventilation (mechanical or non-invasive) or dying by Day 14. The results have not yet been published. This drug makes sense because it is already used to treat cytokine storms in immunotherapy patients, and a key issue with Covid-19 is cytokine storm. √ WHO announced the launch of Access to COVID-19 Tools Accelerator, a global project focused on developing and producing new treatments, vaccines, and tests for Covid-19, while ensuring global access to the products. √ Among other therapies to add to the long list of drugs in development to treat Covid-19 are:

- AbCellera and Lilly are collaborating on research for development of an antibody to treat Covid-19, and AbCellera got some help (up to \$175.6 million) from the Canadian government’s Innovation, Science, and Economic Development Canada Strategic Innovation Fund.

- BerGenBio’s bemcentinib, an oral selective AXL inhibitor – A 120-patient Phase II trial has started in the U.K. in hospitalized Covid-19 patients.

- CAR T – Researchers at Duke-NUS Medical School in Singapore are studying whether there might be utility for CART and/or TCR-T therapies in Covid-19.

- Karyopharm Therapeutics’ Xpovio (selinexor) – The company announced the first patient was dosed with this cancer drug in a Phase II trial in severely ill Covid-19 patients.

- Johnson & Johnson and Merck's Pepcid (**famotidine**) – given IV at a dose 9-times the over-the-counter dose of this heartburn drug – is being tested in a clinical trial in **New York City by Northwell Health**.
- Sarepta Therapeutics is initiating a discovery program to see if some of its antisense oligonucleotides can inhibit viral infection.

Trends-In-Medicine 5/7/20: Coronavirus Repurposed Drugs Being Investigated for Covid-19 Company Alexion Pharmaceuticals **Ultomiris ravulizumab** C5 complement inhibitor.

Amgen Otezla **apremilast** PDE4 inhibitor

AstraZeneca Farxiga **dapagliflozin** SGLT2 inhibitor Johnson & Johnson and Merck Pepcid famotidine H2 blocker

Novartis and Incyte Jakafi **ruxolitinib** oral JAK inhibitor (for ventilator patients)

Novartis Cosentyx **secukinumab** anti-IL-17A Diovan valsartan ARB Ilaris

canakinumab interleukin-1 β inhibitor Xolair **omalizumab**

IgE inhibitor Pulmotect -- **inhaled superoxide** -- Synairgen -- SNG-001 inhaled interferon beta-1a Vaccines.

AstraZeneca is collaborating **with Oxford University** on the vaccine Oxford developed. Oxford took an existing chimp vaccine and engineered it to work for SARS-CoV-2, did efficacy studies in monkeys, and has now started a Phase I safety trial in healthy volunteers. The researchers predicted the vaccine could be ready by fall 2020. v Leukocare, ReiThera, and Univercells are collaborating on development of a novel adenoviral vector-based vaccine for Covid-19. They hope to launch a clinical trial this summer and begin manufacturing alongside clinical development. Moderna, which has the lead in vaccine development and the support of NIAID, is advertising to fill a number of positions across Clinical, Quality, Technical Development, Drug Manufacturing, and Digital.

The Trump administration is working on a Manhattan Project-style initiative, Operation Warp Speed, to spur rapid development of a SARS-CoV-2 vaccine, with the aim of having a vaccine ready for use by the end of this year. The hope is that 3-4 of the 14 promising vaccines already in development will survive and be successful.

An Israeli coronavirus drug that claims to have a 100% success rate among severely ill patients is being tested in the **United States** for the first time.

CBNNews.com [Emily Jones 04-16-2020](#)

[Pluristem Therapeutics Inc.](#), a biotech in Haifa, reported that 7 who were at a **high risk of death due to respiratory failure survived** after receiving the medication.

The patients were treated with **allogeneic placental expanded (PLX) cells** under the compassionate use program and exhibited **respiratory failure requiring intubation in the ICU. 4 of the patients had multi-system organ failure, including heart and kidney failure**. These cells suppress or reverse the

dangerous over-activation of the immune system that causes death in many coronavirus patients. Pluristem uses "donated **placentas at the time of delivery** of healthy, full-term babies, from healthy women under 35 years old, undergoing an elective caesarean section."

All seven of the patients who received the drug survived and four patients saw an **improvement in respiration**. One patient who is still alive saw a continued deterioration of the respiratory system. Now, a critical COVID-19 patient in the US has been treated with PLX cell therapy at **Holy Name Medical Center in New Jersey**.

