I-CARE℠

RSV AND FLU TREATMENT

A guide to diagnosing and managing influenza and Respiratory Syncytial Virus (RSV) infections in adults

January 2023

Updates:

- Added Minocycline

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Disclaimer

The information in this document is our recommended approach to the treatment of Influenza and Respiratory Syncytial Virus (RSV) Infections in adults. Patients should always consult with their provider before starting any medical treatment, as this protocol may need to be personalized based on the patient's age, demographics, and co-morbidities. As this is a highly dynamic topic, we will update these guidelines as new information emerges. Please ensure you are using the latest version of this protocol.

Overview of I-CARE: Flu and RSV Treatment

In adult patients, COVID-19 (Omicron variant), influenza, and RSV present with similar symptoms and physical findings. It may therefore be difficult to distinguish between these infections (particularly COVID-19 and influenza) based on clinical presentation alone.

We would suggest this treatment protocol in those with diagnosed Respiratory Syncytial Virus (RSV); however, in low-risk patients with mild RSV, we would suggest omitting Nitazoxanide/Ivermectin. This protocol should also be used in patients with an undiagnosed flu-like illness, i.e., those who have not been tested or those whose tests are negative.

About Influenza

Influenza characteristically begins with the abrupt onset of fever, nonproductive cough, and myalgia. [1] Other symptoms include malaise, sore throat, nausea, nasal congestion, and headache. Gastrointestinal symptoms like vomiting and diarrhea are usually not part of influenza in adults.

Older adults (≥65 years) and immunosuppressed patients are more likely to have subtle signs and symptoms; they may present without fever and with milder systemic symptoms than other patients; however, older adults have a higher frequency of altered mental status. [1]

To test for influenza, conventional reverse transcription polymerase chain reaction (RT-PCR) assays are preferred, if available; these are the most sensitive and specific tests for diagnosis of influenza virus infection. An alternative diagnostic test for influenza is an antigen detection assay. These assays have low to moderate sensitivity but high specificity.

About Respiratory Syncytial Virus (RSV)

RSV is a negative sense RNA virus that is highly infectious, with an R0 of 8-15. Although virtually all individuals have been infected with RSV by two years old, previous infection with RSV does not appear to protect against reinfection, even in patients with high titers of specific antibodies. Cell-mediated immunity (CMI) may play an important role in eliminating the virus. [2]

RSV pathogenesis is associated with Th2 polarization of the immune response in the lungs. [3] A formaldehyde-inactivated RSV vaccine administered to toddlers in 1996 was associated with a

hospitalization rate of 80% following RSV infection, as compared to 5% in the controls. [3-6] An aberrant Th2-mediated immune response following vaccination was postulated to account for this outcome. [3;4] Furthermore, non-neutralizing antibodies against RSV in seronegative individuals may have primed the patients to develop this aberrant immune response. [3]

During the coronavirus disease 2019 (COVID-19) pandemic, mitigation measures (lockdowns, physical distancing, school closure) were associated with marked reductions in non-COVID-19 respiratory infections in children, including RSV. [7] 2022 has seen a dramatic increase in the number of patients hospitalized with RSV. This may be related to an increased attack rate following the lockdowns as well as a more robust Th2 response. Prior exposure to SARS-CoV-2 may be associated with a predominant Th2 response. [8;9]

The clinical manifestations of RSV vary with the patient's age, health status, and whether the infection is primary or secondary. [2] RSV is a significant cause of death in infants and young children. Healthy adults are infected with RSV repeatedly throughout their lives and typically have symptoms restricted to the upper respiratory tract. Signs include cough, coryza, rhinorrhea, and conjunctivitis. Compared with other respiratory viruses, RSV is more likely to cause sinus and ear involvement with less prominent fever. [2] RSV is an important and often unrecognized cause of lower respiratory tract infection in older adults and immunocompromised adults.

Diagnosis of RSV is based on a PCR test as well as rapid antigen tests. In adults, antigen tests have a high specificity however they are less sensitive than PCR-based assays.

