

Pandemic Plan for the Church

Ministering to the Community in a Time of Crisis

How to Prevent Acute Respiratory Distress (What We've Learned from COVID-19)

The inflammation triggered by the immune response can produce what is called a cytokine storm which can progress into Acute Respiratory Distress Syndrome.

Disclaimer: This material is meant as informative and not as medical advice. Please contact your doctor if you have these symptoms or any questions.

Introduction

Approximately 42% of patients hospitalized with COVID-19 pneumonia developed Acute Respiratory Distress Syndrome (ARDS). ARDS involves severe inflammation, fluid buildup in the air sacs (alveoli) and low blood oxygen levels, requiring intensive care management.ⁱ

Despite the better understanding of the pathophysiology of COVID-19 and Avian Influenza, primarily respiratory diseases that infect both upper and lower respiratory tracts, the search for new interventions remains ongoing. Scientists have taken to study medicines and molecules with anti-inflammatory and strong antioxidant potentials.ⁱⁱ

This document is a summary of some of the over the counter (OTC) medicines that have been put into practice during the COVID-19 Pandemic, in the effort of preventing a cytokine storm that may lead to ARDS.

Cytokine Storm

Cytokines are protein hormone like substances that act as messenger molecules and regulators in the immune system. They are produced primarily in response to pathogens (any agent that can cause disease). When there is an excessive number of cytokines it can cause too much fluid to build up, this is called a *cytokine storm*.

A cytokine storm is defined as an acute overproduction and uncontrolled release of pro-inflammatory markers, both locally and systemically.ⁱⁱⁱ It is a life-threatening condition caused

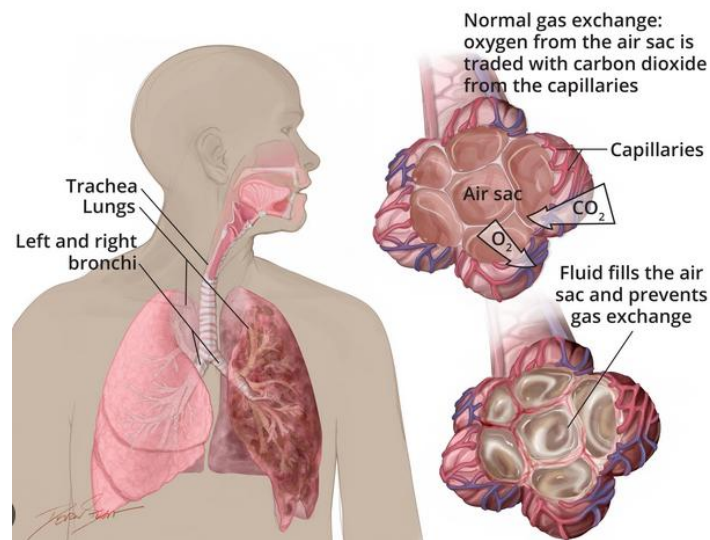
by a severe, uncontrolled immune system inflammatory reaction. Instead of protecting the body, this exaggerated response causes the immune system to overreact and release excessive amounts of pro-inflammatory cytokines into the bloodstream, triggering widespread inflammation that can damage organs and lead to multi-organ failure. This is an excessive immune response, not the amount of viral load.

The phrase “cytokine storm” is a descriptive term to encompass a variety of cascading events that can ultimately result in multi-organ failure and death. It is this inflammation triggered by cytokines that causes the severe complication of acute respiratory distress syndrome (ARDS).

Management of this inflammatory response prevents subsequent infections such as pneumonia or damage to the organs. The HPAI H5N1, SARS, MERS, COVID-19, and the seasonal flu have similar pathologies, and all can trigger cytokine storms. For more information on the pathophysiology of viruses and cytokine storms, please see the document and PowerPoint presentation titled “Pathophysiology of Avian Influenza.”

Acute Respiratory Distress Syndrome (ARDS)

Acute Respiratory Distress Syndrome (ARDS) is a severe, rapidly progressing form of respiratory failure caused by widespread lung inflammation. It occurs in the alveoli (air sacs) and bronchial epithelial cells (cells that line the bronchial tree). Fluid fills the alveoli preventing oxygen from entering the bloodstream. It usually develops within 24-48 hours a major injury or infection, such as pneumonia or sepsis. This accumulation of fluid and hypoxemia (below normal level of oxygen in the blood) leads to a cascade of problems which affect the body’s tissue and organs.