[COLCHICINE](#) (Colcris, Mitigare; Takeda Pharmaceuticals) is an inexpensive, FDA-approved, powerful anti-inflammatory drug used to treat gout and pericarditis. It's currently being studied for its usefulness in mitigating the cytokine storm caused by the novel coronavirus. [Researchers](#) at the Montreal Heart Institute and the University of Montreal hope that colchicine can stop the body's overproduction of immune cells and cytokines, which leads to a cytokine storm that damages lung tissue and leads to acute respiratory distress and multi-organ failure. From *Newsletter Science Xi*: Colchicine is different, said researcher Dr. Priscilla Hsue, a professor of medicine at the University of California, San Francisco (UCSF). "One of the unique aspects is that we're trying to hit this before people need to be hospitalized," Hsue said. Colchicine is the medication of choice for a few reasons, Hsue explained: unlike drugs tested in [hospital patients](#) given by infusion or injection, colchicine is easy to take by mouth, inexpensive, and has a long history of safe use, she added.

IVERMECTIN is a safe single dose treatment effective in reducing the virus. The ScienceDirect journal, *Antiviral Research*, research from Monash U's K Wagstaff, MD, in Melbourne, Australia. The approved and safe common anti-parasite Ivermectin has broad spectrum antiviral activity and is effective inhibiting the coronavirus that causes COVID-19. Ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2) in the TEST TUBE. A single treatment was able to effect ~5000-fold reduction in virus at 48h in cell culture.

https://www.breitbart.com/border/2020/04/04/common-anti-parasite-drug-may-kill-coronavirus-in-under-48-hours-say-researchers/?utm_source=newsletter&utm_medium=email&utm_term=todays_hottest_stories&utm_campaign=20200404

AVIGAN (FAVIPIRAVIR): 14 days of the Japanese flu drug shortens the illness. It is being studied now at Harvard's Massachusetts General Hospital.

EIDD-2801 is investigational affecting human lung and airway cells from patients with COVID-19: [Science Translational Medicine](#). It introduces genetic mutations into coronavirus' RNA. As the RNA copies itself, these damaged mutations, accumulate and render the virus unable to infect, It an ORAL medication rather than an IV like remdesivir, so it can be administered at HOME. According to T Sheahan, PhD, Dept of Epidemiology, U of North Carolina. EIDD-2801 is also effective against OTHER RNA viruses, several strains of influenza, respiratory syncytial virus, chikungunya, Venezuelan equine encephalitis, and Eastern equine encephalitis.

- Convalescent plasma. • Hyperimmune globulin – GigaGen is working on this.

More information: Shilei Hao et al. QTY code-designed water-soluble Fc-fusion cytokine receptors bind to their respective ligands, *QRB Discovery* (2020). DOI: [10.1017/grd.2020.4](https://doi.org/10.1017/grd.2020.4)

- Monoclonal antibodies – e.g., Bii Biosciences, Tsinghua University, and 3d People's Hospital of Shenzhen which are collaborating on developing fully HUMAN NEUTRALIZING MONOCLONAL ANTIBODIES Covid-19/CoV2-19. To speed development of potentially safe and effective treatments of Covid-19, the FDA set up a new program – the Coronavirus Treatment Acceleration Program (CTAP) – which uses all the tools the Agency has to help get therapies to patients quickly. Health and Human Services Secretary Alex Azar said, “As part of this new program, the FDA is cutting red tape, redeploying staff, and working day and night to review requests from companies, scientists, and doctors who are working toward therapies.” FDA staff in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) are providing regulatory advice, guidance, and technical assistance as quickly as possible. And the FDA is triaging requests from developers and scientists working on new drugs and biologics. Other drugs worth watching include:

- Fujifilm/Toyama Chemical's AVIGAN (FAVIPRAVIR) – The company started a Phase III trial in Japan of this antiviral flu drug, an RNA polymerase inhibitor, to see if it shortens Covid-19 recovery time. TRENDS-IN-MEDICINE April 1, 2020/Coronavirus

- NeuroRx and Relief Therapeutics' AVIPTADIL – The FDA gave the green light for the start of a Phase II trial of this erectile dysfunction drug to treat acute respiratory distress in Covid-19 patients.

