

Position statement of expert panel of the Polish Allergology Society (PTA) on the management of patients with bronchial asthma and allergic diseases during the SARS-CoV-2 pandemic

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A. Introduction

The dynamically changing epidemiological situation related to SARS-CoV-2 infection poses challenges also for allergists. Both allergic diseases affecting many organs, especially the respiratory system, and the procedures used by allergists give rise a number of questions about the proper procedures during the pandemic. This position statement aims to provide allergists with recommendations on the proper management of allergic patients in the current epidemiological situation. One should be aware of the limited amount of documented information on the COVID-19 disease itself, as well as the association of allergic diseases with the same. Therefore, we would like to point out that in individual situations the final decision on the procedure is to be made by a doctor who has direct and full knowledge of the patient's condition and expectations, as well as viable options available. Both the limited amount of data on the association between COVID-19 and allergies, and the fact that only few organizations of allergists have developed current guidelines of conduct so far, have made it necessary for us to reach a consensus on the recommendations among Polish experts.¹

B. General recommendations for dealing with the SARS-CoV-2 pandemic

Asthma and allergy patients should follow general principles of prevention, which can reduce the risk of infection. It is particularly reasonable to limit social contacts, maintain appropriate physical distance from other people and systematically wash one's hands. (Recommendations for allergists attending patients during the SARS-CoV-2 pandemic are presented in the final chapter.)

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c. Susceptibility of patients with bronchial asthma and allergies to SARS-CoV-2 infection

Asthma patients show a reduced local immune response, with lower production of type I and III interferons in response to rhinovirus and paramyxovirus infections associated with common cold^{2,3}, although this has not been confirmed by all studies^{4,5}. Respiratory viral infections in asthmatic patients are more frequent and cause serious exacerbations. Coronaviruses (mild strains) are found relatively often during exacerbations of bronchial asthma; one of the meta-analyses have shown that they are present on average in 8.4% of exacerbations⁶.

There is no data indicating a higher susceptibility of asthma patients to coronavirus infections or a more severe course of viral disease. Reports from China and South Korea do not indicate asthma as a risk factor for SARS-CoV-2 infection – the proportion of asthmatic patients among SARS-CoV-2 infected individuals and the severity of the infection are similar to the general population^{7,8,9}. Thus, while heart disease and metabolic diseases are often found among coronavirus-infected patients, asthma, COPD and bronchiectasis are even less frequent¹⁰. However, it shall be noted that most of these data comes from Asian countries (China, South Korea) and the data on the European population is very scarce today. The differences in COVID-19 mortality rates between Asian and European patients observed after just a few weeks of the pandemic may indicate that these populations are not only culturally and socially distinct, but may also differ in terms of genetically determined sensitivity to the severity of the disease. Due to the low prevalence of SARS-CoV-2 infection in children, there is no data on this age group as yet.

It is not known if the SARS-CoV-2 causes exacerbation in asthmatic patients, and if so, what is the course of the disease. Given that coronaviruses of other strains are detected in the airways in patients with asthma exacerbations, it cannot be ruled out that SARS-CoV-2 may also cause asthma exacerbations.

In patients with **allergic rhinitis (AR)**, a different immune response to rhinoviruses and paramyxoviruses is found in the airway epithelium¹¹. However, at present it cannot be determined whether patients with AR are more likely to be infected with the SARS-COV-2 coronavirus compared to the general population. However, the probability of infection among patients with AR may be higher in case of suboptimal treatment or discontinuation of treatment which may lead to increased itching of the eyes and nose, sneezing and nasal discharge. All these symptoms naturally force patients to have much more frequent contact of their hands with their eyes and nose, both on a reflex and conscious basis. As a result, patients with AR should, be encouraged to maintain treatment that provides full control of their symptoms and should strictly comply with the sanitary regime.

There is no data on the SARS-CoV-2's association with or effect on other allergic diseases: allergic skin diseases, food, drug or Hymenoptera venom allergies.

Continuation of the existing treatment as the basic principle for allergic patients' management during COVID-19 pandemic.

Treatment of bronchial asthma

Inhaled corticosteroids (ICS) are the most effective controllers in chronic bronchial asthma and during the SARS-CoV-2 epidemic they should be used in both non-infected and infected asthmatic patients in line with the accepted standards¹². There is no indication that inhaled corticosteroids may increase susceptibility to coronavirus infections or affect their course in infected individuals. On the contrary, experience with respiratory tract infections caused by other viruses shows that good asthma control associated with effective treatment with inhaled corticosteroids reduces the risk of exacerbations that are mostly associated with viral infections. Reduction or withdrawal of ICS may therefore result in loss of asthma control and potentially increased susceptibility to SARS-CoV-2 infection. Moreover, the loss of control may result in the patient's need to visit a hospital emergency ward or be hospitalised, which may further increase the risk of infection. Optimal treatment of asthma is crucial not only for the patient themselves, but also for their the immediate vicinity. Insufficient asthma control may manifest itself i.a. in more frequent coughing attacks, which, even with the asymptomatic course of COVID-19 disease in a patient with asthma, may significantly increase the risk of transmission of the infection to people in the immediate vicinity.