Acute Respiratory Distress Syndrome^{iv}

Signs and symptoms of ARDS include:

- Severe shortness of breath
- Rapid breathing
- Fingernails, lips or skin may turn blue (cyanosis)
- Extreme fatigue
- Low blood pressure
- Confusion

ARDS vs Pneumonia

ARDS is a severe, life-threatening, systemic inflammatory condition that requires medical attention. Pneumonia is an infection that causes inflammation in one or both lungs. Pneumonia is caused by bacteria, viruses, or fungi. ARDS is usually the secondary condition triggered by pneumonia, sepsis, or trauma.



Different Lung Pathologies^v

Many studies were performed throughout the COVID-19 pandemic to find medications and supplements that help in the prevention or resolution of ARDS. This document summarizes

some of the supplements and over-the-counter medications that have proved to be helpful. Each includes scientific studies with evidence to back up the claims.

Vitamin D and Respiratory Health

Vitamin D is a fat-soluble nutrient essential for bone health, immune function, and calcium absorption. A study performed through the COVID-19 outbreak shed more light on the use of vitamin D and its effects on respiratory health. We have long known that sunlight can boost serotonin levels and improve mental health by increasing vitamin D production. Studies now have shown that having low levels of vitamin D in your system may in fact increase the risk of severe COVID-19 symptoms and even lengthen your recovery.^{vi}

There is evidence that vitamin D may prevent or improve outcomes in many infectious and inflammatory conditions, including acute and chronic respiratory infections. There is also an increasing understanding of its immunomodulatory and anti-inflammatory functions. A recent study found a 70% reduction in viral respiratory tract infections among persons with vitamin D deficiency receiving vitamin D treatment.^{vii} Studies have indicated that there is a high prevalence of vitamin D deficiency worldwide.^{viii}

Vitamin D and the Immune System and Inflammation

These studies have also found other benefits to Vitamin D while treating COVID-19. It has been found to boost your immune system and help control inflammation.

Dr. James Mullin of Lankenau Institute for Medical Research states:

“The benefits, however, are so clear and the risks so minimal that we believe physicians should be recommending supplemental Vitamin D right away,” Mullin said. “Cytokine storms, where the body’s immune response kicks into overdrive and can result in severe disease and death in COVID, compromise the body’s airway barrier function. We already know from past studies that Vitamin D blunts cytokine storms in cases of flu. In cases of COVID-19, vitamin D therapy may allow time for a patient’s own immune defenses to kick in before it’s too late.”^{ix}

Vitamin D and Sunlight

Vitamin D is a fat-soluble vitamin, different from others in that a major source comes from the sun’s UV light. Exposure to the sun allows your skin to convert vitamin D from cholesterol and is the best way to get vitamin D. Dietary sources include fortified foods and supplements.

Vitamin D3 vs Vitamin D2

Vitamin D is found in supplements in two different forms; one is vitamin D3 (cholecalciferol) and the other is vitamin D2 (ergocalciferol). Vitamin D3 is found in the skin after sunshine converts cholesterol into the pre-vitamin cholecalciferol. It is D3 that is found in egg yolks, oily fish, some fortified foods and some supplements. Vitamin D2 can be found in supplements that come from plant and/or fungal sources such as mushrooms.

Vitamin D3 is the form naturally found in the body and in normally manufactured supplements. Vitamin D2 is contained in vegan supplements. Studies have shown that vitamin D3 increases levels of calcidiol (the molecule in your blood that is measured to calculate levels) more efficiently than vitamin D2.^x

Recommended Dietary Allowances for Vitamin D

Many people are deficient, or don't get enough. This is especially true if you're older, don't eat healthy foods, or have a darker skin tone. And those low levels may raise your risk of severe COVID-19 if infected.^{xi}

Currently, different recommendations exist. The Institute of Medicine has placed the recommended dietary allowance, or RDA, for vitamin D at 600 international units (IU) per day for young adults and 800 IU per day for adults older than 70. Other experts suggest that adults' vitamin D needs are much higher. For example, the Endocrine Society recommends up to 1,500 to 2,000 IU of vitamin D daily for adults. Mayo Clinic recommends that adults get at least the RDA of 600 IU. However, 1,000 to 2,000 IU per day of vitamin D from a supplement is generally safe, should help people achieve an adequate blood level of vitamin D, and may have additional health benefits.^{xii} Below is a table of recommended dietary allowances of Vitamin D from the National

Age	Male	Female	Pregnancy	Lactation
0-12 months*	10 mcg (400 IU)	10 mcg (400 IU)		
1-13 years	15 mcg (600 IU)	15 mcg (600 IU)		
14-18 years	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)
19-50 years	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)
51-70 years	15 mcg (600 IU)	15 mcg (600 IU)		
>70 years	20 mcg (800 IU)	20 mcg (800 IU)		

Institutes of Health^{xiii}.

If you are not currently taking Vitamin D as a daily supplement, as a guard for your respiratory health, you should start right away.

