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Allergy and Immunotherapy During the Pandemic

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Abstract

Purpose of Review To summarize and review recent literature on the role of allergen immunotherapy in the setting of a worldwide pandemic.

Recent Findings At the start of the SARS-CoV-2 pandemic, most elective ambulatory patient care services, including allergen immunotherapy, were suspended. Now with medical practices reopening, allergists must establish plans and protocols for resuming care of allergy patients, including strategies for restarting allergen immunotherapy. While there are no published evidence-based protocols for resuming allergen immunotherapy, limited scientific data and expert opinion suggest that the major factor in dose adjustment is the time elapsed from the last dose.

Summary Resuming outpatient allergy services in the setting of the COVID-19 pandemic poses many challenges to the practitioner. Allergy specialists are now faced with developing prudent and evidence-based strategies for safely resuming allergen immunotherapy, while also maintaining a safe environment for staff and patients.

Keywords Immunotherapy · COVID-19 · SARS-CoV-2

Introduction

Since the first reports of infected patients and clustered disease outbreaks of SARS-CoV-2 in China in 2019, the coronavirus disease has evolved into a worldwide pandemic. On March 11, 2020, the World Health Organization (WHO) declared the "coronavirus disease 2019 (COVID-19)" a global pandemic [1]. With countries struggling to contain the spread of disease, many municipalities imposed "stay at home" orders. These enforced social distancing and quarantine measures generated an inherent disruption to traditional healthcare delivery across all specialties, including allergy, as most elective and ambulatory patient care was suspended. As the pandemic persisted, and now over 2 years into our new COVID-19 era, healthcare providers have been forced to adapt new approaches to patient care. Allergists have been faced with establishing new protocols and planning resumption of clinical care in a changed healthcare landscape.

General Considerations

SARS-CoV-2 has a varied clinical presentation, ranging from asymptomatic spread to a severe acute respiratory syndrome and fatality. Despite the availability of a vaccine for COVID-19, new variants of the virus have emerged, characterized by enhanced transmissibility and increased risk of severe disease. The continued evolution of viral variants has led many scientists and clinicians alike to consider the fact that COVID-19 may become endemic, highlighting the importance of establishing practical clinical protocols for the management of allergy patients, even in the setting of highly transmissible respiratory illness.

The clinical presentation of COVID-19 has significant overlap with many of the symptoms which prompt patients to visit an allergy specialist. Symptoms of COVID-19 include but are not limited to fever, cough, sore throat, smell and taste dysfunction, headache, body aches, weakness, nasal congestion, and shortness of breath [2••]. Less likely are gastrointestinal symptoms such as nausea, vomiting, and diarrhea. One caveat facing the allergy practitioner

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is that many of the symptoms of asthma or allergic rhinitis which may prompt a patient to seek consultation with an allergy provider may mirror the symptomatology of COVID-19. This can pose a challenge in the pre-visit screening of patients, and appropriate pre-visit COVID-19 testing per national and local public health protocols may be advisable. Additionally a telehealth visit can also be an excellent tool to allow for patient assessment and planning of care prior to face-to-face visits [3].

Prevention and Control in the Office

All physicians, including allergists, are posed with the challenge of caring for patients while still ensuring protection for themselves, their office staff, and other patients in the office. The strategies one employs to mitigate risk of COVID-19 spread in the medical setting remain in evolution as the pandemic has grown more chronic, but certain measures have been consistently shown to provide benefit. A majority of COVID-19 is spread person-to-person via respiratory droplets, produced by talking, coughing, and sneezing. Ways to help reduce community spread include maintenance of social distance (approximately 6 feet); avoidance of large crowds and poorly ventilated spaces; mask-wearing; vigilant hand-washing and use of hand sanitizer with at least 60% alcohol; and regular cleaning and disinfecting of frequently touched surfaces [4].

Employing social distancing measures in a busy allergy practice can be challenging. Simple recommendations which help to reduce the number of people in the office include limiting family members in the clinic and providing precise appointment times (even for allergy shots) to decrease the density of patients in the waiting room. Scheduled immunotherapy administration visits may be preferable to "walk in" immunotherapy visits in order to limit the number of patients seen per hour. Consideration may be given to extending shot clinic hours to accommodate a slower hourly flow. One specific issue which arises in a busy allergy immunotherapy clinic is the issue of patients waiting for observation after an allergy injection. The American Academy of Allergy, Asthma and Immunology (AAAAI) continues to recommend that patients receiving injections should remain in the office for a post-injection monitoring period as specified in the immunotherapy practice parameters [5]. Waiting in a car, or outside of the immediate office space, after receiving an injection is not an acceptable alternative as the patient cannot be directly observed. When patients are waiting following injections, they should be spaced at least 6 feet away from other patients.

The use of personal protective equipment (PPE) for all healthcare professionals and office staff is paramount in limiting the spread of COVID-19 and keeping both patients and staff safe. When resuming in-person allergy office visits, as well as allergy immunotherapy, healthcare providers should have available gloves, gowns, masks, hair coverings, and eye protection. These supplies are also necessary for mixing allergy extracts, as well as for administration of injections in the office. The adequacy and specific type of PPE to be used during immunotherapy administration depend upon federal, state, and local regulations, as well as supply chain and practical considerations [6]. Vigilant handwashing and use of hand sanitizer with a minimum 60% alcohol content must be enforced.