Treatment of COVID-19, Influenza, and RSV

(in order of priority, not all required)

- **Nasal Spray/Irrigation**; 2-3 times a day.
  Influenza, SARS-CoV-2, and almost all respiratory viruses replicate primarily in the nasopharynx. A 1% povidone-iodine nasal spray and a nasal spray with Iota-Carrageenan are potent inhibitors of SARS-CoV-2 and influenza virus, and dramatically alter the course of infections with these viruses. [10-16] The spray should be administered 2-3 times per day. Nasal irrigations with saline as well as neutral electrolyzed water may also be of some benefit. [17;18]

- **Mouthwash**; 2-3 times a day.
  Antiseptic-antimicrobial mouthwashes have been shown in multiple research studies to inhibit the replication of multiple respiratory viruses, including SARS-COV-2, influenza, respiratory syncytial virus, etc. We suggest using a mouthwash/gargle in addition to a nasal spray. We recommend products containing chlorhexidine, povidone-iodine, cetylpyridinium chloride, or the combination of eucalyptus, menthol, and thymol (Listerine™). Gargle with these solutions 2-3 times a day.

- **Elderberry**; 4 times a day, according to manufacturers' dosing guidelines.
  Black elderberry (*Sambucus nigra*) has traditionally been used to treat cold and flu symptoms. Elderberries contain a great variety of flavones, isoflavones, flavanols, anthocyanins, phenolic acids, lectins, and many vitamins. The active chemicals include anthocyanins, primarily cyanidin 3-glucoside (C3G) and cyanidin 3-sambubioside, which have been shown to have antiviral, antibacterial, antidiabetic, antitumor, antioxidant, antidepressant, and immune-boosting properties. [19;20] Oral ingestion of elderberry results in detectable levels of these anthocyanins in blood plasma. The antiviral properties include activity against coronaviruses and influenza viruses. [19;20] The active compounds have been demonstrated to bind to H1N1 virions, blocking host cell entry and/or recognition. [21;22]

  In addition, elderberry cyanidin 3-sambubioside binds to influenza neuraminidase blocking the enzyme active site. [23] Torabian et al demonstrated that elderberry juice had both direct effects by blocking influenza viral glycoproteins as well as indirect effects by increased expression of IL-6, IL-8, and TNF. [24]

  Elderberries have been demonstrated to be highly effective and safe in the treatment of influenza. [22;25] A recent meta-analysis demonstrated that supplementation with elderberry was found to substantially reduce upper respiratory symptoms in patients with influenza. [26] In addition, elderberry supplementation has been demonstrated to reduce the duration and severity of symptoms in patients with the "common cold". [27] We, therefore, recommend the use of elderberry syrups or supplements in patients with viral upper respiratory tract infections. A triple combination containing elderberry, Vitamin C, and Zinc may be a convenient approach.

  Some authors have suggested that elderberries should be used with caution in patients with autoimmune diseases as well as in patients receiving immunosuppressive drugs, as this nutraceutical is believed to "activate the immune system". [28] However, the effects of the cyanidin-3-glucoside (the bioactive compound in elderberries) on the immune system are complex with anti-inflammatory, anti-allergic, and immunomodulatory properties. In a human intestinal cell line model, Serra et al demonstrated that cyanidin-3-glucoside (C3G) was effective in inhibiting the release of cytokine-induced proinflammatory mediators. [29] In a murine rheumatoid arthritis model C3G reduced the concentrations of the inflammatory cytokine IL-6 and IFN-γ and increased the levels of the anti-inflammatory cytokine IL-10 in the peripheral blood and synovial fluid. [30] Pyo et al demonstrated that C3G suppressed IL-4 and IL-13 produced by activated Th2 cells. [31]

  As discussed above, the preferential switching to a Th1 response may be particularly important in limiting the severity of RSV infection and elderberries may be a valuable treatment modality in patients with allergic diathesis.

While the data is somewhat contradictory, the preponderance of evidence suggests that elderberries have anti-inflammatory properties; this suggests that this nutraceutical is likely safe in patients with autoimmune disease when used for 2 weeks or less. However, such patients need to monitor their symptoms closely.

It should be noted that C3G interacts with the gut microbiome and the intestinal mucosal immune system to maintain gut health. [32]

Elderberries have not been reported to have drug-food interactions. [33] Elderberries do not contain phytochemicals known to increase the risk of miscarriage, cause birth defects, change hormonal function, or reduce breast milk supply. However, animal and human studies are lacking, and therefore there is insufficient data to recommend this nutraceutical during pregnancy or breastfeeding. [28]

Elderberry fruit extracts have most often been used by adults in doses up to 1200 mg a day orally for 2 weeks. Elderberry is available in many different types of products, including syrups, tablets, gummies, and mouth rinses. Elderberry supplements, gummies, and syrup may be obtained from your local pharmacy (e.g. NatureMade Elderberry with Vitamin C and Zinc) or from the following suppliers/manufacturers (https://thepowerofelderberries.com/, https://www.NorthernElderberry.com, https://www.puritan.com/, https://www.amazon.com/, https://gobblemountain.com/).

