Leo Galland M.D.

20 Fifth Avenue, New York, N.Y. 10011

**Coronavirus Protection**

I have written this to supply useful and practical information for those concerned about the present corona virus epidemic and also to correct some misinformation that is circulating.

BACKGROUND: AN EMERGING PICTURE

Corona viruses are a family of viruses made from RNA instead of DNA. There are many species that produce respiratory and gastrointestinal illness in humans and animals. Four strains cause the common cold. The pandemic corona virus, COVID-19, first identified in Wuhan, China, has certain distinctive features, some of which are receiving attention in the media: Chinese data indicate that 80% of infected people have minimal symptoms and do not seek medical attention, whereas 15% become moderately to severely ill with cough and shortness of breath and 5% require intensive care. About half the Chinese patients admitted to hospitals do not have a fever and a fifth failed to develop fever despite having pneumonia, so—unlike with influenza—the presence or absence of fever is not a useful diagnostic aid.

COVID-19 appears to spread readily from person to person, usually as droplets from coughing or sneezing. It is also shed in stool, so food-borne or water-borne infection is possible but not yet demonstrated. Corona viruses remain viable on surfaces for up to 9 days (more about this below), but spread of infection from touching of a contaminated surface has not yet been demonstrated. The incubation period from exposure to illness is 2 to 14 days, with an average of 5 days. Unlike the flu, illness from COVID-19 appears to start gradually with fatigue, aches and pains and a sore throat. These symptoms typically last for 5 days and are followed by recovery. This is Phase One and for 80% of people it is the only phase. For 20%, however, Phase Two starts after 5 days, with cough and shortness of breath, symptoms of pneumonia. Both groups will continue to shed the virus in secretions for several weeks and may still be contagious after symptoms end.

Because people who are infected but not sick are able to infect others, widespread dissemination is likely. For this reason, healthy young people need to take the same precautions their grandparents take, if the pandemic is to be controlled. Infants and young children, even when heavily infected, are especially resistant to sickness from this virus, which is the opposite of the flu. Severe illness and mortality increase with age and are more likely in smokers and in people with diabetes, high blood pressure and heart disease. The reason for these differences and for the two phases of illness is explained below, in the sections on the Coronavirus Biology and ACE-2 Enhancement.

Unlike influenza, in which pneumonia is due to a secondary bacterial infection, responsive to antibiotics, corona virus pneumonia is viral and produces a characteristic pattern on chest X-ray or CAT scan. The mortality rate of COVID-19 varies with the population being studied. The clearest data for mortality among ambulatory, well-fed individuals comes from the Diamond Princess cruise ship, because all of the 3500 people on board were tested. So far, 706 have tested positive for the virus and 6 have died, a case fatality rate of 0.85%, almost 10 times greater than the typical seasonal flu. In nursing homes or homeless shelters the COVID-19 case fatality rate is likely to be much higher. Dr. Anthony Fauci of the National Institutes of Health puts the case fatality rate for COVID-19 in the U.S. at 1%.

It is not presently known whether recovery from infection with COVID-19 produces immunity to the virus. There are cases reported of apparent re-infection, but they might represent flare-up of an infection that had been suppressed and not cured. Without individual immunity, vaccines will not work and there will be no herd immunity.

PERSONAL PROTECTION

Avoidance of exposure should be the number one strategy and has received the most attention. Methods of avoidance are described in the section below called Anti-Viral Hygiene. By avoiding infection, you help prevent spread to other people and benefit the entire community.

If you are exposed or infected, there are measures you can take, based on the biology of the virus, which may diminish the likelihood of severe illness. These are not treatments for disease; they are preventive strategies to help place you among the 80% with mild to minimal illness and they have the greatest chance of succeeding if implemented before you are exposed.

