

# Managing childhood allergies and immunodeficiencies and handling of immunotherapy in the COVID-19 pandemic



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## Introduction

- Currently, the world is faced with a major pandemic due to a novel coronavirus, SARS-CoV-2, leading to COVID-19 disease.<sup>1</sup>
- COVID-19 affects all age groups, adults as well as children.<sup>1</sup>
- Patients with pre-existing comorbidities may be particularly vulnerable.<sup>1</sup>
- This guidance outlines the European Academy of Allergy and Clinical Immunology (EAACI) recommendations for the management of children with allergies and immunodeficiencies and for patients on allergen-specific immunotherapy (AIT) during the COVID-19 pandemic.<sup>1,2</sup>
- With the increasing need to distinguish between COVID-19 and certain allergy-related symptoms, the guidance aims at supporting paediatric allergists and all physicians performing AIT in their current daily practice with clear recommendations on how to proceed with treatment during the pandemic and in SARS-CoV-2-infected patients.<sup>1,2</sup>

- The guidance is based on four statements released by:
  - » EAACI, ‘Managing childhood allergies and immunodeficiencies during respiratory virus epidemics—the 2020 COVID-19 pandemic’ (*Brough et al. 2020*)
  - » EACCI: ‘Handling of allergen immunotherapy in the COVID-19 pandemic: an ARIA-EAACI statement’ (*Klimek et al. 2020*)
  - » BSACI: ‘Modifications for paediatric allergy services during COVID-19 pandemic’ (*Fox A and Ball H 2020*)
  - » PTA: ‘The position of the expert group of the Polish Allergology Society on the management of patients with asthma and allergic diseases during the SARS-CoV-2 pandemic’ (*Kowalski et al. 2020*)

## What is coronavirus disease 2019 (COVID-19)?

- In March 2020 the World Health Organization (WHO) declared a worldwide pandemic of an infectious disease ‘coronavirus disease 2019’ (COVID-19).<sup>2</sup>
- COVID-19 is caused by a novel strain of human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>1,2</sup>
- Common signs of COVID-19 are respiratory problems, fever, cough, shortness of breath, and difficulties in breathing.<sup>2</sup>
- In severe cases infection with COVID-19 can cause pneumonia, severe acute respiratory syndrome, kidney failure, and death.<sup>2</sup>
- Because COVID-19 is caused by a newly identified viral strain, there are as of yet, no proven effective therapeutics or vaccines and no known pre-existing immunity in the population.<sup>2</sup>
- Coronaviruses are believed to be transmitted through contact with contaminated fomites (i.e., objects, materials, surfaces, etc.) and inhalation of large respiratory droplets generated by sneezing or coughing.<sup>2</sup>

## COVID-19—what is different in children?<sup>1</sup>

- Compared with adults, children affected by COVID-19 are often less likely to present with symptoms, and when they do, these symptoms are less likely to be severe.
- Reliable data from more than 72,000 case reports reviewed by the Chinese Centre for Disease Control showed that fewer than 1% of cases were aged under 10 years.
- The most common clinical signs included cough and pharyngeal erythema; fever was observed in 41.5% of cases and 64.9% were diagnosed with pneumonia. Asthma and allergies were not mentioned in this case series.
- Another study in 2,143 Chinese children reported that 94 patients (4.4%) were asymptomatic, 1,091 (50.9%) had mild disease, 831 (38.8%) had moderate disease, whereas 125 (5.8%) were severe/critical cases.
- In the USA among 149,082 laboratory-confirmed COVID-19 cases, only 2,572 (1.7%) were children aged under 18 years. Of the 345 paediatric cases with information on underlying conditions, 80 children (23%) had at least one underlying condition including asthma.
- The reason for the relatively milder presentation in children is unknown. Several hypotheses have been posited including host factors such as immature expression of the receptor for coronaviruses (e.g., ACE-2) and direct competition from presence of other viruses in the respiratory tract mucosa. Unlike adults, children with COVID-19 infection may not mount a generalised ‘cytokine storm’ leading to respiratory distress syndrome and multi-organ failure. Children also have fewer chronic comorbidities.
- It is important to note that although children have less severe COVID-19 disease, they are still able to pass on the virus even while asymptomatic.

