# Subpages for the World Health System



## Pharmaceutical Interventions to Defeat COVID-19

We present here a summary of the most promising potential pharmaceutical interventions to prevent infection, to kill the coronavirus, and to alleviate deadly complications.

### Treatments and Vaccines

Pharmaceutical interventions can save lives and reduce disease in several ways. *Vaccines* "teach" the immune system about a pathogen, allowing it to immediately fight it when encountered in the future. *Antiviral medications* can target the virus itself, by preventing its entry into cells or its replication. *Antibodies*, derived from the blood of recovered patients or produced in a laboratory, can help the immune system fight the virus. *Combating cytokine storms* is a fourth approach, which could reduce the deadly respiratory effects of the virus, while not fighting the virus itself.

#### Vaccines

Vaccines "prime the pump" of the immune system, to be able to rapidly mount a defense against a pathogen. They are used in advance to protect people from contracting a disease. People who are vaccinated against a disease are able to quickly fight it off if they come in contact with it, since their bodies are already prepared to do so. Some diseases that mutate rapidly, such as the seasonal flu, require new vaccines every year. Will this be the case for SARS-CoV-2? At present, research on the rate of mutations — and their nature — suggests that immunity against SARS-CoV-2 may be longer lasting. It is possible that new vaccines will be required if new strains of SARS-Cov-2 develop.

On March 16, phase I trials began in Seattle for an experimental coronavirus vaccine: mRNA-1273, produced by Moderna and first shipped from that laboratory to the National Institute of Allergy and Infectious Disease on February 24. The primary purpose of these initial trials, in which 45 healthy individuals were administered varying doses of the vaccine, is to make sure that the vaccine doesn't cause harm. Blood samples, first taken in mid to late May will also test whether the body has made antibodies to neutralize the spike protein of SARS-CoV-2, giving preliminary data about the candidate vaccine's potential effectiveness.

### Antiviral Medications

At a Beijing press conference on March 17, Zhang Xinmin, director of the National Center for Biotechnology Development, under China's Ministry of Science and Technology, reported that Avigan (known as favipiravir or favilavir) had shown clinical promise in trials conducted in Wuhan and Shenzhen, involving 240 and 80 patients, respectively. The figures reported included a reduction in time of fever from 4.2 to 2.5 days in Wuhan, and a median recovery time of 4 days with the drug as opposed to 11 without it. The Shenzhen study saw improvements in chest x-rays for 91% of patients given the medicine, compared to 62 for those not treated with it. The drug is now included in China's treatment plan. The drug was originally developed by Fujifilm to treat the flu. Fujifilm is now running Phase II trials in the United States and Phase III trials in Japan. The White House has urged the FDA to issue an Emergency Use Authorization for Avigan.

Another antiviral continues to be used in China, and ongoing controlled studies are testing its effectiveness: Remdesivir, originally developed as an Ebola treatment by Gilead Sciences, which has experience in creating drugs to treat other viral infections such as the seasonal flu, HIV, and hepatitis. Two studies in China will begin reporting results this month (April 2020).

Chloroquine, an anti-malarial drug used to treat COVID-19 patients in China, was reported to be an effective treatment by Xinhua on February 17. During February, at least 200,000 doses of chloroquine were imported into China from neighboring Pakistan. The use of hydroxychloroquine, which has a better safety profile than chloroquine, has become widespread, following additional studies in France (most famously by Didier Raoult et al.) and word-of-mouth discussions among physicians, whose practice in treating patients is evolving more rapidly than peer-reviewed publications can keep up. The mechanism of action by which (hydroxy)chloroquine prevents cell replication has been studied in cell cultures.

### Plasma of Recovered Patients / Antibodies

Blood plasma from recovered individuals contains antibodies created by the immune systems of those recovered patients. Blood from healthy, recovered individuals is drawn, the plasma is isolated, and it is given intravenously to a patient in need. It is necessary to match blood types for this treatment. During the last weekend in March, Houston Methodist Hospital became the first facility in the United States to perform these transfusions, and appeals on social media are now recruiting recovered COVID-19 survivors to donate their blood to help others.

Antibodies, which attach to specific regions of antigens and other substances in the body, can also be created in the laboratory, by using yeast, mice, or other animals to produce them for harvesting. Drug names ending in -mab — such as adalimumab (Humira) — are of this type; they are monoclonal antibodies. Once the antibody binds to the troublesome agent, it is inactivated, and, if it is a virus, it can be more easily defeated by the immune system. According to a list at biocentury.com, at least a dozen groups are working on creating antibodies against SARS-CoV-2. Regeneron, a U.S. company, has identified promising antibodies from among those found in recovered humans and mice and plans to begin manufacturing a cocktail of the antibodies in April, for use in summer testing. It is also testing an antibody that would target the effects of the virus, rather than the virus itself.

### Preventing Cytokine Storms

An advanced stage of COVID-19, in which severe and life-threatening respiratory problems develop, is associated with an increase in specific cytokines, small proteins that serve a signaling function in the body. An excess of these cytokines can cause an immune response that damages healthy lung cells in addition to those harboring the virus. Interleukin-6 (IL-6) is one such cytokine that has been found to reach extremely high levels in COVID-19 patients. Two monoclonal antibody therapies — Kevzara (sarilumab) and Actemra (tocilizumab) — are being used to reduce this immune response. These monoclonal antibodies (mabs) attach themselves to IL-6, deactivating it.

Both of these drugs are being used in studies as well as by physicians eager to save the lives of their patients.

