ASK DoctorMurray

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Supporting Your First Line of Defense Against Viral Infections

The worldwide COVID-19 pandemic brought focus to the prevention of viral infections, both in terms of reducing risk through good hygiene as well as measures to bolster the immune system. But even before our immune system comes in contact with a coronavirus or any microorganism, there are natural barriers to infection. As it relates to the respiratory viruses, the first line of defense is the lining of the airways or respiratory tract—nasal cavity, sinuses, throat, trachea, and bronchi.

Why is the mucous membrane important in fighting respiratory infections?

In order for any virus to infect the throat, sinuses, airways or lungs it must first pass through or enter the body through the mucous membranes or *mucosa*. It is the first barrier to infection; the immune system is the second line of defense. There are two routes for respiratory tract viruses like influenza and coronavirus to enter the lungs and cause serious damage. The primary route is through the respiratory tract; the other route is through the gastrointestinal tract.

The respiratory tract mucous membrane that lines the airways is the first line of defense. It consists primarily of cells known as *ciliated epithelial cells*. These cells have their external surface covered by hair-like structures called *cilia*. The cilia are formed into bundles and act like brushes to move the respiratory tract secretions, micro-organisms, and debris up and eventually out of the nose or mouth. On top of the ciliated epithelial cells are two layers of mucus. The mucus is produced by another type of epithelial cell called a *goblet cell.* A thinner version of mucus lies intermixed with the cilia bundles while a thicker layer sits on top of that layer. The mucus is composed of *mucin*, which refers to a network of proteins complexed with sugars.

The mucous membrane and mucus are specially designed to protect against any microorganism or particles from getting into the lungs. Inside the lungs is composed of specialized epithelial cells that do not have cilia. Nor are there goblet cells in the lungs. In the lungs, there are only very thin epithelial cells, connective tissue, and blood capillaries all designed to perform the function of delivering oxygen to the blood and exchanging it for carbon dioxide that is then exhaled through the airways. When particulate matter or microorganisms make it to the lungs, it is a very serious situation as there is very little protection there. The importance of the health of the mucus and the lining of the airways in preventing COVID-19 infection cannot be overstated as conditions associated with poor functioning of this line of defense is associated with an increased risk of more serious infection.

Can viruses travel from the gut to infect the lungs?

The secondary route of infection for many respiratory tract viruses like COVID-19 coronavirus entering the body is through the gastrointestinal tract. Within the GI tract, there are a number of protective factors beyond the mucus lining. The most notable additions are digestive secretions such as stomach acid and digestive enzymes. The immune system structure in the gut is also much larger. If a virus is able to avoid these protective factors and infect the GI tract, it is able to enter the bloodstream and also infect the lungs.

Interestingly, this ability of coronaviruses to travel from the gut to the lungs was confirmed with **Middle East respiratory syndrome coronavirus (MERS-CoV)** by increasing the gastrointestinal replication of the virus by infecting animals with viruses orally while at the same time giving them an acid-blocking drug known as a proton pump inhibitor.[1] Obviously, this begs an answer

to the question: *Does taking a proton pump inhibitor increase the risk for viruses that can attack the lungs by increasing the secondary route of access to the lungs?* The answer is **yes**.

Another factor that greatly increases the risk of the secondary route of infection is a lack of digestive enzymes. It is well established that pancreatic enzyme insufficiency is a major risk factor for all viral respiratory infections. In fact, enzyme replacement therapy is the key medical approach to reduce the risk of lung infections in these patients. Enzymes that digest protein, *proteases*, are able to digest not only proteins in food but also the proteins on the cell walls of the virus. Viruses contain proteins protruding from their cell membranes that play critical roles in the infection process. Without these proteins, the virus simply cannot enter human cells. Supplemental proteases are also effective in supporting the mucus barrier in the airways as well (discussed below).

What determines the severity of COVID-19 infection?

The difference between a mild vs. a severe COVID-19 infection appears to be based on a few key factors. The infection equation is like a mathematical equation where one plus two equals three. In the infection equation, the interaction of the host's immune system with the infecting organism determines the equation's outcome.

Each day, every one of us is exposed to organisms that have the potential to make us sick, yet we don't always fall prey to these "bugs" because our immune system is generally stronger than the organism. If the "bug" is extremely powerful, the viral load of the exposure is extreme, or our immune system is compromised, an infection can occur. From preliminary data it looks like as many as perhaps 90% of people exposed to COVID-19 remain asymptomatic. In other words, even though they have been exposed to the virus, they have not developed symptoms. On the flip side, it is clear already that in people with compromised immune systems or those who are smokers or have a pre-existing health issue when they are exposed to COVID-19, it often leads to a fulminant infection and death.

The initial viral load of the exposure also appears to be a key factor. If exposure is a small dose of COVID-19, in most cases, in healthy individuals, it will lead to no symptoms or they will experience only mild symptoms. If the viral load a person is exposed to is quite high, then it greatly increases their risk for a more moderate to severe infection. That is why healthcare workers are especially vulnerable. They are often exposed to a very high viral load.