We recommend elderberries be taken four times a day as per the manufacturer's dosing guidelines.

Don’t consume green, unripe, uncooked elderberries. They contain toxins and can be poisonous.

- **Vitamin C**; 500-1000 mg, 4 times a day.
  Vitamin C has important anti-inflammatory, antioxidant, and immune-enhancing properties, including increased synthesis of type I interferons. [34-39] Vitamin C increases interferons and the innate antiviral response mediated by RIG-I-mediated signal transduction pathways. [40] The effects of Vitamin C on the course of upper respiratory tract infections have long been recognized. [41]

  We recommend a dose of 500-1000 mg taken four times a day. Oxidant injury plays a major role in the pathogenesis of RSV lung disease; [42] a combination of antioxidants including Vitamin C, NAC, and melatonin may therefore play a major role in ameliorating this disease.

- **Nitazoxanide**; 500 mg, 2 times a day.
  Nitazoxanide (NTZ) is an oral antiparasitic drug having activity against many protozoa and helminths and – like ivermectin – has been shown to have antiviral, anti-inflammatory, and immune-modulatory effects. [14;15] NTZ has broad-spectrum antiviral activity that includes

influenza virus, respiratory syncytial virus (RSV), and SARS-CoV-2 [15-18] Nitazoxanide appears to be highly effective against influenza. NTZ inhibits the replication of a broad range of influenza viruses, including neuraminidase inhibitor-resistant strains, blocking the maturation of viral hemagglutinin at the posttranslational level. [19]

The US Nitazoxanide Influenza Clinical Study Group randomized 622 patients for at least one respiratory symptom, and one constitutional symptom of influenza within 48 hours of symptom onset to receive either nitazoxanide 600 mg, nitazoxanide 300 mg, or placebo two times a day for 5 days. [20] The median duration of symptoms for participants receiving placebo was 116·7 h (95% CI 108·1–122·1) compared with 95·5 h (84·0–108·0; p=0·0084) for those receiving 600 mg nitazoxanide and 109·1 h (96·1–129·5, p=0·52) for those receiving 300 mg nitazoxanide (median difference of 21.2 hr for the 600 mg group). Adverse events were similar between the three groups. It is interesting to note that the duration of symptoms was significantly shorter in the NTZ group that was viral culture negative.

It should be noted that while NTZ is relatively cheap in most countries (approx. $0.31 per tablet), the main distributor in the United States (Alinia™) charges exorbitant prices (> $500 for 6 tablets). Therefore, we suggest tablets be ordered from a compounding pharmacy in the U.S. or a reliable pharmacy abroad.

- **Minocycline;** 200 mg loading dose, then 100 mg twice a day for 1 week
  Minocycline has anti-cancer, antioxidant, anti-inflammatory, and anti-apoptotic properties (prevents a type of cell death). In addition, in-vitro studies have demonstrated that minocycline has antiviral activity against influenza virus and RSV infection. [43;44]

- **Ivermectin**; 0.4 mg/kg per day for 5 days
  In-vitro (test tube) studies suggest that ivermectin has broad antiviral activity against RNA viruses including influenza virus. [45-47] It is likely that ivermectin has clinical efficacy in patients with influenza. However, there is no (published) clinical data on the use of ivermectin in the treatment of influenza. Therefore, we recommend ivermectin as part of a multi-drug regimen when nitazoxanide is not available. We suggest a dose of 0.4 mg kg per day for 5 days. Ivermectin is best taken with a meal. This drug should be avoided in pregnancy and in patients taking calcineurin inhibitors (cyclosporine and Prograf).

