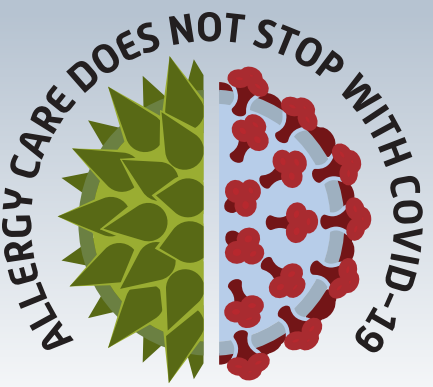


WORLD ALLERGY WEEK 2020
28 JUNE - 4 JULY

PHYSICIAN BRIEF

Authors: Motohiro Ebisawa, MD, PhD; Bryan Martin, DO; Sandra González Díaz, MD, PhD; Elham Hossny, MD, PhD; Michael Levin, MD, PhD; Mário Morais Almeida, MD; José Antonio Ortega Martell, MD; and Gary WK Wong, MD

Note: This document is a reference for physicians during World Allergy Week 2020. It is not medical advice. This information is current as of 19 June 2020. Stay updated, because experts are still learning about SARS-CoV-2 and COVID-19.

Definition of COVID-19

COVID-19 is short for "coronavirus disease 2019." According to the U.S. Centers for Disease Control and Prevention (CDC), it is a new respiratory disease spreading around the world, caused by infection with SARS-CoV-2, a new strain of coronavirus. Patients with symptoms are very contagious, but those who have mild manifestations can still infect others. There is no available vaccination against COVID-19, but researchers are currently working to develop a vaccine.[1]

SARS-CoV-2, which causes COVID-19, primarily spreads from person-to-person through respiratory droplets suspended in the air when an infected person coughs or sneezes. Because droplets usually fall within a few meters, the likelihood of transmission decreases if people remain at least two meters (six feet) apart. Transmission through the inhalation of aerosols (viruses suspended in air) is still under study. Diagnosis of COVID-19 is usually based on detection of SARS-CoV-2 by PCR testing of a nasopharyngeal swab or other specimen. Infection control and prevention efforts focus on personal protective equipment for health care workers, social distancing, testing, and contact tracing.[2]

Children are as likely as adults to become infected with SARS-CoV-2, but they are less likely to be symptomatic or develop severe symptoms. However, their ability to transmit infection even when asymptomatic remains an issue. On the other hand, the elderly and people of all ages with chronic conditions such as heart disease, lung disease, and diabetes, seem to be at higher risk of developing serious COVID-19.[3,4]

The pathology of severe cases of COVID-19 do indeed resemble certain immunopathologies seen in SARS-CoV-1 and MERS-CoV infections, such as CRS (cytokine release syndrome). However, in many other ways, immune responses to SARS-CoV-2 are distinct from those seen with other coronavirus infections. SARS-CoV-2 has a longer incubation period and higher rate of transmission than other coronaviruses but also speaks to significant differences in the host immune response, such as mechanisms for viral escape from innate sensing, hyper-inflammation associated with coagulopathy, and lymphopenia marked by T cell and NK cell dysfunction.[5]

COVID-19 and Bronchial Asthma

Viral infections, in general, are known to precipitate asthma exacerbations, and poor levels of asthma control make viral-induced exacerbation more severe.[6] There is some evidence that patients with asthma are overrepresented among the adult patients admitted to hospitals with COVID-19.[7] That is why asthma is listed as a risk factor for COVID-19 morbidity especially in the elderly.[8]

Good asthma control is mandatory during the COVID-19 pandemic. Adherence to the same asthma maintenance medications is recommended during the pandemic.[7,9] Since all methods of optimizing asthma control – whether they be inhaled steroids, combination inhaled steroid plus long acting bronchodilator therapies – have been shown to substantially reduce exacerbation risk. All standard asthma therapies should continue to be used to optimize asthma control, with certainty that this will reduce the risk of adverse outcomes with COVID-19.[8] It

is a recommendation supported by a recently published statement from the Section on Pediatrics of the European Academy of Allergy and Clinical Immunology (EAACI).[10] Proper treatment might prevent unnecessary visits to clinic, emergency department, or urgent care, and hence lower the risk of exposure to SARS-COV-2.