## Children with asthma and allergic diseases<sup>1</sup>

- The US Centres for Disease Control and Prevention (CDC) states that people of all ages with chronic lung disease including moderate-to-severe asthma are at high risk of COVID-19. However, pre-existing allergies have not been classified as a risk factor.
- In children with asthma, regular use of inhaled corticosteroids (ICS) may not increase the risk of pneumonia or other respiratory infections.
- Other commonly prescribed allergy medicines such as antihistamines, bronchodilators, and leukotriene receptor antagonists should not be considered as increasing the risk of COVID-19.
- EAACI expert opinion states that biologics may be continued in healthy patients during the COVID-19 pandemic. Nonetheless, biologics should be paused until recovery in SARS-CoV-2-positive patients.

## Patients with immunodeficiencies

- Patients with immunodeficiencies should be carefully followed during COVID-19.<sup>1,2</sup>
- In paediatric patients with secondary immunodeficiencies such as those receiving immunosuppressant drugs for autoimmune or severe allergic diseases it is recommended to continue treatment.<sup>1</sup>
- Precautionary recommendations for patients with immunodeficiencies follow national guidelines for the general population and include strict hygiene and social distancing measures to limit exposure.<sup>1</sup>

## Prevention and control of COVID-19 in allergic patients receiving allergen-specific immunotherapy (AIT)<sup>2</sup>

- EAACI recommends using the infection prevention and control measures in any patient receiving AIT according to European Centre for Disease Prevention and Control (ECDC) and WHO.
- This implies following recommended prevention and control measures for individual countries or regions.
- Allergy services and all primary care staff should be aware of the following:
  - » the current COVID-19 epidemiologic situation in their country and globally
  - » known risk factors for infections
  - » clinical symptoms and signs of COVID-19
  - » recommended infection and control measures in their country or region
  - » procedures for reporting and transfer of persons under investigation and probable/confirmed cases.
- Appropriate personal protective equipment (PPE) should be available onsite for all personnel.
- At each facility a dedicated member of staff (e.g., head doctor/nurse) should lead the COVID-19 preparedness and control measure policies.
- Signs should be posted at all entrance doors listing the main COVID-19 symptoms and informing persons with any of these symptoms not to enter the clinic. Everyone within the clinic should adopt appropriate hand hygiene measures, using soap and water or an alcohol-based hand rub.
- Based on a case-by-case risk assessment, the use of PPE for AIT should be considered.
- The suggested set of PPE for droplet, contact, and airborne transmission (gloves, goggles, gown, and FFP2/FFP3 respirator) can be adapted for the clinical assessment of suspected COVID-19 cases. If available, provide a surgical mask for patients with respiratory symptoms.

## Managing AIT during the COVID-19 pandemic<sup>2</sup>

- Most AIT products (SCIT or SLIT) authorised for use in Europe recommend that patients experiencing an acute respiratory tract infection should temporarily discontinue AIT until the infection is resolved.
- EAACI recommends taking similar action in COVID-19.
- Confirmed cases should discontinue AIT (SCIT or SLIT) independent of disease severity until symptoms have completely resolved and/or an adequate quarantine has been performed.
- Patients who recover from COVID-19 or have a sufficient SARS-CoV-2 antibody response after asymptomatic disease can be started or continued as planned.
- The possibility of expanding injection intervals in the continuation phase may be beneficial.