If you acquire a respiratory illness, COVID-19, or HPAI H5N1, some doctors have found a link between the disease and vitamin D deficiency. It has been determined that increasing supplementation either 5,000 to 10,000 IUs a day, (taken 5,000 IUs 2 times a day) to correct or prevent deficiency while someone is sick or admitted in the hospital.^{xiv}

How to Take Vitamin D

Vitamin D is fat-soluble, meaning it does not dissolve in water, and is absorbed best when taken with high fat foods. You can take it at any time of the day, but some suggest that taking it in the morning may improve absorption.

Taking Vitamin K2 along with Vitamin D will help transport calcium out of your arteries, this will enhance your bone and cardiovascular health.

How to get more vitamin D

More sunlight and foods rich in vitamin D are the best ways. Exposure to sunlight for 15 to 30 minutes, three days a week is good source. Foods that are good sources of vitamin D are:

- Oily fish (like salmon, rainbow trout, tuna, sardines)
- Red meat
- Egg yolks
- Food with vitamin D added
- Raw mushrooms
- Fortified orange juice
- Fortified milk
- Almond milk
- Rice milk

Antihistamines

Scientists who have been studying the pathophysiology of COVID-19 have found that like the H5N1, the disease is a result of histamine activated pathways which can lead to a cytokine storm which may result in acute respiratory distress syndrome (ARDS).

Histamine plays a crucial role in the immune system and sends messages between cells. It is a chemical compound produced by basophils and mast cells that are part of the innate immune

system (the body's rapid, first line, non-specific defense present from birth. Acts within minutes to hours of infection.). They release inflammatory mediators like histamine and cytokines. Some functions of histamine in the human body include:

- Tells your stomach cells to make acid
- Helps your brain to stay awake
- Increases blood flow and causes inflammation in nearby tissue
 - Widening of blood vessels
 - Causing leaking
 - Causing tissues to swell
- Helps protect us from foreign invaders (antigens) by expelling the antigen
 - Runny nose
 - Sneezing
 - Watery eyes
 - Itchy skin
- Histamine effects also include:
 - Anaphylaxis
 - Rash/urticaria
 - Increase in heart rate

Substances that may trigger an overreaction of the immune system and activate histamines are:

- Food.
- Dust
- Pollen
- Venom
- Antigens

Histamine pathways can trigger inflammation responses such as ARDS, deep vein thrombosis, and damage to organs. There are four classes of histamine receptors H1, H2, H3, and H4, all of which play a role. However, Of the histamine receptors, H1 and H2 have gained the most

clinical attention in treatment strategy for ARDS. H1 receptors mediate allergic reactions, inflammation, and smooth muscle contraction. H2 receptors stimulate gastric acid secretion. Historically, using the combination of H1 and H2 receptor antagonists (antihistamines) has been classic treatment strategy.^{xv}

H1 Inhibitors

H1 inhibitor antihistamines should be included in symptom management, by modulating the histamine pathways and suppressing viral growth. One study by practicing pulmonologists states that starting treatment with antihistamines every 12 hours at the first symptoms. Those recommended include: ^{xvi}

- Dexchlorpheniramine (Polaramine) 2 mg
- Cetirizine (Zyrtec) 10 mg
- Loratadine (Claritin) 10 mg

H2 Inhibitors

Mast cells are responsible for releasing substances called mediators that result in inflammation. These mediators are chemicals, such as histamines, that can cause an inflammatory cascade. By including an H2 inhibitor that binds with the H2 receptors in mast cells, it reduces the release of certain proteins in the body causing inflammation. Recent studies show COVID-19 symptoms improved with the use of an H2 inhibitor.

A drug that binds to H2 receptors is Pepcid AC, also known as famotidine, which is used to treat gastrointestinal conditions. The drug binds histamine H2 receptors that are present not only in the stomach but also in mast cells.^{xvii}

In addition to inhibiting histamine release, it also reduces other inflammatory mediators which are responsible for the release of cytokines (molecules that allow communication between cells). Thereby, Pepcid AC may improve symptoms by reducing histamine-induced cytokine release and inflammation.^{xviii}

It is recommended that a sick person take famotidine at 80 mg three times per day for a maximum of 14 days.^{xix} Side effects can include headache, constipation, or diarrhea. Pregnant women should consult their doctor. Children younger than 12 should not take this medication, and older adults may be more sensitive to its side effects.