The Global Initiative for Asthma (GINA) recently stated that patients with asthma should not stop their prescribed inhaled corticosteroid controller medication (or prescribed oral corticosteroids). Stopping inhaled corticosteroids leads often to potentially dangerous worsening of asthma, and avoiding oral corticosteroids during severe asthma attacks may have serious consequences. Long-term oral corticosteroids may sometimes be required to treat severe asthma, and it may be dangerous to stop them suddenly.[11] Again, the British Thoracic Society does not recommend stopping oral steroids in the management of asthma or avoiding it for an acute asthma attack, even if it is due to COVID-19.[12]

Nebulization routinely for care of asthma exacerbations in offices or emergency rooms should be avoided, if possible, as it may generate aerosolization of SARS-CoV-2 leading to transmission of infection. Particularly in health care settings, metered-dose or dry powder inhalers are preferred over nebulizers, except in life-threatening asthma.[10-12;,14,15]

Thus, asthma and allergies should be treated according to the usual protocols. One exception to this is the advice to withhold biologics during acute COVID19 disease.[10] Non-infected allergic patients may be able to continue biologic therapy at home with prefilled syringes to avoid repeated contact in health care settings.[7]

Allergen Immunotherapy during the COVID-19 Pandemic

Although immunotherapy is not contra-indicated during the COVID-19 pandemic, the treatment must have safeguards in place to protect both patients and the health care team.

Little is known about the relation between COVID-19 and allergen specific immunotherapy (AIT). Data from patients infected with other viruses including influenza deny any adverse effect of AIT. In non-infected individuals or recovered patients after COVID-19 infection, interrupting subcutaneous (SCIT) or sublingual immunotherapy (SLIT) is not advised. SLIT can be taken at home, and preparedness of the allergy clinic is imperative to cope with COVID-19 in accordance with the World Health Organization (WHO) guidelines, and this mandates availability of appropriate personal protective equipment (PPE) for all personnel at the point-of-care. On the other hand, both subcutaneous and sublingual immunotherapy should be discontinued in symptomatic COVID-19 patients or those in contact with SARS-CoV-2 positive individuals (RT-PCR).[16]

The Impact of Smoking on COVID-19 Outcome

Chronic obstructive pulmonary disease (COPD) and ongoing smoking history attribute to the worse progression and outcome of COVID-19.[17] A review of studies by public health experts convened by the WHO on 29 April 2020 found that smokers are more likely to develop severe COVID-19 disease compared to non-smokers. Smoking impairs lung function, making it harder for the body to fight off coronaviruses and other diseases. Tobacco is also a major risk factor for non-communicable diseases like cardiovascular disease, cancer, respiratory disease, and diabetes, which put people with these conditions at higher risk for developing severe illness when infected by COVID-19.[18]

Allergic Rhinitis Management during COVID-19

COVID-19 expression or severity does not seem to increase significantly in other forms of allergy such as allergic rhinitis (AR), urticaria, and atopic dermatitis.[19,20] Allergists should be aware of the resemblance between AR and nasal symptoms of COVID-19 in order not to miss or over suspect cases.[10]

The use of inhaled and nasal steroids will not increase the susceptibility to COVID-19. A position statement of the Allergic Rhinitis and its Impact on Asthma (ARIA) and EAACI noted that patients with COVID-19 infection can continue intra-nasal corticosteroid therapy (including spray) for allergic rhinitis at the recommended dosage.

Oral steroids should be limited to emergency use only. Suppression of the immune system has not been proven with such therapy, and more sneezing after stopping may cause more spreading of the virus. These recommendations are conditional since there is a paucity of data, and they should be revised regularly with new knowledge.[21] Quantitative smell testing demonstrates that decreased smell function, but not always anosmia, is a major marker for SARS-CoV-2 infection.[22]

Even when wearing a mask during the COVID-19 pandemic, the eyes remain unprotected in patients suffering from allergic conjunctivitis. The results of a survey conducted by members of an EAACI Working Group on the management of ocular allergy during the COVID-19 pandemic showed agreement on using anti-allergic drugs as a first choice treatment, with the addition of topical corticosteroids as second-choice. The use of systemic immunosuppressants or topical calcineurin inhibitors was not a consensual decision.[23] Immunosuppression, even localized to the ocular surface through the topical use of cyclosporine and tacrolimus, has the potential to increase susceptibility, persistence, and reactivation of any viral infection. Although the presence of SARS-CoV-2 in tears has rarely been detected,[24] conjunctivitis may be a sign of COVID-19, prior to or after the onset of respiratory symptoms.[25]