CORONAVIRUS BIOLOGY, WHAT YOU NEED TO KNOW

In order to cause disease, any virus must enter a human cell, replicate, and damage the cell, escaping to infect adjacent cells. COVID-19 enters human cells by attaching to a protein on the cell surface called ACE-2. The pattern of COVID-19 pneumonia matches the distribution of ACE-2 in the lungs. ACE-2 is actually an enzyme with strong beneficial effects in the organs that produce it. When corona virus binds to ACE-2, the protein loses its enzyme activity. In the words of one scientist, COVID-19 produces “ACE-2 exhaustion”. Scientists believe that ACE-2 exhaustion is responsible for the severity of pneumonia and catastrophic effects like heart failure and circulatory collapse. Laboratory studies have shown that restoring ACE-2 dramatically reduces the severity of pneumonia in animals infected with the SARS virus, a close relative of COVID-19. The resilience of ACE-2 may explain the diversity of responses to corona virus infection. ACE-2 activity is highest in the young and decreases with age. The conditions associated with death from COVID-19 infection (advanced age, diabetes, high blood pressure, heart disease, cigarette smoking) are all associated with diminished baseline ACE-2 activity. The second phase of COVID-19, the progression from a minor viral illness to severe pneumonia, probably reflects ACE-2 exhaustion, occurring several days after the initial symptoms. This protocol for protection will present aids to enhancing ACE-2 resilience.

Once they have entered human cells, corona viruses replicate by hijacking a human protein called mTOR, which is present in all cells. The body uses specialized proteins called Sirtuins to control mTOR activation. Nutritional activation of Sirtuins can inhibit mTOR.

Once they have multiplied, corona viruses damage human cells by producing an enzyme called 3CL protease, which allows them to spread to adjacent cells. 3CL protease has been called “the Achilles heel” of corona virus and is the subject of new anti-viral drug development. There are some dietary flavonoids that inhibit 3CL protease, which may limit severity of infection.

In order to accomplish the 3 steps just described, viruses also need to avoid the natural, intrinsic protection provided by the human innate immune system, a series of cells and proteins that kill viruses on contact. Corona viruses have many mechanisms for evading the innate immune system, so it isn’t clear that stimulating innate immunity will offer much protection, but weakened innate immunity is likely to contribute to severity of illness, so measures to optimize innate immunity are warranted. Once pneumonia develops and disease severity increases, the role of the immune system changes. Much of the damage is due to over activity of immune responses, what is termed a “cytokine storm.” Immune boosting therapies may be contra-indicated during phase two of COVID-19 infection.

PROTECTION THROUGH NUTRITION AND NATURAL PRODUCTS

A few natural products have shown anti-corona virus effects in laboratory studies, including results in animals. Some of these have a long history of human use for treating infections.

ACE-2 Enhancement

Regular aerobic exercise and a plant-based whole foods diet are associated with improved ACE-2 function. Natural products shown to enhance ACE-2 include **curcumin** (a set of flavonoids found in the spice turmeric**), resveratrol** (a polyphenol found in red grapes and other foods**), rosmarinic acid** (a polyphenol found in spices like rosemary and oregano), ***Panax notoginseng*** (an herb used in some traditional Chinese medicines—the active Panax fractions for strengthening ACE-2 are called saponins), and **alpha-lipoic acid** (an anti-oxidant). ACE-2 as an enzyme produces a peptide called **Ang 1-7**, which is responsible for many of its cellular benefits. Ang 1-7 is made up of 7 amino acids and is absorbed if taken orally. Through a positive feedback loop, administration of Ang 1-7 also increases activity of ACE 2. Ang 1-7 may soon be available through a compounding pharmacy.

mTOR Modulation

The best known nutritional stimulator of Sirtuin function, and hence the most studied natural modulator of mTOR, is **resveratrol**. **Quercetin**, a flavonoid found in apples, onions and many spices, also inhibits mTOR. In the case of resveratrol, repeated exposure decreases the amount that’s needed for viral inhibition. Because resveratrol and quercetin are poorly absorbed, it is best to start taking them long before exposure, so that levels in cells can accumulate. Both have high safety profiles and anti-inflammatory effects.