- **Zinc**; 50-90 mg per day.
  Zinc is essential for innate and adaptive immunity, with zinc deficiency being a major risk factor for influenza. [48-50] Due to competitive binding with the same gut transporter, *prolonged* high-dose zinc (> 50mg day) should be avoided, as this is associated with copper deficiency. [51]

  Commercial zinc supplements contain 7 to 80 mg of elemental zinc and are commonly formulated as zinc oxide or salts with acetate, gluconate, and sulfate. [48-50]

- **N-acetylcysteine (NAC)**; 600-1200 mg orally, 2 times a day
  NAC is the precursor of reduced glutathione. NAC penetrates cells where it is deacetylated to yield L-cysteine, thereby promoting glutathione (GSH) synthesis. [52] NAC has a broad range of antioxidant, anti-inflammatory, and immune-modulating mechanisms, and has demonstrated benefit in both experimental models and in patients with COVID-19, influenza, and RSV infections. [52-61] A dose of 600-1200 mg orally twice a day is suggested.

- **Sunlight and photobiomodulation (PBM)**; 30 minutes a day
  PBM is referred to in the literature as low-level light therapy, red light therapy, and near-infrared (NIR) light therapy. Our forefathers roamed the earth and were exposed to sunlight daily, likely with profoundly important health benefits. [62] The spectral radiance of solar radiation extends from 10 nm to about 3000 nm i.e., the spectrum from ultraviolet (10 -400 nm), visible (400-700 nm with red light 600-700 nm), near-infrared radiation (750-1500 nm (NIR-A)) and mid-infrared radiation (1500- 3000 nm (NIR-B)).

  Sunlight has great therapeutic powers. Indeed, during the 1918 influenza pandemic, "open-air treatment of influenza" appeared to be the most effective treatment for seriously ill patients reducing hospital mortality from 40% to about 10%. [63] The Surgeon-General of Massachusetts reported that "plenty of air and sunshine" was highly effective for the treatment of influenza pneumonia. He reported that "very little medicine was given after the value of plenty of air and sunshine had been demonstrated." Further, he commented: "from being discouraged, the medical staff became enthusiastic, and the patients were treated with the confidence that at last something had been found which would give good results."

  Apart from UV radiation stimulating Vitamin D synthesis, red and NIR-A radiation have a profound effect on human physiology, notably acting as a mitochondrial stimulant and increasing ATP production. [64] Furthermore, IR light profoundly modulates inflammatory pathways and inflammatory genes. [64;65]

  Based on this data, we suggest that patients expose themselves to about 30 mins of midday sunshine. When this is neither feasible nor practical, patients can expose themselves to red and NIR radiation emitted from LED panels or incandescent lamps.

- **Melatonin**; 5-10 mg nightly
  Melatonin is a potent antioxidant with important anti-inflammatory effects. We suggest a dose of 5-10 mg at night. [66-72] Slow- or extended-release preparations are preferred, as this minimizes the risk of bad dreams. If 10 mg is not well tolerated, cut the dose to 5 mg, and slowly increase as tolerated.

- **Symptomatic treatments**.
  In highly symptomatic patients, over-the-counter "flu" preparations with acetaminophen, antihistamines, and a decongestant are suggested**.**

- **Documented COVID-19 infection**. (See I-CARE: Early COVID Treatment Protocol for more information)
  In patients with proven COVID-19 infection (PCR or Antigen test positive), we would suggest the combination of ivermectin and hydroxychloroquine in place of nitazoxanide. However, as nitazoxanide has proven clinical efficacy in patients with COVID-19, this drug is a reasonable alternative to the combination of ivermectin and hydroxychloroquine. [73;74]

    a. **Ivermectin:** 0.4 to 0.6 mg/kg – one dose a day for at least 5 days or until symptoms resolve. If symptoms persist longer than 7 days, consult a healthcare provider.
    b. **Hydroxychloroquine (HCQ):** 200 mg twice a day for 5 to 10 days. Best taken with zinc. HCQ may be taken in place of, or together with, ivermectin. While ivermectin should be avoided in pregnancy, the FDA considers HCQ safe in pregnancy.
    c. **Home pulse oximeter.** Monitoring of oxygen saturation is recommended in symptomatic patients, due to asymptomatic hypoxia. Take multiple readings over the course of the day and regard any downward trend as ominous. Baseline or ambulatory desaturation under 94% should prompt consultation with a primary or telehealth provider, or evaluation in an emergency room.

Table 1. How to Calculate Ivermectin Dose

Note that Ivermectin is available in different tablet strengths (e.g., 3, 6 or 12 mg) and administration forms (tablets, drops) depending on the country (please refer to the package information). Tablets can be halved for more accurate dosing.