- Roche's Activase (ALTEPLASE, tPA) – An article, published in the Journal of Trauma and Acute Care Surgery, suggests that this stroke drug might be useful in Covid-19-associated acute respiratory distress syndrome (ARDS), particularly in patients who need a ventilator but can't get one. Their reasoning: “The risk of adverse events...is far outweighed by the certainty of death in patients meeting the eligibility criteria for this treatment.” It has been found beneficial but heparin was not after the alteplase infusion A 12-patient compassionate-use study is planned.

- VITAMIN C – A meta-analysis of 8 studies, published in the *Journal of Intensive Care*, found that giving vitamin C (4-12 grams a day) to ICU patients on a ventilator reduced the length of

time on the ventilator by 14% vs. control. The patients with the most benefit from vitamin C were those on the ventilator the longest. A person in good health maintains a normal plasma vitamin C level with an intake of ~0.1g/day. Critically ill ventilator patients may need much higher doses – grams/day.”

[The HIV protease inhibitors ritonavir and lopinavir are being studied for early use, but so far have proven ineffective for CoV2-19.](#)

Preventive Medicine Center general suggestions and thoughts based on fact, judgment, reasoning, and experience:

Avoid MILK-DAIRY products 100 (100!!!) %. My belief is that ANY MILK-DAIRY thickens the mucus reducing clearance of the invading virus, allowing it to “settle in and invade.” It is my belief-knowledge that a single drop of any milk dairy begins this allergic type adverse pathway. It is 100% milk-dairy avoidance or incorrectly have as much as you want. SWEETS, including dried fruits, and juices except for Pom Wonderful pomegranate juice, function as sweets = sugar = reduce/immobilize immune functioning at multiple levels. Basically, consume an organic unprocessed whole foods diet, ideally “macrobiotic” grains-vegetables-beans-fruit-nuts-seeds = GVBfns. See the www.thepmc.org website for general wellness information + this paper + how to prevent and/or reverse where possible high blood pressure, diabetes, high triglycerides, overweight at the 95+% level and the need for open heart surgery, angioplasty.

Read <http://williamspear.com/2020/03/12/covid-19/> Bill Spear’s summary letter on CoV2-19 & his Macrobiotics Primer: Bill states in a personal letter to me (minimally edited) 4/5/20: “As we know, the virus isn’t actually “living”, it’s just anxious to find a host in your lungs, and when it gets there all hell breaks loose. So, the real job of prevention is to strengthen the host’s blood supply to cells, i.e., alkalinity (HRS states that is similar to the hydroxychloroquine discussion above). My layman’s point of view is that just as the fatty outer coating is broken by sudsy, soapy wash (and stronger) externally, acidic blood breaks that cellular fatty wall internally releasing the cascade of inflammation and lung damage that ensues. Whether that’s accurate or not, relevantly I know of long time macrobiotic people who are caring for CoV2-19 positive non-macrobiotic family members in the same house, and they all have experienced only very minor symptoms. That may not be causal insofar as their seeming “immunity” but such an interpretation is reasonable”-HRS agrees.

For cooking, rely on *The Changing Seasons Cookbook*. Make 1 recipe EXACTLY according to directions-avoid as many processed foods, and wheat products as possible therein. Organic MISO, tamari, rice noodles are processed and acceptable/even desired. Take the recipe with you to the natural food store. Be sure to get the exact ingredients in that one recipe. Miso soup with kombu, millet + cauliflower, scallions and daikon; brown rice with pickled shiso are specifically recommended for now as is live refrigerated organic sauerkraut. CLEANING solutions: 4 teaspoons of bleach in a quart of water, 0.125% peroxide, 80% ethanol, and 75% isopropyl alcohol are effective cleaners that kill the virus.

MEDICINE, SUPPLEMENT, AND GENERAL CONSIDERATIONS HERE ARE TO BE SPECIFICALLY DECIDED ON BETWEEN YOU AND YOUR PHYSICIAN: These Preventive Medicine Center thoughts are “invitations to consider” and require your