- 1) ****It is recommended to continue anti-inflammatory treatment with inhaled corticosteroids in asthmatic patients during the SARS-CoV-2 epidemic.**
- 2) ****ICS should be administered via metered dose or dry powder inhalers.**
- 3) ****The use of nebulisers is discouraged as it may cause increased aerosolization of virus particles in the ambient air and promote the spread of infection.**

Systemic corticosteroids (SCS) are used chronically in about 5% of patients with severe bronchial asthma, but emergency oral corticosteroid bursts are often administered during disease exacerbation. In asthma patients with chronic oral corticosteroids there is no justification for interruption or reduction of doses due to threatening or present COVID-19 disease. Discontinuation of oral corticosteroid therapy in these patients could result in exacerbation of the underlying disease; in addition, it can lead to the development of acute adrenal insufficiency, which could cause increased susceptibility to viral infections.

******It is justified to continue treatment with oral corticosteroids in patients taking these drugs on a chronic basis.**

For the time being, however, it is not possible to present an unequivocal opinion on the administration of SCS during asthma exacerbation in a COVID-19 patient. Although the World Health Organization (WHO) and the US Centre for Disease Control and Prevention (CDC) recommend avoiding oral corticosteroids in patients with COVID-19^{13, 14}, there are also reports indicating the beneficial effects of SCS on the course of SARS-CoV-2 infection in hospitalised patients⁽¹⁵⁾. Therefore, it can be assumed that in asthma patients without symptoms and

without a confirmed SARS-CoV-2 infection, treatment with oral corticosteroids is acceptable during the exacerbation of the disease. In asthmatic patients with SARS-CoV-2 infection, the decision remains in the hands of the attending physician.

There is no data indicating that the use of other anti-asthmatic drugs (short- and long-acting beta2 adrenergic agonists or antileukotriene medications) is relevant for the course of COVID-19 disease.

Biologic therapy in the management of asthma

Anti-IgE antibodies and IL-5 neutralising agents, which are currently available under the programmes of the National Healthcare Fund, help to achieve and maintain disease control in patients with severe bronchial asthma. There is no data indicating possible immunosuppressive effects of anti-IgE and anti-IL-5, which could affect susceptibility to SARS-CoV-2 infection or the course of the COVID-19 disease. According to the recommendation of the Ministry of Health, biologicals, in the absence of alternative methods of treatment, should be administered according to the existing rules.^{16,17}

4) **It is recommended to continue biologic therapy with anti-IgE or anti-IL-5 in patients with severe asthma.**

5) **It is acceptable to start and then continue biologic therapy with anti-IgE or anti-IL-5 antibodies in patients with severe bronchial asthma in accordance with the current Biological Treatment Programme of the National Health Fund.**

However, it may be justified to limit additional testing (e.g. spirometry) as requested by the drug programme – this requires the approval of the National Health Fund (NFZ).

Allergic rhinitis

It should be noted that the symptoms of conjunctivitis – often accompanying the symptoms of allergic rhinitis (AR) – may occur in the early stages of coronavirus infection. The primary treatment of AR includes antihistamines and intranasal corticosteroids.¹⁸ There is no data that would justify limiting the use of antihistamines or local corticosteroids in patients with AR.

6) **In patients with AR, the existing therapy should be continued and adequate treatment, including local corticosteroids, should be implemented in patients with expected seasonal symptoms.¹⁹**

Allergic skin diseases

There is no evidence of a direct link between the presence of allergic skin diseases (atopic dermatitis, chronic urticaria, angioedema) and susceptibility to SARS-CoV-2 infection or the course of the COVID-19 disease. However, it cannot be ruled out that chronic stress associated with allergic skin diseases, which has an adverse effect on immune system function, may result in such susceptibility (limitations on the use of diagnostic procedures in these diseases during the pandemic are discussed below).

Frequent washing of hands and the use of antibacterial and disinfectant preparations recommended during the pandemic increase the likelihood of weakening the natural skin barrier. It is therefore necessary to protect the skin from drying out and damaging the integrity of the epidermal barrier by using appropriate emollients.

******8) After application of disinfectants, especially in patients with allergic skin diseases, the epidermal barrier shall be protected by the use of adequate emollients, including barrier creams and medicinal creams.**

During the pandemic, patients with symptoms of severe chronic spontaneous urticaria, in whom the four-fold dose of modern antihistamine is ineffective, may still be eligible for biologic therapy with omalizumab, according to the current drug programme of the National Health Fund.

******9) Continuation and, in specific cases, initiation of biologic therapy with anti-IgE antibodies (omalizumab) in patients with severe chronic urticaria is acceptable.**

In the current epidemiological situation, the initiation of urticaria treatment with immunosuppressants (e.g. cyclosporine) is not recommended due to the possibility of increasing susceptibility to viral infections. If treatment with cyclosporine has already been taken, reduction to a one-half of the usual dose should be considered.

Other allergic diseases

Food and drug allergies are not directly related to COVID-19 (limitations on the use of diagnostic procedures are discussed below).

