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Missed Doses of Allergen Extracts Contribute to Serious Reaction

Allergen immunotherapy involves the administration of gradually increasing doses of selected allergens to a patient to treat stinging insect hypersensitivity, allergic rhinitis or conjunctivitis, or allergic asthma.[1] The treatment plan is usually prescribed by an allergist, who is a specialist in the diagnosis and treatment of allergies, asthma and immunologic disorders. The treatment is commonly carried out by practitioners in family practice or community clinics and involves the administration of an allergen extract. ISMP Canada recently received a report of a preventable incident that caused harm to a patient who was being treated with allergen immunotherapy. The case is shared to alert primary care practitioners as well as allergy specialists, about the potential risks associated with this treatment and to urge medical offices and clinics that provide immunotherapy to evaluate their processes to prevent a similar incident.

Medication Incident

A patient with allergies to both mould and birch trees received 2 boxes of allergen extract from his allergist in connection with planned allergen immunotherapy. One box contained a vial of Aspergillus/Penicillium (ASP/PEN) extract and the other a vial of Birch/Tree Mix/Ragweed (BIR/TRE/RAG) extract. The intention was that he take both extracts to his own practitioner for concurrent administration according to a specific hyposensitization treatment plan. However, the patient took only the ASP/PEN extract to his medical clinic. Serial dose increments of the ASP/PEN extract were administered for several months according to the schedule provided by the allergist, and the patient tolerated this build-up phase. When the vial was empty, the patient was advised to order more. The following week, he took in the vial he previously received containing BIR/TRE/RAG extract, which was initiated in the clinic according to the schedule included in the box. He tolerated increasing doses of this extract over a period of a few months.

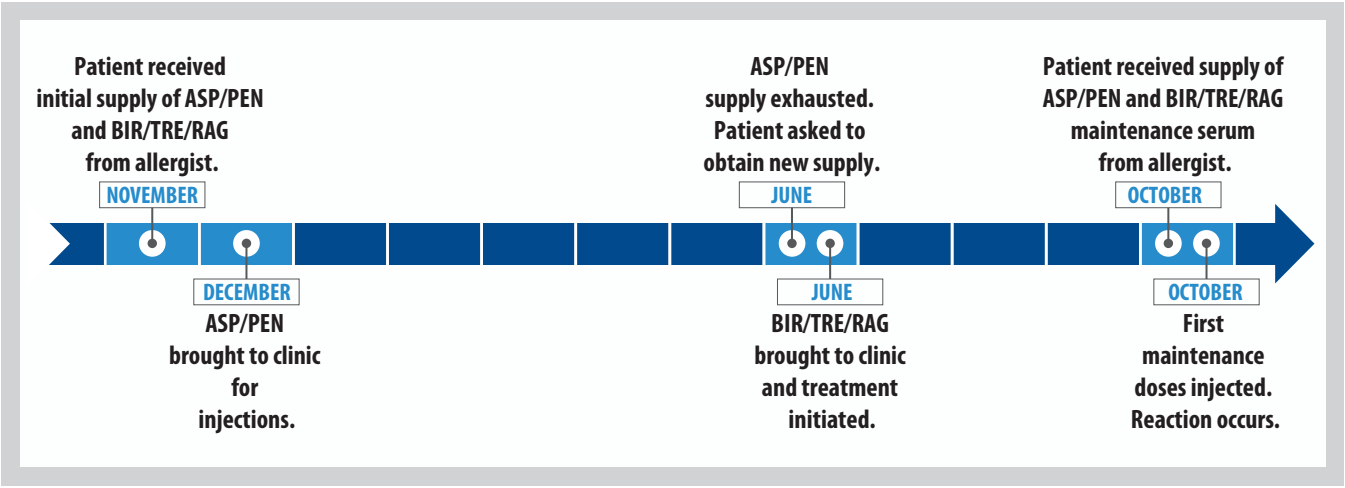
The patient received vials for maintenance therapy of the ASP/PEN and BIR/TRE/RAG extracts, which had been sent automatically by the allergist, and brought them to his clinic. A full maintenance dose of each extract was administered according to the schedule provided by the allergist.

Thirty minutes after receiving the first maintenance doses, the patient returned to the clinic exhibiting bright red hives and feeling unwell. The patient was treated with intramuscular diphenhydramine and oral prednisone, and he recovered without complications. It was later discovered that the patient had missed doses of both extracts during the build-up phase in the preceding months, which likely contributed to the reaction. Figure 1 highlights the events leading up to the patient's reaction.