personal judgment. If there are questions or concerns, please contact the Preventive Medicine Center. Usual suggestions are that supplements be taken daily for 2 weeks and then 5 DAYS A WEEK thereafter. Chew gum to keep your throat lubricated in order to "wash out" the virus. For colds or CoV2-19: the PMC position is to take vitamin C 500 mg 3 times a day, and in treatment 4-12 grams IV vitamin C per day reduced respirator use 25%, vitamin D3 5.000 units a day 5 days a week, Immune Renew (a yeast based immune stimulating beta glucan) 2 twice a day (Host Defense & OM manufacturers also have beta glucan immune stimulating products), as is Brewer's yeast. AHCC 2 twice a day (as just said, 5 days a week) is the top selling supplement in Japan. Manuka honey has anti-bacterial and possibly anti-viral properties. Pau d'arco is an herbal anti-inflammatory as is nano-curcumin. Berberine functions similarly to metformin, spirulina is the origin of phycocyanobilin -> anti-inflammatory heme oxygenase production, & glucosamine. SINGULAIR (montelukast) is a lung leukotriene inhibitor that reduces lung inflammation and is worth considering in the armamentarium. If you are taking high blood pressure medication, try to have it be an ARB (angiotensin receptor blocker such as losartan). If on cholesterol lowering medicine, Livalo/pitavastatin seems more beneficial than Crestor/rosuvastatin or Lipitor/atorvastatin. Personally, my guess is that the gout treatment medication ALLOPURINOL would be helpful for serious CoV2-19 infection.

An excellent air purifier company: <https://www.airpurifiersandcleaners.com/sun-pure-sp-20-portable-air-purifier>. Dulera inhaler for bronchial cough issues. Zantac (or Pepcid as famotidine once daily) is off market + Zyrtec (for complete histamine blockade) twice a day for nasal congestion. Immediate (!) use of these combined antihistamines can actually stop the development of "colds." Fish oil is generally anti-inflammatory: Carlson's Cod Liver Oil (2 teaspoons = "a swig") once or twice a day. Elderberry capsules for further immune enhancement. For a bothersome cough for my patients I recommend elderberry syrup 2 tsp 3 times a day. Generic or trade Robitussin plain 2 teaspoons 3 times a day as necessary also only for a bothersome cough. The DM = dextromethorphan may be deleterious in CoV2-19. For chest issues, the glutathione supporting antioxidant NAC 600 mg 2 or 3 a day. If there is a deep cough, in order to prevent scarring due to fibrosis/scarring consider taking anti-fibrosis serrapeptase 2 capsules three times a day. If there is bacterial invasion in the lungs = pneumonia development, antibiotics should be chosen based on sensitivity. HCQ (HCQ \$0.40 per pill) + AZITH would be the first choice. Otherwise, if treatment is begun without a culture, doxycycline + azithromycin would be my antibiotics of choice as they also have an anti-inflammatory effect.

Tetracyclines may be effective in the treatment of novel coronavirus (COVID-19) in a 4/8/20 letter to the editor online now in *Pharmacotherapy*. Reuters Health News 4/17/20. Drs. Mahyar Etminan and Mohit Sodhi of the U of British Columbia, Vancouver, Canada.

"Tetracyclines have shown to have antiviral activity in other viruses (independent of their antibacterial activity)." They also have "powerful" anti-inflammatory effects "and, of course, inflammation is an important pathological attribute of COVID-19," he explained. The anti-inflammatory capabilities of tetracyclines include down regulation of the **NFKB** pathway as well as a decrease in levels of **inflammatory cytokines such as tumor necrosis factor alpha, interleukin-1-beta, and interleukin-6**. These cytokines have been **shown to be significantly elevated** when SARS-CoV-2 is exposed to lung tissue in addition to exacerbating the pathogenesis of the infection itself, they point out. Tetracyclines also have "good absorption in the lungs, where COVID-19 attacks, and are relatively safe, safer than hydroxychloroquine."

"For all of these reasons, we think there should also be a focus on examining this drug in clinical trials as both a prophylactic agent or treatment in early and late disease," he said. Tetracyclines

might be potential therapeutic agents for COVID-19 that are "hiding in plain sight," write Dr. Etminan and Dr. Sodhi. "We strongly urge international research groups to consider investigating the potential therapeutic efficacy of tetracycline antibiotics in treating COVID-19."

Read the 2020 *Progress in Cardiovascular Diseases* article by Mark McCarty et al. regarding nutraceuticals inhibiting NOX2, thereby stimulating type 1 interferon response via Toll Receptor 7 (TLR7). HO-1 (heme oxygenase-1) enhancement to treat RNA viruses. Discussed/ "recommended" in that article are alpha lipoic acid, sulforaphane, ferulic acid, resveratrol, spirulina (phycocyanobilin). EGCG as capsules or as green tea, with white tea for its high antioxidant content.