Certain procedures performed in an allergy clinic are higher risk for aerosolization. These include the use of spirometry, fractionated exhaled nitric oxide (FeNO) measurement, peak flow monitoring, and nebulizer treatment [7]. In the height of the pandemic, all aerosolizing procedures were put on hold unless considered absolutely essential. As the pandemic has become more prolonged, more selective use of these procedures has resumed, but the healthcare provider must be judicious in their use. For example, peak flow monitoring may not always be necessary before allergy injection. Spirometry and FeNO measurement may only be done in select cases, and after COVID-19 testing. The use of a metered dose inhaler (MDI) is preferred over use of a nebulized treatment [8••].

Resuming Allergy Immunotherapy

As the COVID-19 pandemic has stretched on, it has become important to consider how to restore ambulatory medical services which limit progression of preventable disease and improve quality of life. As such, allergen immunotherapy is the only disease-modifying treatment for patients with allergic disease and helps to substantially reduce symptoms in a majority of patients with type I (immediate hypersensitivity) atopic disease [6]. Allergen immunotherapy is most traditionally administered via subcutaneous immunotherapy (SCIT) but can also be administered via sublingual immunotherapy (SLIT). Established over 100 years ago and an internationally recognized procedure, allergen immunotherapy efficacy for the treatment of allergic asthma and allergic rhinoconjunctivitis has been supported by large systematic reviews and meta-analyses [9, 10]. At the start of the pandemic, many immunotherapy services were suspended. For example, immunotherapy was only continued for patients with life-threatening allergies, such as those patients receiving venom immunotherapy. SLIT also offered some clear advantage given the fact that it could be administered at home. Now with progressive reopening and resumption of clinical services, the question has become how physicians can safely restart allergy immunotherapy for their patients.

For patients receiving subcutaneous immunotherapy, re-starting allergy injections after a prolonged absence can theoretically increase the risk of a severe systemic adverse event. Since safety is of paramount importance in considering protocols for re-starting injections, it is advised that the dosing of allergy immunotherapy be reduced for all patients who had a disruption to their immunotherapy schedule, with a more gradual resumption of immunotherapy. While there is no clearly established, evidence-based protocol for resuming immunotherapy after a prolonged disruption, there is limited scientific data and expert opinion on how one may consider resuming therapy.

In the 3rd update to the practice parameters on allergen immunotherapy, the authors highlight the absence of data and wide variation of missed dose adjustments noted among practicing allergists. Nevertheless, the importance of time elapsed since the missed dose is emphasized. Additional factors of relevance noted include the concentration of extract to be administered as well as the individual patient's history of systemic reaction [5]. Also, the clinical features of each individual patient must be examined, including the severity of underlying allergic disease, time of year for pollen allergy, history of anaphylaxis or mast-cell disorder, and health status including comorbid conditions and medication usage, as well as asthma severity and control [11]. In a 2012 study, in which 1201 members of the AAAAI were surveyed, it was shown that the vast majority of allergy specialists dose adjust based on the date of the last administered dose. While most reduce by a certain number of "steps" or "doses" backward, some do dose adjust based on percentage or volume [12].

As a general rule, patients who have been receiving maintenance doses will be able to tolerate higher dosing schedules than those in the escalation phase of therapy, and the starting immunotherapy dose will need to be more significantly reduced if the interval of time since receiving allergy immunotherapy is more lengthy. One possible algorithm for resuming allergy immunotherapy shared by the American Academy of Otolaryngic Allergy is included in Fig. 1, accounting for these factors outlined above. This is not based on clear scientific data but again an example based on expert opinion [13]. An important take-home message in considering this algorithm, or any other suggested algorithm, is the recognition that treatment of individual patients will always require careful analysis of an individual patient's medical condition and individual dosing of specific immunotherapy. Certainly, a lesson learned from the disruption to allergy services during the COVID-19 pandemic is the need for prospective data to better inform more clearly established dose adjustment strategies after a gap in therapy [11].

Finally, as the pandemic stretches on and many patients remain hesitant, or even unable, to access traditional medical