## Allergen sensitisation testing during the COVID-19 pandemic

- Allergen-specific IgE testing is the only test approved to be used for allergy diagnosis during the COVID-19 pandemic.<sup>3</sup>
- Skin prick testing and other tests should be replaced with IgE testing in order to maintain social distancing.<sup>3,4</sup>

- Children with newly diagnosed or recurrent idiopathic anaphylaxis should be prioritised with laboratory and allergy-specific IgE testing as appropriate.<sup>3</sup>
- Diagnosis of allergic rhinitis should be conducted via allergen-specific IgE tests.<sup>3</sup>
- Patients should be advised on symptom management via the telephone, if telemedicine is supported by the clinic.<sup>3</sup>

## Recommendations for the management of paediatric patients with allergies and immunodeficiencies during the COVID-19 pandemic<sup>1</sup>

<b>Fact 1.</b> Children are at lower risk of COVID-19 infection and have a less severe course of the disease.	<b>Recommendation 1.</b> Paediatric allergists should seek to gain the best control of current allergic symptoms and instruct patients on current recommendations for hygiene and social distancing to reduce the risk of infection.
<b>Fact 2.</b> Whenever possible, diminish or remove risk factors.	<b>Recommendation 2.</b> Uncontrolled asthma is a risk factor. Paediatric allergists should aim for optimal asthma control with appropriate medications.
<b>Fact 3.</b> Initial symptoms of seasonal allergy might be misleading as suggestive of COVID-19.	<b>Recommendation 3.</b> Paediatric allergists must not be over-suspicious of, and yet should not miss, COVID-19 in allergic patients.
<b>Fact 4.</b> Treat your allergic patients according to usual guidelines	<b>Recommendation 4.</b> Paediatric allergists should treat patients with allergic asthma, allergic rhinitis, or other allergy conditions according to usual guidelines, without restricting the use of any specific medication. One exception to this is the advice to withhold biologics during acute COVID-19 disease
<b>Fact 5.</b> Current knowledge may evolve and guidelines may change.	<b>Recommendation 5.</b> Allergists should be flexible to revisions of current recommendations
<b>Fact 6.</b> Patients with immunodeficiency have increased risk for infections with respiratory viruses.	<b>Recommendation 6.</b> To avoid disease exacerbations, patients should stay on their regular medication for their underlying disease. Patients with suspected COVID-19 infection should remain in close contact with their attending physician even during reduced staffing (e.g., via telemedicine) and resolve any clinical symptoms immediately.

## Allergen immunotherapy (AIT): recommendations in non-infected individuals during the COVID-19 pandemic or recovered patients after infection<sup>2</sup>

- Interrupting subcutaneous immunotherapy is not advised.
- Interrupting sublingual immunotherapy is not advised.
- Sublingual immunotherapy may be taken at home.
- Both subcutaneous and sublingual immunotherapy can be continued in non-infected individuals in the current COVID-19 pandemic.
- Preparedness of your allergy clinic is imperative to cope with COVID-19.
- These recommendations are conditional since there is a paucity of data and they should be revised regularly with incoming new information on COVID-19.

## Allergen immunotherapy: recommendations in COVID-19 diagnosed cases or suspected for SARS-CoV-2 infection<sup>2</sup>

- Interrupting subcutaneous immunotherapy is advised.
- Interrupting sublingual immunotherapy is advised.
- Both subcutaneous and sublingual immunotherapy should be discontinued in symptomatic patients with exposure or contact to SARS-CoV-2-positive individuals, or patients with positive test results (RT-PCR).

## References

1. Brough HA, Kalayci O, Sediva A et al. Managing childhood allergies and immunodeficiencies during respiratory virus epidemics - the 2020 COVID-19 pandemic. *Pediatr Allergy Immunol*. 2020. doi: 10.1111/pai.13262.
2. Klimek L, Jutel M, Akdis C et al. Handling of allergen immunotherapy in the COVID-19 pandemic: An ARIA-EAACI statement. *Allergy*. 2020. doi: 10.1111/all.14336.
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4. Kowalski ML, Bartuzi Z, Bręborowicz A. The position of the expert group of the Polish Allergy Society on the management of patients with asthma and allergic diseases during the SARS-CoV-2 pandemic'. 2020. <https://www.pta.med.pl/wp-content/uploads/PTA-COVID19-Stanowisko-31.03.2020.pdf>