Antivirals:

New vaccine platform for CoV2-19 4/8/20 by [University of Bristol](#) Edited for concision.

COVID-19/CoV2-19 SPIKE PROTEIN mediates cell entry. Imophoron's ADDomer-based vaccine presents exactly (just) these parts to the immune system, giving rise to SPECIFIC antibodies in order to neutralize the virus/protect against infection.

Most COVID-19 vaccines present the ENTIRE SPIKE to the immune system, which reacts by making antibodies. This usual approach RISKS inducing antibodies that bind to the WRONG parts of the spike and could make the disease even worse. In vaccines for SARS-CoV-1 (note "1"), this sometimes resulted in severe lung tissue damage. Imophoron's vaccine presents only very SPECIFIC parts of the spike essential for cell entry and are much less prone to this risk.

This Imophoron ADDomer platform is a new, highly adaptable, easy-to-manufacture, rapid-response platform for vaccines to combat present and future infectious diseases. It is a synthetic, self-assembling, nature-inspired virus-like particle (VLP). This type of vaccine is extremely stable and requires no refrigeration, enabling unrestricted distribution world-wide.

MIT's SHERLOCK: PCR tests require complex instrumentation and are usually performed by skilled personnel in an advanced laboratory setting. An alternative method is [SHERLOCK](#), a nucleic acid-based test developed at MIT stemming from the CRISPR gene editing tool that does not need complex instrumentation and can be read out using a paper strip akin to a [pregnancy test](#), without any loss of sensitivity or specificity. The test is also low-cost and can be performed in less than an hour.

Frederic Garzoni, Founder/CEO at Imophoron: "We ... can design and roll-out potential vaccines in about two weeks ...& contribute to resolving the major health and economic threats caused by emerging viruses such as COVID-19."

More information: Charles Vragliau et al. Synthetic self-assembling ADDomer platform for highly efficient vaccination by genetically encoded multiepitope display, *Science Advances* (2019). DOI: [10.1126/sciadv.aaw2853](https://doi.org/10.1126/sciadv.aaw2853)

The University of Michigan publication authored by Martha Berg implies that if there were universal anti-tuberculosis BCG immunization in the USA, the USA would have only suffered an estimated 94 deaths total, which would have been only 4% of the actual [death](#) toll of 2,467 in this country on March 29.

The report "Mandated Bacillus Calmette-Guérin (BCG) vaccination predicts flattened curves for the spread of COVID-19" is an analysis of reports of COVID-19 cases and related deaths in more than 50 countries. Researchers say countries that have a current policy mandating the anti-TB BCG vaccination have significantly slower growth of both cases and deaths, as compared to all other countries. This vaccination may or may not be related to these statistics, but it does affect general immunity.

[AbbVie](#): the company is collaborating with select health authorities and institutions to determine the antiviral activity of lopinavir/ritonavir ([Kaletra](#)) against COVID-19.

[AIM ImmunoTech](#): developing Ampligen, a broad-spectrum antiviral that will be tested as a potential treatment for COVID-19 in Japan. A significant survival effect was observed in a trial evaluating mice infected with the earlier Severe Acute Respiratory Syndrome (SARS) coronavirus.

[Gilead](#): developing remdesivir (costs \$4000.00 as opposed to CHQ at \$0.40/pill and azith = \$0.63/pill), a broad-spectrum intravenous antiviral agent that is being investigated in a [double-blinded, placebo-controlled study](#) sponsored by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH). In addition, Gilead is initiating two phase 3 trials to evaluate the safety and efficacy of remdesivir in adults diagnosed with COVID-19, following a rapid review and acceptance by the Food and Drug Administration (FDA) of the investigational new drug filing for the novel antiviral.

Immunotherapies and other investigational therapies:

The Israeli company MIGAL (see further below) says it HAS A VACCINE that will be finalized in 2 weeks and ready for distribution in 80 days. J Craig VENTER, the team leader who first sequenced the human genome and an originator of chromosome insertion, has his own California institute that in all probability will quickly develop an efficient CoV2-19 testing and an effective CoV2-19 vaccine. Distributed Bio/Dr Jacob GLANVILLE is using computational-guided immune-engineering to create an antibody that neutralizes the virus in 20 minutes. It binds the spot that the virus uses to gain entry into your cells.