How much do I weigh?		What dose does the protocol say?			
In pounds	In kilos	0.2 mg/kg	0.3 mg/kg	0.4 mg/kg	0.6 mg/kg
70–90	32–41	6-8 mg	10-12 mg	13-16 mg	19-25 mg
91–110	41–50	8-10 mg	12-15 mg	17-20 mg	25-30 mg
111–130	50–59	10-12 mg	15-18 mg	20-24 mg	30-35 mg
131–150	60–68	12-14 mg	18-20 mg	24-27 mg	36-41 mg
151–170	69–77	14-15 mg	21-23 mg	27-31 mg	41-46 mg
171–190	78–86	16-17 mg	23-26 mg	31-35 mg	47-52 mg
191–210	87–95	17-19 mg	26-29 mg	35-38 mg	52-57 mg
211–230	96–105	19-21 mg	29-31 mg	38-42 mg	58-63 mg
231–250	105–114	21-23 mg	32-34 mg	42-45 mg	63-68 mg
251–270	114–123	23-25 mg	34-37 mg	46-49 mg	68-74 mg
271–290	123–132	25-26 mg	37-40 mg	49-53 mg	74-79 mg
291–310	132–141	26-28 mg	40-42 mg	53-56 mg	79-85 mg

Not recommended

- **Tamiflu**

  The Tamiflu saga summarized below highlights the fraud, deception, and abuse perpetrated by Big Pharma and the federal agencies (e.g., FDA) with which they conspire.

  Since the first pandemic scare of this century (H5N1 avian influenza in 2004), governments have been stockpiling the neuraminidase inhibitors zanamivir (Relenza) and especially oseltamivir (Tamiflu) in vast quantities. [75] The United Kingdom, United States, and many other countries hold enough stocks of these antivirals to offer courses of treatment to a quarter of their population. Most European states have oseltamivir as a core feature of their response, according to their published pandemic response plans.

  The recommendation to use oseltamivir was based on a 2003 pooled analysis by Laurent Kaiser and colleagues, which in turn was based on 10 randomized controlled trials, of which only two had been published. [76] Most of the data supporting oseltamivir's claim to reduce lower respiratory tract complications had never seen the light of day (another example of Big Pharma playing the fraudulent Disinformation Playbook). [77] The British Medical Journal and reviewers from Cochrane contacted the authors of the 2003 paper but were told the authors did not have the data on the missing eight studies. [75] The Cochrane team then went to the source, the manufacturer, Roche. The company refused to release the data unless the reviewers signed a confidentiality agreement with a secrecy clause. [75] The reviewers weren't prepared to do so, as it could stop them from reporting their findings. So began a campaign of public pressure that lasted four years.

  A freedom of information request shook loose 20,000 pages of incomplete oseltamivir data from the European Medicines Agency in 2011. Later in 2011, Roche finally relented and released 77 full clinical study reports of oseltamivir trials. Importantly, none of the trials was independent of the drug's manufacturer; in addition, all were against placebo rather than against standard drugs for relieving symptoms, such as acetaminophen. [78] Furthermore, many of the published studies were ghost-written, and in many instances, it was impossible to work out who actually carried out the research. [78;79]

  A Cochrane review in 2014 that used the newly released data found insufficient evidence to support claims that oseltamivir reduced lower respiratory tract complications or impeded viral transmission. [80;81] There was no significant reduction in the risk of pneumonia, bronchitis, otitis media, sinusitis, or any complication classified as serious and no reduction in the risk of hospitalization. The reviewers also raised new questions about the drug's harm profile, stating *"the use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children."*

  An additional analysis demonstrated that Oseltamivir had no protective effect on mortality among patients with 2009A/H1N1 influenza. [82] Furthermore, data suggest that Tamiflu

does not have antiviral properties but rather acts as an antipyretic (fever reducer). [75] As treatment with Tamiflu only suppresses symptoms, *"then infected people could be going to work and school feeling fine, while passing on the flu virus."* [75] Despite these data, pandemic stockpiles are still being scrupulously topped up and the "influenza pandemic" response plans of the UK and US have not changed in over a decade (another example of the Pharma-Government fraudulent collaboration). [75]

- **Antibiotics**

  Patients with upper respiratory tract infections should NOT empirically be treated with antibiotics unless they develop a documented complicating bacterial infection.

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