3CL protease inhibition

**Elderberry** fruit (*Sambucus nigra*) and the medicinal herb ***Houttuynia cordata*** both inhibit the viral enzyme 3-CL protease and have been shown to inhibit coronavirus activity in cells. Both are also potent stimulators of anti-viral immune responses. Elderberry seems to be most effective if started before infection and continued through the initial period of infection. It may be contra-indicated in Phase Two of COVID-19, because of its immune enhancing effects. Elderberries’ 3CL protease inhibition is related to its content of flavonoids, especially those called anthocyanins, and its immune stimulating activity is related to its complex sugars (polysaccharides). When taking elderberry, make sure its flavonoid or anthocyanin content has been standardized. Elderberry extracts are safer than raw elderberry fruit. The leaves, bark and roots of elderberries contain a toxic substance, which is removed by cooking or extraction. Concerns have been raised about the immune stimulating effects of elderberries. These are addressed in the next section,because they apply to all immune enhancing therapies. There are several other dietary flavonoids that inhibit coronavirus 3CL protease. The most potent according to one detailed study, was herbacetin, which is primarily found in ground flax seed.

Enhancement of Innate Immunity

The innate immune system is present at birth and is ready to attack microbes on contact. Its function is supported by adequate sleep and moderate exercise. The most important dietary component for its maintenance is protein. Protein deficiency impairs innate immunity, but there is no evidence that excess dietary protein improves it beyond the effects of a normal healthy diet. Your protein intake in grams should be about half your lean body weight in pounds.

**Vitamin D**, vitamin A and zinc are essential for innate immunity but excess levels of these actually impair immune function. Almost everyone should supplement with Vitamin D through the winter, but the dose needs to be individualized over a range of 1000 to 5000 IU/day. Vitamin D is best absorbed with a large meal. Vitamin A (in the form of retinol) and zinc should only be supplemented if blood levels are low. Many integrative physicians make the mistake of measuring zinc in red blood cells or whole blood; this is not an accurate reflection of zinc status. Plasma zinc or white blood cell zinc is much more meaningful.

Elderberry polysaccharides are potent stimulators of innate immunity, so, like resveratrol, elderberry extract can help on two fronts. The COVID-19 pandemic has created a run on elderberries and warnings about elderberries, because of their known benefits in fighting flu. All elderberry products are not the same, however, and some may be of little value. Alcohol extraction of elderberries leaves the polysaccharides behind. The best elderberry products for both flavonoid content and polysaccharide content are produced by ultrafiltration.

Medicinal and dietary mushrooms also contain polysaccharides that can stimulate innate anti-viral immunity. The most studied are **turkey tail** (*Coriolus*), **maitake**, **shiitake** and **reishi**.

Probiotics and prebiotics may impact innate immunity by creating a gut microbiome that stimulates the immune system. Research in this area is in its infancy. Prebiotics with the best evidence for immune stimulation include **beta-glucans**, **arabinogalactans** and **galacto-oligosaccharides**. These are readily available as powders. Probiotics with the best evidence for immune stimulation are *Lactobacillus* species, especially ***Lactobacillus plantarum***, which is found in sauerkraut and other fermented plant foods, and spore-forming bacteria of the genus *Bacillus,* which are normally found in soil. Several preparations are commercially available. Because COVID-19 has many mechanisms for evading innate immunity, even when it is strong, immune enhancement by itself is not a promising approach for preventing severe infection.

The lung damage of advanced corona virus pneumonia is due to an overactive immune response, so these immune boosting therapies should be used for prevention or early infection only, and not for severe illness. If you suffer from an autoimmune disease, it may not be advisable to use mushrooms, elderberry or probiotics that stimulate innate immune function. If you have been sick with COVID-19 for 5 days and have evidence of pneumonia, you should stop the use of mushrooms, elderberry and immune-enhancing probiotics.

ANTI-VIRAL HYGIENE

The first step is to develop these habits: Wash your hands with soap and water for 20 seconds before eating, touching your face, after being with other people and when you return home. A face wash is also a good idea. Do not use antibacterial soap; it will not kill viruses and will only damage your skin’s microbiome. Because corona virus can live on hard surfaces for days, avoid touching doorknobs or elevator buttons with your hands.