“We have generated extremely potent picomolar antibodies that block known neutralizing ACE2 epitopes, blocking the novel coronavirus-19 from infecting human cells.”

[Algeron Pharmaceuticals](#): developing ifenprodil, an N-methyl-d-aspartate (NDMA) receptor glutamate receptor antagonist, which is being prepared for US clinical trials for COVID-19 based on results of an animal study that showed the investigational therapy significantly reduced acute lung injury and improved survivability in H5N1 infected mice.

[CEL-SCI](#): developing an immunotherapy using LEAPS, a patented T cell modulation peptide epitope delivery technology, to stimulate protective cell-mediated T cell responses and reduce viral load.

[Innovation Pharmaceuticals](#): developing brilacidin, a defensin-mimetic, that mimics the human innate immune system and causes disruption of the membrane of pathogens, leading to cell death. It has already been tested in humans in phase 2 trials for other indications.

[Mesoblast Limited](#): investigating remestemcel-L, an allogeneic mesenchymal stem cell (MSC) product candidate, as a treatment for patients with acute respiratory distress syndrome caused by COVID-19. Remestemcel-L, which is comprised of culture-expanded MSCs derived from the bone marrow of an unrelated donor, is administered in a series of intravenous infusions and is believed to have immunomodulatory properties to counteract inflammatory processes.

[Q BioMed](#): partnering with Mannin Research to develop a potential treatment that addresses vascular leakage and endothelial dysfunction, which may potentially help patients with severe cases of COVID-19.

[Takeda](#): developing an anti-SARS-CoV-2 polyclonal hyperimmune globulin (H-IG) to treat high-risk individuals with COVID-19 (TAK-888). Pathogen-specific antibodies from plasma will be collected from recovered patients (or vaccinated donors in the future) and will be transferred to sick patients to improve the immune response to the infection and increase the chance of recovery.

[Tiziana](#): developing TZLS-501, which has been shown to rapidly deplete circulating levels of interleukin-6 (IL-6) in the blood, a key driver of chronic inflammation. Excessive production of IL-6 is believed to be associated with severe lung damage observed with COVID-19 infections.

Vaccines:

University of Pittsburgh in EBioMedicine “Band Aid” Vaccine.

https://www.westernjournal.com/american-ingenuity-covid-vaccine-simply-applied-skin-believed-stopped-virus/?utm_source=Email&utm_medium=CTBreaking&utm_campaign=breaking&utm_content=conservative-tribune

Researchers at the U of Pittsburgh published in EBioMedicine have created a mouse-tested and easily scalable vaccine for coronavirus-19 that is "delivered through a fingertip-sized patch" with "a microneedle array" that would inject the vaccine through 400 small needles applied like a Band-Aid. The vaccine created "a surge of antibodies" sufficient to eliminate the coronavirus but hasn't been followed long term. This U of P vaccine has potential advantages over the vaccine being tested [developed by Moderna](#) which uses a more experimental method. This U of P vaccine was developed along the line of the flu shots, "using lab-made pieces of viral protein to build immunity."

From *Trends -In-Medicine*: [Altimune Inc](#): developing a single-dose, intranasal vaccine against COVID-19 using its proprietary NasoVAX technology. The vaccine is moving toward animal testing.

[Applied DNA Sciences](#): collaborating with [Takis Biotech](#) to develop a DNA vaccine candidate using PCR-based DNA ("LinearDNA") manufacturing systems; preclinical testing in animals is expected to begin in the second quarter of 2020.

[Codagenix Inc](#): co-developing a live-attenuated vaccine with the Serum Institute of India using viral deoptimization.

[GlaxoSmithKline](#): collaborating with [Clover Biopharmaceuticals](#) to develop a protein-based corona virus vaccine candidate (COVID-19 S-Trimer) using Clover's proprietary technology (Timer-Tag©) and combining it with GSK's pandemic adjuvant system.

[Inovio Pharmaceuticals](#): developing a DNA vaccine (INO-4800) to address COVID-19; human trials to begin in the US in April.

[Johnson & Johnson](#): partnering with the Biomedical Advanced Research and Development Authority (BARDA) to develop a vaccine using Janssen's AdVac® and PER.C6® technology, which provide the ability to rapidly upscale production of an optimal vaccine candidate.

