Coronavirus Clinical Considerations

We have already seen an increasing number of questions come in asking about Coronavirus disease 2019, now known as COVID-19, and we would like to offer our health care practitioner community a summary of the observed clinical course of COVID-19 and what evidence base we can find on coronaviruses.

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Additionally, we encourage all practitioners to be very careful in how they speak in marketing communications and communications to patients, and ensure that you also do not claim or imply that you have options to prevent, mitigate, or treat coronavirus-related illnesses.

Observed Clinical Course for COVID-19

The median age for those infected is around 50 years old, with a slightly higher incidence in men. Children appear less vulnerable to infection and appear to have milder symptoms than adults. There have been no reports of deaths in children aged 0-9 years of age. One very small study of 9 infants under 1 year of age infected with COVID-19 found that none of the infants experienced severe illness or complications[i]. Pregnant women do not appear to be at higher risk than the general population.

Most infected people appear to have mild infections, with mild cold-like symptoms and fever. There are even case reports of asymptomatic carriers. Most people who contract COVID-19 have symptoms including:

- Fever, muscle aches
- Uncomplicated upper respiratory symptoms (cough, sore throat, nasal congestion, headache)

Some patients will experience more severe symptoms, which may include:

- Difficulty breathing
- Mild pneumonia
- Severe pneumonia
- Acute Respiratory Distress Syndrome (ARDS)
- Sepsis and septic shock
- Death

Outside of Hubei Province, China, the fatality rate appears to be likely no more than 1-2%[ii]. To reframe that, 98-99% of individuals who contract this coronavirus will recover.

Research on Natural Agents and Other Coronaviruses

COVID-19 is a novel illness, and we do not have data showing any evidence of protection or treatment with any agent, and drug and vaccine testing are currently underway with existing and novel antiviral medications[iii]. There have been studies showing effects of specific agents with other coronaviruses, such as the SARS coronavirus in 2003. It is essential to note that these studies are primarily human cell lines or animal studies, not in vivo human clinical trials.

- Garlic (doses vary depending on preparation)
- Elderberry (doses vary depending on preparation)[iv]
    - Research is on Sambucus formosanaNakai, which is different than Sambucus nigra, which contains higher levels of caffeic acid, but Sambucus nigra has data showing activity with other viruses
- Lactoferrin, 300-500 mg 2-3 times daily
    - Tested against SARS-CoV virus and showed participation in host immune response to prevent invasion with the virus by enhancing NK cell activity and stimulating neutrophil aggregation and adhesion. In ex vivo studies, lactoferrin inhibited at the viral attachment stage, blocking the binding of the spike protein in a dose-dependent manner. Lactoferrin may bind to heparin sulfate proteoglycans and lock the preliminary attachment between the virus and host cells[v].
    - In addition to lactoferrin's role in viral attachment and immune response, it may also help ameliorate or balance resultant inflammation in the lung (and other tissues) after exposure to an infectious agent[vi].
- Resveratrol: 250 mg 3x daily
    - In a cell study, resveratrol significantly inhibited MERS-CoV infection and prolonged cell survival after MERS infection. Resveratrol also down-regulated apoptosis of affected cells induced by MERS-CoV in vitro[vii].
- Rhizome Rhei (Da Huang), Radix & Caulis Polygoni multiflori (He Shou Wu, which has resveratrol as a constituent). Doses vary based upon preparation
- Flavonoids have been shown to inhibit the proteolytic activity of SARS-CoV 3C-like protease in cell studies, including[viii].
    - Apigenin
    - Luteolin
    - Quercetin
    - Daidzein

Dr. Peter D'Adamo has been working to summarize these agents into an easy-to-digest resource which can be found here. Dr. D'Adamo has no affiliation with Emerson Ecologics, but has graciously granted permission for us to share this resource with integrative providers for their own reference and research