Another factor that determines the severity of COVID-19 infection may be the ability of the virus to travel down the respiratory tract into the lungs. A respiratory tract viral infection generally starts in the nose and travels down the airways. The deeper it goes, the more severe the infection. Remember, the lung cells have little protection. During a viral infection of the lungs, not only are the lung epithelial cells damaged by the infecting virus, but they are also damaged by the body's immune response to the infection. If the response and clean-up by the immune system is quick, the infection can be contained and cleared in a few days. But if the immune response is either insufficient or over-aggressive, it can lead to significant damage.

How do I support the first line of defense?

From the above discussion, it should be clear that the first step in supporting our host defenses against COVID-19, or any organism that targets the respiratory tract, is to support the production of an effective mucosal barrier. Here are some key strategies:

- Adequate hydration.
- Supply key nutrients for epithelial function and the production of mucin (the components of mucus).
- Utilize protease enzyme formulas.
- Take N-acetylcysteine.

Why is adequate hydration important to the mucous membranes?

Water is critical to the health of the mucous membranes for several reasons. The mucin that the epithelial cells make is made "dry," otherwise there would not be enough space in the cell itself. Mucins are able to bind 1,000 times their weight in water. Without sufficient water they are not able to grow. Remember grow toys? Those cheap little toys that get bigger after you leave them in water. That is how mucus is formed. So, sufficient water is critical to mucus function. Humidifiers may help keep the airways moist, but insuring sufficient hydration from the inside out is critical to ensuring proper barrier function.

What are the key nutrients for epithelial function and the production of mucin?

A deficiency of any essential vitamin and mineral can lead to an altered mucosal barrier. The epithelial cells need a constant supply of nutrients in order to replicate properly, and to perform both their structural role as well as manufacturing role. It is not just mucin that these cells manufacture, they also manufacture many other protective substances critical in fighting off viruses

and harmful organisms. Taking a multiple vitamin and mineral formula is crucial. Take one that provides at least the recommended dietary intake level for key nutrients like vitamin A, C, and D; B vitamins; and zinc as these nutrients are especially important. Since most multiples now contain beta-carotene as the vitamin A source, I would also recommend taking additional vitamin A in the form of retinol during a virus outbreak or increased exposure to particularly virulent forms of respiratory tract viruses. This form of vitamin A has more direct anti-infective action.

Vitamin A was the first fat-soluble vitamin to be discovered, but that is not the only reason why it was called "A"—it was given the name to signify its "anti-infective" properties. Vitamin A is absolutely critical to the health and function mucous membranes. Vitamin A deficient individuals are more susceptible to infectious diseases in general, but especially viral infections. Vitamin A supplementation has been shown to produce significant benefits in improving immune function during viral infections, especially when fighting respiratory tract viruses in children.[2]

Dosage ranges for vitamin A reflect intent of use. During the cold and flu months, to support the health of the mucosa and immune system, a dosage of 3,000 mcg (10,000 IU) for men and 1,500 mcg (5,000 IU) for women is safe. During an acute viral infection, a single oral loading dosage of 15,000 mcg or 50,000 IU is safe as long as there is ZERO chance of pregnancy. Because high doses of vitamin A during pregnancy can cause birth defects, women of childbearing age should not supplement with more than 1,500 mcg (5,000 IU) of vitamin A per day. The same warning applies during lactation.

Vitamin D is also important to take a little extra of than what is typically found in a multiple vitamin and mineral formula. There is a growing body of science that show low levels of vitamin D increase the risk for viral respiratory infections.[3] Since we can make vitamin D in our skin when it interacts with sunlight, there is obviously a natural tendency for many people to make less vitamin D during the winter months. Supplementing the diet with additional vitamin D can help prevent this winter-time drop in vitamin D levels. Beyond that, it appears that vitamin D functions in the body in a way that prevents viruses from infecting cells. Research has shown that vitamin D supplementation prevents respiratory infections in adults and children. During the winter months, most vitamin D experts recommend taking 5,000 IU per day for adults and children over 10 years of age. For children under the age of 1 year the dosage is 1,000 IU; for children between the ages of 2-4 years 2,000 IU; and for children between the ages of 4 through 9 the suggested dose is 3000 IU daily. During an acute viral infection, a single loading dose of up to ten times these suggested dosages is appropriate.

What are protease enzyme formulas?

Certain protease enzymes have shown benefits in improving the composition, physical characteristics, and function of mucus. Proteases are often used in digestive formulas to aid in the breakdown of dietary protein. When taken on an empty stomach away from food, these proteases are absorbed into the bloodstream to exert systemic effects including beneficial effects on mucus composition and function.