As another example, I-Mab Pharmaceuticals is researching an antibody that attaches to another cytokine, GM-CSF.

Steroids can be used to reduce the immune auto-response, but weakening the immune system of patients suffering from a viral infection has obvious downsides. They are also becoming widely used by physicians, although definitive research has not yet been performed and analyzed.

These agents, if successful, could reduce the death rate from COVID-19, even if they do not combat the virus directly.

# Equipment and Manufacturing Requirements to Defeat COVID-19

## Ventilators

The total global inventory of ventilators is hard to determine, but there are certain figures that point to the problems of dealing with COVID-19 in impoverished nations lacking health infrastructure. The United States has a total of about 170,000 ventilators for its 330 million people, which is about 500 ventilators for every million people. Germany has about 25,000 ventilators for its 83 million people, about 300 ventilators per million — the highest per capita level in Europe.

The picture in Africa, however, is absolutely devastating. According to *Time*, there are 500 ventilators for the 200 million people of Nigeria, which comes out to 2.5 ventilators for every million people — about 200 times less than the United States on a per capita basis. In Sudan, there are 1.9 ventilators for every million people. The Central African Republic (population nearly 5 million) has a total of three ventilators, and Liberia, with a population of 4.7 million people, has none.

Estimates by the Brookings Institution and the *Financial Times* are that India has approximately 20,000 ventilators, which would be 15 ventilators for every million people.

For the entire world to be at the United States per capita level of ventilators would require a global inventory of 4 million.

## Ventilators

A 2005 planning study by the U.S. Department of Health and Human Services considered the health care needs to treat a hypothetical pandemic influenza in which 30% of the U.S. population became infected at some point. They concluded that for a moderate pandemic like the 1957–1958 influenza (which killed 1.1 million of the planet's population of 2.9 billion at the time), U.S. hospitalizations would reach 865,000, with 130,000 patients requiring ICU care, and 65,000 requiring ventilators. For a pandemic like the 1918 influenza (which claimed the lives of 20–50 million of the planet's 1.6 billion people), U.S. hospitalizations would reach 9.9 million, with 1.5 million people requiring ICU beds and 750,000 requiring ventilators.

Projecting from these figures to the present world population, the world would require, using the range of the two scenarios, 1.7 to 20 million ventilators. Africa would need 0.26–3.0 million in these two scenarios, respectively, and Latin America would need 0.14–1.6 million. India would require 0.29–3.3 million. With international collaboration and sharing of resources, those figures could obviously be far less, assuming the general seasonal characteristic of pneumonia-inducing diseases.

### Medical equipment

Numerous companies have expressed interest in retooling for the production of ventilators, from automakers to aerospace companies. General Motors and Ventec Life Systems have teamed up to produce 10,000 units a week by May. Ford Motor Company and General Electric have also teamed up to produce 7,200 units a week by May, committing to 50,000 total produced by July 4. Other automakers like McLaren and Jaguar Land Rover, both based in the UK, are also looking at retooling to produce ventilators. Germany based VW Group is looking at employing their 125 industrial-grade 3D printing machines to produce ventilators. Aerospace companies like Brazil-based Embraer, Europe-based Rolls Royce and Airbus, and the American firm SpaceX have also expressed interest in producing ventilators.

Existing producers of ventilators are ramping up production. One example is Philips, which is doubling production to 2,000 per week, and Getinge, which will increase production to 3,750 per week. Drager has a deal with the German Government to make 10,000 ventilators; Vyaire has a contract with the U.S. Government for 8,000, Smiths Group has a contract with the UK government for 10,000. With the figures just presented, at full production capacity and by fulfilling contracts, that would supply an additional 300,000 ventilators by July. There are many other producers and other companies discussing retooling, and figures of global production capabilities are in flux, both increasing due to upgrades and becoming unsteady due to supply chain limitations. An April 9 Politico article reports that estimated demand solely from the United States and several Western European nations was for one million ventilators; the world's needs will be higher.

## Respirators

A properly fitted N95 respirator protects the wearer from 95% of particles over 0.3 microns in size. While the SARS-CoV-2 coronavirus itself is smaller than this size, the virions do not float around entirely on their own and are effectively blocked by N95 respirator masks.

A 2015 study by the U.S. National Library of Medicine — National Institutes of Health, estimated that if 20–30% of the U.S. population were to become ill, the best case scenario would see 1.7–3.5 billion N95 respirators would be needed by healthcare and emergency services personnel as well as for patients seeking care. The intermediate demand scenario would demand 2.6–4.3 billion and the maximum demand scenario would require 7.3 billion.

Extrapolating this figure to the world's population, the global requirements could be anywhere from 40 billion to 180 billion N95 masks for the duration of the outbreak. Africa alone would require 6 to 28 billion. Latin America's needs would be in the range of 3.4 to 15 billion. India would require between 7 and 30 billion.

## Supply Chains

The effects of decades of globalization are being felt in the formerly industrialized nations that now find themselves unable to supply their own needs for medical equipment or even such basic manufactured products as masks and hospital gowns. The importance of having domestic production is becoming clear. This is not only for specific goods, but also for potential retooling.

### Has 'Just-in-Time' Become 'Way Too Late'?

The just-in-time approach to manufacturing means keeping stocks of supplies and parts down to a minimum, relying on extensive logistics to supply components as they are needed. The resulting low inventories mean that disruptions to supply chains effectively shut down production. This approach is not limited to private businesses. Public health systems have seen hospital beds declining — the US has less than half as many hospital beds today as it did fifty years ago.

## Wuhan’s Successful Response to COVID-19