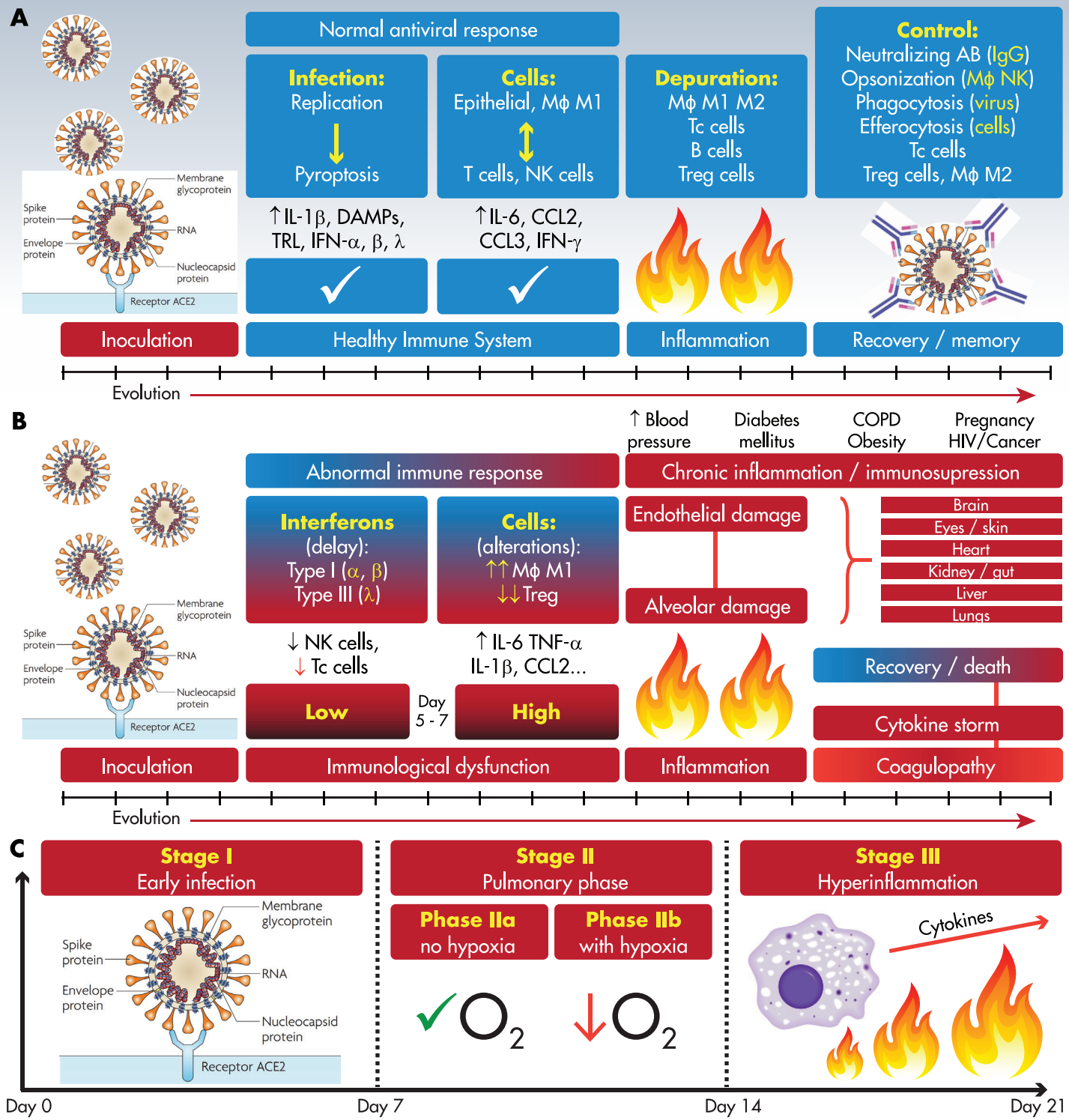
The Role of Telemedicine

During the ongoing pandemic while social distancing is being encouraged, most allergy/immunology care could be postponed/delayed, or handled through virtual care. With the exception of many primary immunodeficiency patients, patients on venom immunotherapy, and asthma patients of a certain severity, there is limited need for face-to-face visits under such conditions. These suggestions are intended to help provide a logical approach for quickly adjusting service to mitigate risk to both medical staff and patients. Importantly, individual community circumstances may be unique and require contextual consideration. The decision to enact any of these measures rests with the judgment of each clinician and individual healthcare system.[7] Routine spirometry testing should be suspended to reduce the risk of viral transmission, and if absolutely necessary, adequate infection control measures should be taken.[26]