A highly studied protease is *mucolase* —a special fungal protease with confirmed actions on respiratory tract mucus. One clinical study looked at the effect of mucolase on mucus in patients with chronic bronchitis. The patients were randomly assigned to receive either the protease or a placebo for ten days. While the placebo had no effect on the mucus, mucolase produced significant changes in both viscosity (thickness) and elasticity (stretchiness) at the end of treatment. In fact, the improved mucus structure and function was apparent up to eight days after the end of treatment.[4] In another ten-day double-blind study, mucolase was shown not only to improve the viscoelasticity of mucus, but also reduce airway inflammation.[5] Key benefits in fighting any sort of respiratory tract infection.

Other proteases, like *bromelain* and *serratiopeptidase*, have shown similar effects. Mucolase, bromelain, and serratiopeptidase decrease the thickness of the mucus, while at the same time increasing mucus production and dramatically increasing the ciliary transport of the mucus.[6-10] The net effect is the production of much more mucus that is effective in neutralizing microbes and moving them out of the body. In addition to enhancing the mechanical effects of mucus, proteases may enable special protective factors within mucus to more effectively neutralize invading organisms. Some of the protective factors secreted in mucus are *secretory IgA*, various white blood cell-derived protease inhibitors that block viruses, nitric oxide, and lactoferrin.

For best results, use protease formulas that contain mucolase from well-respected brands. Be sure to take these enzymes away from food and follow label dosage instructions.

Do protease enzymes exert antiviral activity?

While proteases are capable of attacking and digesting proteins on viruses within the digestive tract, within the respiratory tract any antiviral action of proteases is likely much more complex than simply taking out the proteins

that attach to epithelial cells. In fact, the most significant antiviral effect may be mediated by just the opposite effect—protease inhibition. When proteases are taken into the systemic circulation or interact with our immune system, it results in an increase in the production of protease inhibitors being produced by the body, particularly white blood cells as a compensatory mechanism. Protease inhibitors secreted by our own white blood cells, as well as in drug form, are known antiviral agents. In particular, white blood cells within the lining of the mucosa of the respiratory tract secrete a protease inhibitor that protects the epithelial cells from microbial proteases that promote infection and spreading. This not only protects the cells from infection, but also exerts antimicrobial effects as well. More technically, *secretory leukocyte protease inhibitor (SLPI)* is particularly important in airway secretions because of its broad-spectrum antibiotic activity, including its antiviral effects. And, the protection of SLPI goes even further by blocking viral attachment and also protecting the lungs against attack by our own immune system.

One of the hallmark features of severe COVID-19 infection is massive destruction to lung tissues caused not so much by the virus, but rather by our immune system. Much of this damage is caused by the release of proteases from our own white blood cells. SLPI is one of the major defenses against the destruction of the lungs by our own immune system. My feeling is that people most susceptible to the lung damage in COVID-19 infection is the result of lower levels of SLPI. Studies with influenza virus shows that when there is a decrease in respiratory tract protease inhibitors, it leads to increased activation and replication of the influenza virus.[11] The same scenario is likely happening with COVID-19 pneumonia.

What is N-Acetylcysteine and how does it support the respiratory tract?

N-acetylcysteine (NAC) is a sulfur containing amino acid that has an extensive history of use as a mucus modifying agent to support the respiratory tract. It is also used in the body to form the *glutathione*—the major antioxidant for the entire respiratory tract and lungs. People who are exposed to smoke or other respiratory toxins, who suffer from conditions associated with inflammation such as diabetes, obesity, and other chronic conditions, have lower levels of glutathione. Low levels of glutathione may be responsible for these conditions also being risk factors for more severe outcomes with COVID-19. NAC supplementation can boost glutathione levels and help protect the lungs and respiratory tract.[12]

NAC is also a mucus modifying agent. It has been used orally with great success, as well as in hospitals through breathing tubes to help people dealing with inefficient or thick mucus in acute and chronic lung conditions such as emphysema, bronchitis, chronic asthma, and cystic fibrosis. NAC helps to reduce the viscosity of bronchial secretions. NAC has also been found to improve the ability of cilia in the respiratory tract to clear mucus, increasing the clearance rate by 35%. As a result of these effects, NAC improves bronchial and lung function, reduces cough, and improves oxygen saturation in the blood when the respiratory tract is being challenged. For protection and boosting glutathione levels in the lung the dosage is generally 500 to 1,000 mg daily. For use in reducing mucus thickness, the typical dosage is 200 mg three to four times daily.[12-14]

Do protease enzymes and/or NAC help during an active respiratory tract infection?

The mucus modifying effects of supplemental proteases and NAC are well-displayed during an acute respiratory infection. By decreasing the viscosity, ciliary action is improved, leading to less mucus congestion, thereby not only reducing symptoms of congestion, but also the likelihood of a secondary bacterial infection. Thick mucus is a breeding ground for disease-causing bacteria. NAC and formulas that contain protease enzymes like mucolase, bromelain, or serratiopeptidase should be used whenever mucus is thick or viscous to reduce the risk of infection.

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