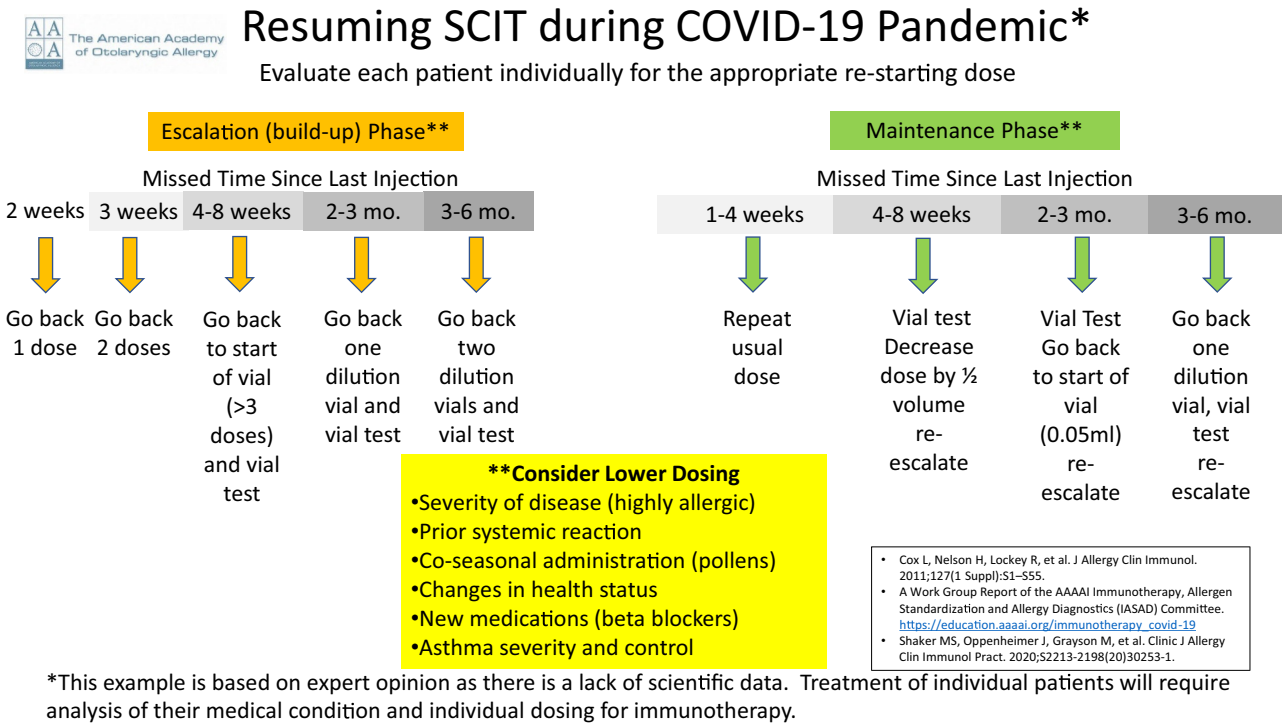

Fig. 1 Resuming SCIT during COVID-19 pandemic. (with permission from the American Academy of Otolaryngic Allergy; https://www.aaoallergy.org/wp-content/uploads/2020/04/Resuming-SCIT-During-COVID-19-Pandemic-AAOA.pdf.)

delivery outlets, sublingual therapy remains a viable treatment option. Increasingly used over the last two decades as an alternative to subcutaneous immunotherapy, SLIT has been demonstrated to be efficacious in the treatment of the allergic patient [14].

Since SLIT enjoys an improved safety profile compared to SCIT, with the risk of severe systemic reaction quite low, it may be reasonable to convert SCIT patients to SLIT on a permanent basis so as to avoid disruption to immunotherapy [15]. At minimum, SLIT is a safe and reasonable tool in the allergist's armamentarium, particularly in the face of a pandemic with perhaps more limited access to hospital and clinic sites.

Resuming Allergy Immunotherapy After COVID-19 Infection

When patients have had disruption to their immunotherapy schedule due to COVID-19 infection, the allergist must exercise clinical judgment about the timing of safely restarting immunotherapy. For patients recovering from mild COVID-19 infection, it is reasonable to consider restarting allergy immunotherapy once the individual is no longer infectious and asymptomatic. Alternatively, for patients recovering from moderate to severe COVID-19 infection, a multi-system evaluation may be necessary prior to resuming allergy immunotherapy. Keeping in mind that COVID-19 infection may be characterized by a severe systemic inflammatory response and multi-organ dysfunction, laboratory evaluation as well as multi-disciplinary consultation (i.e., cardiac, renal and pulmonary) may be required prior to resuming allergy immunotherapy [2••]. Particularly for asthmatic patients, lung function studies may be important in deciding the safety of restarting allergy immunotherapy.

Conclusion

The SARS-CoV-2 pandemic has presented organized medicine with unprecedented challenges relative to how one delivers safe and efficacious medical care in an ambulatory setting. Limitations on face-to-face medical encounters necessarily impacted the delivery of allergy services, especially routine allergen immunotherapy, and, as the pandemic has stretched on, it has become apparent that the face of medical care may be forever changed. As such, physicians specializing in allergy must be adaptable and modify their practices to still meet the needs of their patients and keep both their staff and patients healthy and safe. Strategies for restarting allergen immunotherapy have been proposed based on limited published data and expert opinion; the pandemic highlights the need for more large-scale evidence-based evaluation of how to best manage patients with disruptions to allergen immunotherapy. While SARS-CoV-2 has presented clinicians with previously unimaginable challenges, the healthcare community has been quick to pivot and adapt practices, including delivery of allergy services, to continue to provide optimal and safe patient care.

Compliance with Ethical Standards

Conflict of Interest The author declares no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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