Background

Allergen immunotherapy (also called allergy vaccine therapy, hyposensitization therapy, or allergy shots) is a recognized treatment for allergic symptoms caused

Figure 1. Timeline of events leading up to patient's reaction.



by various allergens, such as tree and grass pollen, dust mites, some animals, certain stinging insects, and mould. It involves desensitization of a patient's immune response by the repeated injection of small amounts of the allergen. Some hyposensitization therapies are seasonal and limited in duration (e.g., those for pollen allergy), whereas others are continual and are administered indefinitely. The dose is gradually increased over time to promote development of the patient's tolerance of the allergen, with the goal of preventing or minimizing symptoms associated with environmental exposure to the allergen.[1] In the case of indefinite therapy, once a patient is desensitized, consideration may be given to maintenance therapy.

Patients with a definitive diagnosis of type I allergy mediated by immunoglobulin E (IgE) confirmed by skin testing are candidates for allergen immunotherapy.[1,2] The allergist will perform an assessment and then prepare a care plan for suitable patients. The allergen extract, accompanied by an injection schedule, is commonly mailed to the patient's home, with instructions for the patient to take the extract to his or her doctor's office or clinic for administration. Some patients may have the family doctor or one particular clinic administer all of the injections, whereas other patients are less consistent about who carries out the treatment plan. At each scheduled visit, the patient is assessed and the extract administered according to the schedule.

Because allergen immunotherapy involves administration of a substance known to cause a reaction in the patient, this type of treatment does have the potential for unpredictable adverse effects, ranging from minor localized reactions to more severe harm or even death from anaphylaxis.[3] For this reason, it is recommended that injections be administered in a setting that allows for prompt recognition and management of adverse reactions, such as the prescriber's office or a clinic.[1,3] In addition to adverse reactions, medication errors also pose a risk to patients. Among the problems associated with allergen immunotherapy identified in a survey of allergists were allergic reactions, missed doses, early doses, wrong doses, wrong extracts, wrong schedules, expired extracts, and poor storage.[4] In another survey of allergists, dosing error was reported to be the second most common factor contributing to near-fatal reactions after immunotherapy injections.[5]

Discussion

The following factors potentially contributing to the medication incident were identified:

- There was a knowledge deficit about allergen immunotherapy on the part of the patient, who seemed unaware of the treatment plan and did not know that the two extracts were for different allergens and were intended to be used concurrently.

- The process of administering the allergen extracts at the clinic lacked robust controls:
  - There was reliance on the patient to be familiar with his allergen extracts, their administration schedule (Figure 2), and the overall treatment plan.
  - The clinic did not have a process for verifying, before each injection, the patient's identification or the name, dose, and schedule of each extract (against the overall treatment plan).
  - Injections were administered according to the schedule provided with each extract, but there was no method of verifying that the allergist's overall treatment plan had been followed, which resulted in some of the missed injections in this case.
  - There was limited documentation for checking and comparing previous treatment schedules or allergens against new schedules and extracts, to ensure safety and appropriate continuity.
- There was no clear, systematic communication process among the 3 parties (patient, allergy clinic, medical clinic). This process deficiency allowed the errors in allergen scheduling and administration to occur and be perpetuated.
- Allergen extract packaging is remarkably similar from one extract to another (see Figure 3), which makes changes or variances difficult to appreciate and increases the risk that the incorrect extract will be selected.
- Different allergy specialists use different extracts and schedules for the same allergen; it is therefore fairly common for general practitioners to see variations in treatment plans from one patient to the next, even for patients who have the same allergy.
- The patient did not stay in the clinic for 30 minutes after the injection (although he did remain in the general vicinity of the clinic).

Safe Practice Recommendations

Allergy Specialists

- Counsel patients about the potential adverse effects of allergen immunotherapy, including both immediate and delayed systemic reactions, and how to manage them. Educate patients about when to seek medical attention.[2] Reinforce the need to adhere to the schedule and overall therapy plan to optimize safety and effectiveness.
- To ensure that patients understand their allergy vaccine therapy, provide them with written information outlining the overall treatment plan, including the type and number of injections, the anticipated administration schedule, the process for ordering more extracts and the timing for a return visit for reassessment.
- Communicate promptly with the referring physician (and to the clinic carrying out the plan, if

Figure 2. Example of injection schedule for allergy immunotherapy and associated documentation.