D. Allergen immunotherapy

Allergen immunotherapy (AIT) is used in the treatment of seasonal and perennial inhaled allergies and in Hymenoptera venom allergy. There is no data indicating possible adverse effects of AIT on susceptibility to or on the course of the COVID-19 disease.

Continuation of AIT

In patients with inhaled allergy, the continuation of AIT in line with the principles followed to-date (minimum 3 years) is crucial for maintaining control of the disease and ensuring the effectiveness of this procedure, carried out with great effort by the patient and the doctor. Justification for termination or suspending the AIT before the lapse of 3 years may be justified due to epidemiological (fear of infection during the visits) or organisational (e.g. problems with availability of the allergist's office) considerations. If immunotherapy is suspended, the patient should be informed in detail about the principles and schedule for AIT continuation after the stabilisation of the epidemiological situation.

******10) In patients with inhalant allergy undergoing subcutaneous immunotherapy it is justified to continue AIT for at least 3 years.**

******11) Taking into account the epidemiological and organisational aspects, the doctor, in agreement with the patient, may consider a temporary suspension of the AIT with a view to its resumption under conditions of full safety.**

A possible alternative treatment for inhaled allergies is to offer patients sublingual immunotherapy. It should be stressed that the final decision in an individual case is made by the doctor in consultation with the patient.

In the case of Hymenoptera venom allergy, continuation of venom immunotherapy (VIT) is critical to ensure the safety of the patient – it is a life-saving procedure. This justifies the continuation of VIT for 5 years, or for an unlimited period of time in patients with risk factors for failure of immunotherapy, or for 3 years in the remaining group of VIT-qualified patients.

12) **It is recommended to continue the AIT with insect venom allergens in accordance with current principles for 3 years or more, depending on the presence of risk factors for the failure of immunotherapy.**

Due to the necessity to reduce social contact during the epidemic, it is justified to extend the interval between injections to the maximum period acceptable for a given vaccine: up to 4-6 weeks in the first year of vaccination and to 8 weeks in subsequent years of vaccination. In cases where it is necessary to suspend immunotherapy for epidemiological and organisational reasons, the patient should be informed in detail about the potential risks and benefits of such a decision as well as the principles and schedule for its continuation after the change in the epidemiological situation.

Initiation of AIT

13) ** It is not recommended to start subcutaneous AIT with inhalant allergens during the pandemic .**

14) ** It is possible to undertake the ultra-rush immunotherapy for Hymenoptera venom allergy in patients with absolute indications for such treatment during the pandemic .**

E. Implementation of other allergological procedures during the COVID-19 pandemic

In order to reduce the risk of SARS-CoV-2 infection associated with a patient's visit and stay in a medical unit during the pandemic, only the necessary diagnostic procedures that have a direct impact on the medical procedure should be pursued. It is up to the allergist to assess the necessity of such tests.

15) **It is recommended to limit, during the pandemic, the following allergological procedures to exceptional situations:**

Skin prick tests (SPT)

Intradermal testing (IDT)

Patch tests with contact allergens

Spirometry

PEF measurement in the office

FeNo (exhaled nitric oxide test)

Test of non-specific bronchial hyperreactivity

(Bronchial and nasal) provocation testing with inhaled allergens

Provocation testing with food allergens

Provocation testing with drugs

16) **When indications for the diagnostics of IgE-dependent sensitisation occur, the use of *in vitro* tests for detecting the presence of specific IgE (sIgE) antibodies is recommended instead of SPT.**

17) **Provocation testing with drugs and tolerance tests for alternative drugs (antibiotics, NSAIDs, perioperative and topical anaesthetics) are acceptable in justified cases.**

18) **Drug desensitisation procedures may be performed when indications are present (e.g. for aspirin in coronary artery disease or antineoplastic drugs).**

Principles of allergology clinic activity during the SARS-CoV-2 pandemic

1. Since allergic diseases have chronic course and most patients have their treatment plans at home, allergists should limit the number of office visits to the necessary minimum.
2. In most cases, consultation may/should be given to patients by phone or electronic means of communication (Skype, e-mail) – this form has a full formal justification from the National Health Fund and is accounted for as a traditional visit to the clinic.
3. If a visit at an allergist's office is still necessary, patients should be admitted in dedicated rooms, so as to shorten their route to the place of provision of service as much as possible and to ensure an adequate distance between those waiting for a visit (according to the recommendations of the Ministry of Health).
4. The safety of patients, their appointed legal representatives and medical staff should be ensured if a visit is necessary.
5. An allergist should use personal protective equipment (gloves, masks, aprons) according to the current guidelines of the Ministry of Health.

6. Asthmatic patients who do not have a treatment plan for the exacerbation of the disease should be provided with one via Internet or telephone (SMS).
7. Patients with seasonal allergies should be informed about the upcoming pollen season and recommended to start treatment before the expected season. It may be important to make local pollen calendars available.

In view of the rapidly changing epidemiological situation, the recommendations set out in this position statement will be updated as new information becomes available.

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