    - Epigallocatechin gallate (EGCG from green tea)
    - Kaempferol
- Red Marine Algae
    - Griffithsin, a lectin derived from red marine algae, binds to oligosaccharides on the surface of various viral glycoproteins, including the spike glycoprotein of the SARS-CoV. Binding to this glycoprotein may render the virus less virulent[ix].
- Chinese Skullcap (Biacalensis)
    - A study on human SARS strains in human lung cells detected activity of baicalin against the virus[x].
- Nettle (Urtica diotica)
    - When concentrated, lectins contained in nettle appeared to target early stages of the virus replication cycle and possibly also help neutralize the virus's infectivity by binding to the spike protein[xi].
- Licorice
    - In a 2003 study published in Lancet, glycyrrhizin was the most potent of 5 antiviral compounds tested in inhibiting replication of the SARS coronavirus[xii].
- Quercetin
    - Quercetin has been studied by a Canadian researcher, Michel Chretien, for its effect on coronaviruses. In late February 2020, the Chinese government partnered with his lab to conduct a human clinical trial on quercetin in Wuhan for treatment of COVID-19. No data as of yet, but preclinical data is promising enough to warrant a trial[xiii].
- Intravenous Vitamin C
    - According to Global Research, 3 clinical trials are currently underway studying IV Vitamin C for possible effect in patients with COVID-19. Doses range from 12,000 to 24,000 mg/day by IV. Oral vitamin C is not currently being studied, but the researchers have called for additional studies to see if oral dosing could be effective[xiv].
- Other herbs, including Cimicifuga rhizoma, Meliae cortex, Coptisid rhizoma, Sophora subprostrata and Phellodendron cortex were identified as potential candidates for drug development for SARS due to their ability to inhibit replication of a coronavirus (hepatitis virus A59) in a mouse model[xv].

General Immune Support

During the winter months, it is a great idea to focus on supporting the immune system. Some key considerations for general immune support include:

1. **Ensure adequate vitamin D levels.** A 2015 study in Thorax by Dancer et al. demonstrated that vitamin D deficiency contributed to development of acute respiratory distress syndrome (ARDS) and suggested that serum 25(OH)D levels <50 nmol/L may predispose to the condition. Additionally, in experimental animal models, vitamin D deficiency resulted in exaggerated alveolar inflammation, epithelial damage, and hypoxia[xvi], suggesting that vitamin D is important for optimum respiratory health.

Vitamin D doses of 1000-6000 IU (on a temporary basis) are recommended with serum monitoring to bring serum levels of 25(OH)D between 50-80 nmol/L.

2 **Selenium.** Has also been studied for immune support in response to RNA viruses (which coronavirus is a RNA virus). A state of selenium deficiency can lead to development and mutation of other RNA viruses like coxsackievirus and influenza into more pathogenic strains. Since selenium is important for the function of both the adaptive and innate immune response, adequate selenium is helpful to support immune function and the healthy response to exposure to viruses.

3 **Zinc.** Another mineral known to support immune function

4 **Multivitamins.** A good quality multivitamin is a good place to start to ensure adequate intake of nutrients.

5 **Probiotics.** Probiotics can support immune function and have been found in a Cochrane review to reduce incidence of Upper Respiratory Tract Infection (URTI)[xvii].

Respiratory Support

While we naturally turn to ingredients which may support immune function or target viral replication or infection of host, it's also essential to think about nutrients and botanicals which may support optimal respiratory function. Maintaining healthy respiratory tissues could help ensure that any clinical course affecting the lungs is as mild as possible. An article in Biomed Research International in 2018 summarized this clinical process and how agents may assist in mitigating the negative effects of inflammation on the respiratory tract[xviii].

Some considerations include:

- Andrographis paniculata[xix]
    - A review and meta-analysis on Andrographis showed has a statistically significant improvement in overall symptoms of ARTIs when compared to placebo and also suggested that Andrographis shortened the duration of cough, sore throat and sick leave/time to resolution when compared versus usual care.
- Flavonoids
    - Quercetin, rutin, 1000 mg daily
    - A Cochrane review of flavonoids found that flavonoid supplementation decreased upper respiratory tract infection (URTI) by 33% (95% CI, 31%, 36%) compared with control group with no apparent adverse effects. Sick day count was also decreased by 40%[xx].
- Probiotics
    - Probiotics can support immune function and have been found in a Cochrane review to reduce incidence of Upper Respiratory Tract Infection (URTI). This study showed that in probiotic users, fewer experienced an URTI, and the mean duration of symptoms was decreased[xxi].
- Inflammation-balancing herbs
    - Curcumin[xxii]

- While curcumin has not been studied in coronavirus models, studies have looked at the effect of curcumin on inflammation in the respiratory tract after influenza infection and found that curcumin (in human cell studies and animal models) influences the inflammatory responses of immune cells, especially macrophages. In one such study, curcumin inhibited the NF-kB signaling pathway and downregulated the production of the cytokine. Overactivity and overresponse of the immune system post-infection can lead to complications and increased morbidity and mortality, so consideration of inflammatory response in the respiratory tract may be an additional means to protect the host.

- Honokiol[xxiii]
  - In a mouse study, honokiol was shown to reduce the increased blood lipid peroxidation in mice during sepsis, reversed the inductions of nitric oxide synthase and NF-kB activation in the lungs of mice. It effectively rescued the lung edema, lung pathological changes, and lethality in septic mice. Other studies in animal and cell models have reported similar immune effects[xxiv] [xxv].

Top Resource

World Health Organization

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