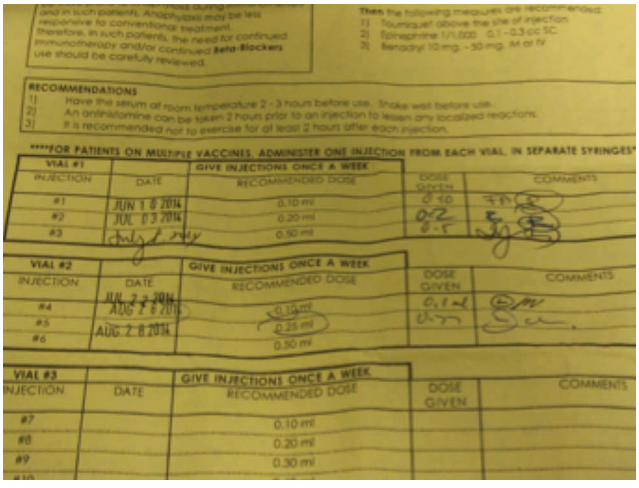


Figure 3. Example of vials for a single allergen extract in ascending concentration.

different) to provide the details about the treatment plan, how the extract will be supplied as well as when follow-up is required.
- Advise patients to use the same clinic consistently to reduce the risk of miscommunication, scheduling mix-ups, or misidentification and to ensure that documentation of previous injections is available to the practitioner who is administering injections.
- Expand the availability of injection clinics at the allergist's office to allow more convenient hours for patients, reducing their need to go to other clinics, where their history and care plan may not be available. Alternatively, partner with a convenient primary care, walk-in, or after-hours clinic where all necessary documentation can be consistently available.
- Design allergen kits which are patient-specific and include all necessary extracts, schedules, and treatment plans in the same package.
- Arrange delivery of the allergen extract to the clinic where it will be administered, to best assure maintenance of the cold chain.
- Create a process whereby primary care clinics can access the allergist for general advice about extracts or for information about a patient's treatment plan by telephone or through web-based communications, especially outside normal office hours.
- Consider approaching regulatory colleges or professional specialist associations to develop a standardized documentation record for allergen immunotherapy, to standardize the allergen extracts used for particular allergies, and to standardize, as far as possible, the treatment plans and labelling for each allergen.[4] Standardization would reduce the variability experienced by practitioners and clinics providing injection services and would also highlight potentially unsafe deviations.

Family Practice / Clinic Practitioners

- Review the office's processes for managing allergy immunotherapy, which may include some or all of the following steps:
  - Obtain the overall care plan from the allergist and ensure that the plan is available in the patient chart (whether paper or electronic) before initiating allergen administration.
  - Provide the complete chart, not just the documentation for the immunotherapy injections to the practitioner at the time of injection.
  - Use a checklist[6] to confirm the patient's identity and health status, to verify the care plan and to document the name, lot number, expiry date, and concentration of the extract.[1]
  - Develop a process whereby clinic staff and the practitioner administering the injection conduct an independent double check to verify patient identification, extract, and schedule against the treatment plan.
  - Periodically review storage of allergen extracts and associated documentation: audit refrigerated extracts for expiry dates, duplicates or changes, and ascertain the availability of treatment plans and administration records.
- At each patient clinic visit:
  - Remind patients about the management of potential adverse effects of allergen immunotherapy, as well as when to seek medical attention.[2] Ensure that patients understand any restrictions or potential alarming symptoms.
  - Reiterate the need to adhere to the appropriate post-administration observation period. Ask the patient to remain in the office for 30 minutes after the injection, and to receive a check of the injection site before leaving.[1,2,4,5] Consider implementation of an office policy to not administer allergy shots to patients who refuse to stay in the office for the appropriate observation period.
  - Reinforce adherence to the treatment schedule and overall therapy plan to optimize safety and effectiveness.
  - Explain how use of the same clinic for all injections is the best strategy to ensure optimal continuity of care.
- Because an allergic reaction can occur at any time, even if the schedule is followed correctly, it is essential to maintain an emergency box containing rescue medication and resuscitation equipment in the clinic where allergy shots are given. Conduct and document monthly expiry date checks of these supplies.
- Develop a process to review and report all incorrect injections and near-miss events within the clinic and externally (e.g., to ISMP Canada) to inform others and to prevent similar incidents.

Conclusion

Allergen immunotherapy has an important role in the long-term management of allergy-related conditions. However, the risks associated with this treatment and the potential for medication incidents when carrying out the treatment plan are under-appreciated.[3] It is hoped that this case review will assist in the prevention of similar incidents by the development and implementation of system safeguards such as increased collaboration between allergists and primary care practitioners, as well as improved office management of patients receiving allergen immunotherapy.

If your organization has successfully implemented any of the above-mentioned or alternative strategies that have enhanced the safe administration of allergen immunotherapy, please contact ISMP Canada at info@ismp-canada.org to share your experiences.

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