Zinc

Zinc is an essential mineral that your body uses in many ways. It is necessary for the development and function of T cells in your immune system, which are responsible for fighting infections. It also plays a significant role in regulating cytokine expression and suppressing inflammation.^{xx}

Zinc has been proven to have antiviral effects by reducing replication of the influenza virus. It also helps to inhibit the viral load. In cell culture studies, zinc has shown to inhibit the replication of the coronavirus causing severe ARDS. It's mechanism of inhibition is the inactivation of the RNA replication.^{xxi}

Life Stage	Recommended Amount
Birth to 6 months	2 mg
<u>Infants</u> 7–12 months	3 mg
Children 1–3 years	3 mg
Children 4–8 years	5 mg
Children 9–13 years	8 mg
Teen males 14–18 years	11 mg
Teen females 14–18 years	9 mg
Adult males	11 mg
Adult females	8 mg
Pregnant teens	12 mg
Pregnant adults	11 mg
Breastfeeding teens	13 mg
Breastfeeding adults	12 mg

Daily Recommended Zinc Intake:^{xxii}

Zinc is safe at daily intakes up to 4 to 34 mg for infants and children, depending on age, and up to 40 mg for adults. Higher intakes can cause nausea, vomiting, loss of appetite, stomach cramps, diarrhea, and headaches.^{xxiii}

This supplement should be a part of your regimen when fighting off a virus. You may consider an increased daily amount of Zinc as high as 50 mg 2 times a day for a short duration while you are experiencing symptoms from COVID-19 or HPAI H5N1.^{xxiv xxv}

Vitamin C

Vitamin C (ascorbic acid) is an essential organic water-soluble compound. It plays many important roles in the body, and the effect vitamin C has on the immune system is complex. It is

required in collagen synthesis, which provides structure, integrity and repair for skin, bones, blood vessels, muscles, and connective tissue.^{xxvi}

It acts as an antioxidant which protects cells and DNA from free radical damage, caused by stress, damage, and chronic diseases.

The effect of vitamin C on the immune system is complex. It has antiviral properties that are particularly beneficial when fighting a viral infection. Vitamin C stimulates the production of interferons, which are signaling proteins produced by infected cells to alert neighboring cells, inducing enzymes that inhibit viral replication.^{xxvii} This is especially significant as it enhances the antiviral activity of lung epithelial cells.

It also plays role in curbing inflammation. It possesses antioxidant and anti-inflammatory effects thus preventing hyperactivation of immune cells and decreasing inflammatory markers. All of which lead to lowering the uncontrollable inflammatory cytokine production.^{xxviii} This is important in preventing ARDS.

It is found in fruits and vegetables such as citrus and peppers. Deficiencies, though rare, can lead to scurvy. Be aware that vitamin C is water-soluble, which means that it dissolves in water and is not stored in the body.

The recommended daily allowance (RDA) of vitamin C

- Men (19+ years) 90 mg for adult men a
- Women (19+ years): 75 mg
- Pregnant women: 85 mg
- Breastfeeding women: 120 mg
- Smokers need an extra 35 mg per day.

The RDA for children by age is:

- 1-3 years: 15 mg
- 4-8 years: 25 mg
- 9-13 years: 45 mg
- 14-18 years: 75 mg (boys), 65 mg (girls)^{xxix}

High-dose vitamin C supplementation can alleviate inflammatory response and hinder the aggravation of COVID-19.^{xxx} It is recommended that you take 1000 mg of Vitamin C every day while experiencing symptoms. Serious side effects from too much vitamin C are rare. However, amounts greater than 2,000 mg a day are not recommended. High doses can lead to stomach upset, diarrhea, and can even cause kidney stones.

Aspirin

Aspirin is acetylsalicylic acid. A pharmaceutical drug classified as a non-steroidal anti-inflammatory drug (NSAID). Some uses for aspirin are:

- Reduce fever
- Reduce inflammation
- Relieve mild to moderate pain from
 - Muscle aches
 - Toothaches
 - Common colds
 - headaches

Aspirin blocks an enzyme called cyclooxygenase. Cyclooxygenase produces hormones called prostanoids. In the blood, these prostanoids cause platelets to stick together. The role of platelets sticking together is to block cuts and breaks in blood vessels. By blocking the enzyme cyclooxygenase, it reduces the formation of blood clots.

The cascade of inflammatory mediators caused some people to develop blood clots with COVID-19. Because of this it is recommended to take 325 mg of aspirin everyday while experiencing symptoms to prevent blood clots.

Do not take aspirin if you experience the following:

- Allergy to ibuprofen
- Stomach ulcer
- Stroke victim (unless doctor recommended)
- High blood pressure
- Indigestion
- Asthma

- Gout
- Heavy periods
- Pregnant or trying to get pregnant
- Breastfeeding

In addition, do not give aspirin to children or teenagers without checking with your child’s doctor. It can cause a serious illness called Reye’s syndrome.

For further information on treating the sick including sore throat, cough, and fever, please refer to the “Caring for the Sick” PDF document, and “Caring for the Sick” PowerPoint presentations found at www.outrunningthehorses.com.

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