The following substances will kill most viruses, including corona viruses, on hard surfaces with 30 seconds of contact: 70% alcohol, 0.5 % hydrogen peroxide, 0.1 % bleach (hypochlorous acid). The studies have been done on hard nonporous surfaces, so alcohol, peroxide or bleach will work on counter tops but may not work on your skin or other porous surfaces. If you choose to use bleach, make sure you do not mix it with ammonia, because the combination produces a deadly gas. Purelle hand sanitizer is 70% alcohol and might be a good substitute for soap, but remember that contact needs to be maintained for 30 seconds. Clean door knobs, phones and keyboards daily or more often.

If you are sick, stay home and wear a **surgical mask** around other people. N95 respirators are fairly uncomfortable when worn for extended periods of time and should be reserved for health professionals. When coughing or sneezing, cover your nose and mouth with your forearm or with a tissue and dispose of the tissue in a closed container. Avoid shaking hands. Social distancing prevents viral spread; try staying six feet away from other people, especially if you’re sick.

Various metals are being touted for their anti-viral effects. Do not fall for the hype. Copper and its alloys like bronze are the most potent of the anti-viral metals. However, a recent, not yet published study from Princeton found that COVID-19 is relatively resistant to death by copper, needing 4 hours of exposure, unlike cold viruses, which are killed in 60 seconds. Because the mechanisms by which different metals kill viruses tend to be similar, it is unlikely that metals like zinc or silver will be effective at killing COVID-19. Furthermore, the silver preparations tested in scientific studies are different from the colloidal silver that is sold in health food stores, so colloidal silver sprays cannot be relied upon for protection. High levels of zinc kill some corona viruses but are less effective than copper. Although some doctors advocate the use of zinc lozenges to prevent COVID-19, zinc lozenges are unlikely to achieve time of contact or concentration needed to kill this virus. The main side effect of zinc is nausea, which would interfere with your ability to take more useful preventive treatments.

In the Princeton study, COVID-19 survived on stainless steel surfaces for 48 hours. Another interesting finding in this study was the number of viral particles transferred to a cotton swab from different surfaces that had been contaminated by the same amount of virus under experimental conditions. Hard, non-porous surface transferred the greatest number, whereas soft highly porous surfaces transferred the least. The number of particles picked up from cloth was just 1% of the number of particles picked up from a hard surface. Possibly the virus becomes enmeshed in the fabric. At present there is no evidence that COVID-19 is spread to human by any means other than airborne droplets, so it is unclear how much effort should be placed on cleaning surfaces or fabrics.

SUPPLEMENT SUGGESTIONS

These recommendations may change based upon availability of specific products and continuing research. They can be modified because of individual needs. Their function is to address the biology of COVID-19 and human immune response. Possible preventive supplements:

FOR SUPPORTING ACE-2.

1. Liposomal **curcumin** (200 mg) and **resveratrol** (75 mg) twice a day with food. (If unable to get a liposomal form, take curcumin 500 mg and resveratrol 200 mg twice a day).
2. **Rosmarinic acid** 140 mg twice a day with food
3. **Alpha-lipoic acid** 300 mg twice a day with food

FOR mTOR INHIBITION

1. **Resveratrol** as described above
2. **Quercetin** 300 mg twice a day with food.

FOR INHIBITION OF 3CL PROTEASE

1. **Elderberry**, doase depends on product
2. **Houttuynia** **cordata, dose depends on product**
3. **Flax seed meal**  1-2 teaspoons a day

TO ENHANCE INNATE IMMUNITY

1. Elderberry extract as described above.
2. Vitamin D3, 1000 to 5000 IU/day with a large meal
3. Lactobacillus plantarum (refrigerate) 1 capsule twice a day at the start of a meal
4. Beta glucan powder 1 scoop a day
5. Arabinogalactan powder 1 scoop a day
6. Coriolus (turkeytail) supplying 800 mg of polysaccharides a day