Telemedicine (TM) can permit mildly ill patients to get the supportive care they need, without being exposed to severe cases.[27] Video-based communication can be used to assess and triage for COVID-19. The patient can interact with a provider who may obtain a history of symptoms and exposure risk and perform an observational assessment.[28] This may include temperature measurement with a home thermometer, and observing if the patient is appearing ill, exhibiting sweating, or being pale or flushed. The observer can even calculate the respiratory rate, detect the use of accessory muscles of respiration, labored breathing, or interrupted speech, and record the presence of cough whether dry or productive. The oropharynx can be observed for erythema, exudate, enlarged or absent tonsils, or presence of oral ulcers. Patient-directed palpation of the neck can be performed to assess for lymphadenopathy. Accordingly, the patient can be directed for laboratory testing or if found acutely ill, an emergency protocol may be conducted as well as transfer to the nearest treatment facility.[27]

Understanding the Immune Response Is Key to Understanding COVID-19 Outcome

The interaction between innate and adaptive immune responses has been found to be a potential cause for the clinical outcome in patients with COVID-19. The timely and well-controlled immune response may contribute to stop virus replication and minimize tissue damage caused by the inflammatory response. Conversely, the timing mismatch between the two immune responses has a major impact on disease progression with higher severity and mortality in COVID-19 patients. A delayed innate immune response followed by a premature excessive adaptive immune response causes depletion of vulnerable epithelial cells in the lungs and a cytokine release syndrome with hypercoagulability with more severe secondary complications.[29,30] (Figure 1)



Upper Airways	Lower airways	Systemic affection: lung, brain, heart, kidney, gut, liver, skin
Asymptomatic → anosmia, ageusia, fever, cough, headache	High fever, persistent cough, dyspnea PaO2/FiO2 ≤ 300mmHg	Coagulopathy, severe respiratory syndrome → organic failure
IFN-I (α,β), III (λ), NK cells	↑ MϕM1, ↑ Neu, ↓ Treg,	↑↑ IL-6, h↑↑ D-dimer, ↑ ferritin
Viral load: + → ++ → +++	Viral load: +++ → ++	Viral load: ++ → + → 0

Figure 1. COVID-19 Immunopathology and Progression. During the normal antiviral immune response to the SARS-CoV-2 infection (A), the healthy immune system responds timely with the production of type I and type III interferons, as well as pro-inflammatory cytokines and cytotoxic cells to reduce the viral load. An adequate control of the inflammatory response is normally achieved by different mechanisms in order to diminish the tissue damage. If there is an immunological dysfunction (B), the delay of the innate immune response produces an overreactive adaptive and inflammatory immune response. Several comorbidities like diabetes and obesity can predispose to this hyperinflammatory response with a cytokine release syndrome, coagulopathy, and the subsequent alveolar and endothelial systemic damage. The progression of the disease (C), is highly influenced by genetic unknown factors and the viral load of the exposure.[31,32]

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Controlling Allergies Could Help To Defend Better against the Virus

Current guidance from the WHO and GINA, highlights asthmatics as a high-risk group for severe illness from COVID-19.[33,34] Viruses are common triggers of asthma exacerbations and the current SARS-CoV-2 pandemic raises several questions regarding the optimum management strategies.

Allergic asthma exacerbation, a syndrome associated with augmented type 2 inflammation, is known to inhibit anti-viral immunity directly. Corticosteroids and several immunomodulatory allergy treatments, through their suppressive effects on type 2 inflammation, are thus likely to restore impaired anti-viral immunity in asthma as well as other allergic conditions and, in contrast to non-asthmatic subjects, have beneficial clinical effects in the context of SARS-CoV-2 infection.[35]

Find Reliable Sources of Clinical Information

With so much misinformation circulating on COVID-19, it is critical for physicians to get access to reliable sources and help to clarify facts from many myths about the disease. Here are a few resources. As more resources become available for World Allergy Week, find them on www.worldallergyweek.org.

World Health Organization:
https://www.who.int/emergencies/diseases/novel-coronavirus-2019

U.S. Centers for Disease Control and Prevention:
https://www.coronavirus.gov

U.S. National Institutes of Health:
https://www.nih.gov/coronavirus

American Academy of Allergy Asthma and Immunology (AAAAI):
https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Announcements/Transcript-7.pdf

https://education.aaaai.org/resources-for-a-i-clinicians/covid-19

American College of Allergy Asthma and Immunology:
https://education.acaai.org/coronavirus

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