[Moderna Inc](#): vials of the Company's mRNA vaccine (mRNA-1273) have been shipped to the National Institute of Allergy and Infectious Diseases to be used in a phase 1 study in the US.

[Novavax](#): currently evaluating multiple recombinant nanoparticle vaccine candidates in animal models; initiation of phase 1 testing is expected in late spring of 2020. The COVID-19 vaccine candidates will likely include the saponin-based Matrix-M™ adjuvant to enhance immune responses.

[Sanofi](#): collaborating with BARDA to develop a vaccine using Sanofi's recombinant DNA platform. The DNA sequence encoding the antigen will be combined into the DNA of the baculovirus expression platform and used to produce large quantities of the coronavirus antigen which will be formulated to stimulate the immune system to protect against the virus.

**This list is not all inclusive.*

Israel: a Covid 19/CoV2-19 VACCINE

by [Howard Richman](#) 3/15/20

“Israeli scientists at the MIGAL Galilee Research Institute had worked for four years and had successfully developed a Coronavirus vaccine for chickens which passed clinical trials. When they saw the genetic sequencing of the COVID-19 virus, they realized that they could quickly adapt their chicken vaccine to the human virus. Ella Dagan, a spokesman for [MIGAL told Europorter](#):

When the genetic sequence of the new coronavirus COVID-19 was published, the researchers realized that the two viruses have the same infection mechanism similarities so they can use it, with small amount of adaptation, to achieve an effective human vaccine in a very short period of time.

Dr. Shahar, one of the scientists told [nocamels.com](#):

It’s a little bit like fate that we were working on this coronavirus vaccine at the same time that the world was suddenly hit by this epidemic of coronavirus for humans.

MIGAL created its vaccine by synthesizing two proteins. Unlike vaccines that are created by injecting a dead or weakened disease-causing virus, there is little danger that synthetic virus protein segments will give patients a disease.

Its vaccine creates antibodies in the mucosal immune system of the body which consists of thin permeable barriers to infection in the lungs, gut, eyes, nose, throat, uterus, and vagina. Dr. Chen Katz, MIGAL’s biotechnology group leader, gave Europorter a detailed cellular-level description of how MIGAL’s vaccine works:

The scientific framework for the vaccine is based on a new protein expression vector, which forms and secretes a chimeric soluble protein that delivers the viral antigen into mucosal tissues by self-activated endocytosis (a cellular process in which substances are brought into a cell by surrounding the material with cell membrane, forming a vesicle containing the ingested material), causing the body to form antibodies against the virus.

Israel’s Minister of Science and Technology, Ofir Akunis, is expediting the human vaccine through Israel’s approval process. According to Europorter:

The minister has instructed the Director General of the Ministry of Science and Technology to fast-track all approval processes with the goal of bringing the human vaccine to market as quickly as possible.

Dr. Katz of MIGAL told [Times of Israel](#) that Israel’s approval process only involves about two months of actual testing:

The clinical testing experiments themselves are not so long, and we can complete them in 30 days, plus another 30 days for human trials. Most of the time is bureaucracy -- regulation and paperwork.

CEO David Zigdon of MIGAL told Europorter that MIGDAL’s goal is to get their vaccine approved in just three months:

Given the urgent global need for a human Coronavirus vaccine, we are doing everything we can to accelerate development. Our goal is to produce the vaccine during the next 8-10 weeks, and to achieve safety approval in 90 days.

There are at least two American COVID-19 vaccines in the works:

1. Moderna Therapeutics has developed a synthetic virus vaccine made from mRNA and has gotten it approved by NIAID (National Institute of Allergy and Infectious Diseases) for testing with human subjects. Those tests began until [April](#).
2. Regeneron Pharmaceuticals will soon have a treatment that will serve as a vaccine for those who don't have coronavirus and a treatment for those who do. They will inject corona virus antibodies directly into the bloodstream instead of relying upon a vaccine to create those antibodies. They used a similar treatment to prevent and cure Ebola. The Israeli government could approve the Israeli vaccine in as little as three months. President Trump may have to intervene in order to get NIAID moving just as fast with an American vaccine.”

These are thoughts as of 5/8/20

H. Robert Silverstein, MD, FACC
Medical Director, Preventive Medicine Center
1000 Asylum Avenue #2109
Hartford, CT 06105
(860) 549-3444 or (800) 789-PREV fax (860) 549-3569
<http://www.thepmc.org>