

Anaphylaxis—Considerations for Pediatric Patients

a interview with

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Phillip E. Korenblat, MD, is Professor of Clinical Medicine at Washington University School of Medicine, specializing in asthma, allergy and clinical immunology. He completed his fellowship in allergy and immunology at the Scripps Clinic & Research Foundation in California. Dr. Korenblat is a certified clinical investigator and educator who was named the "Outstanding Teaching Allergist for 2003" by the American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI). He has completed over 200 clinical research studies. He has published extensively, including as co-author of two editions of the textbook *Allergy Theory and Practice*. He is listed in *Best Doctors in America*, as well as *America's Top Doctors*, and has received the "Distinguished Service Award" from the Washington University Medical Center Alumni Association. Dr. Korenblat was the founder of Allergy Abroad, a biannual program in its 25th year that occurs at the most distinguished centers for asthma, allergy care and research around the world.

Anaphylaxis is the term given to a severe and rapid multi-system allergic reaction. This reaction may be the result of an immune-mediated allergic or non-allergic event. In some instances the anaphylaxis can be caused by non-immune mechanisms. However, in most instances it is caused by an allergen and occurs when the patient has been exposed to a trigger substance (allergen) to which they have become sensitized. The most common allergens that set off reactions include tree nuts, peanuts, hymenoptera, and medication, but people can be sensitive to a large variety of substances. The reaction will occur following ingestion, injection and, rarely, from inhalation of the allergen. Once the symptoms present, it can escalate quickly into respiratory and/or cardiovascular distress with potential fatal consequences.

The symptoms of anaphylaxis can include respiratory distress, hypotension, fainting, unconsciousness, urticaria, flushed appearance, vomiting, and abdominal pain. This sudden change can, understandably, also cause anxiety. Symptoms can be immediate or delayed—up to several hours after ingestion—and are brought about by the activation of the immune system following a binding of the allergen to the allergic antibody immunoglobulin (Ig)E. This antibody is attached to the mast cells, which then degranulate and release chemical immune modulators including histamine. These chemical modulators can lead to smooth muscle spasms (causing lower airways and the consequent respiratory distress as well as gastrointestinal and uterine contraction resulting in abdominal pain), increase in the permeability of blood vessels, which is responsible for the hypotension, flushed appearance, and swelling (angioedema), which can be localized in the upper airways and cause life-threatening upper airway obstruction.

The visual symptoms that appear on the skin may come and go rapidly and not be present when a patient is initially seen by medical personnel. Anaphylaxis necessitates quick assessment of the patient's mental status, blood pressure, respiratory and cardiovascular status and this will often direct the immediacy of the therapy needed. Given the rapid decline in a patient's health once the symptoms present, the speed of treatment is paramount and a common course of action is to prevent

the anaphylaxis progression, as well as attempt to reverse the event. Treating anaphylaxis often results in the combined uses of epinephrine (to provide a rapid relief of symptoms), antihistamines (to support the epinephrine), and often corticosteroids and intravenous fluids.

Treatment Speed and Considerations

It has been noted by medical staff treating adult patients with severe anaphylaxis that the patients often first experience a 'feeling of impending doom',¹ a reference to the immediate nervous system response to the allergen. Patients are advised to be alert to such feelings and have treatment immediately available. Very young pediatric patients may not be able to communicate this feeling of doom and so quick recognition of the symptoms and the vigilance of their guardians are extremely important, especially in pediatric patients with asthma as it is a marker of greater risk of death from anaphylaxis. "In a study at a pediatric emergency room (ER) in 526 children with generalized allergic reactions, of whom 57 presented with anaphylaxis, 82.5% had cutaneous symptoms but respiratory symptoms were the most common," explains Dr. Philip Korenblat, Professor of Clinical Medicine at Washington University School of Medicine, St. Louis. "Children can have agitation, flush, hives, abdominal pain, and vomiting. These can happen quite suddenly in an otherwise healthy child and this will alert people to something going on. An episode that is not detected as anaphylaxis often results in less prompt treatment, and data shows that there is a higher likelihood of the episode being prolonged, or a return of symptoms later (approximately four to six hours) and these can be worse than the original symptoms. A delay in adequate treatment is often responsible for a 'bad' outcome (often resulting in fatality)."

Epinephrine is recommended as the first-line therapy in the treatment of anaphylaxis; however, there is still reluctance—even by healthcare professionals—to administer it early, preferring to give antihistamines, corticosteroids, and intravenous fluids (again, despite epinephrine being the first choice of medication in significant systemic allergic reactions that are either true anaphylaxis or rapidly progressing toward anaphylaxis).

There are occasions when the initial use of agents other than epinephrine would be considered appropriate, but epinephrine serves to halt or at least prevent the progression of anaphylaxis and does so more rapidly and effectively than antihistamines or corticosteroids.

A multicenter emergency department study looked at patients following an insect sting. Of the systemic reactions, 69% received antihistamines, 50% systemic corticosteroids, and 12% epinephrine. According to Korenblat the “degree of severity in many of these cases may not have [been any] different had they received epinephrine, but I think the study demonstrates the reluctance to administer epinephrine.” Korenblat highlights: “In one study of fatal allergic reactions, epinephrine was used in 60% but only in 14% before cardiac arrest!” The overall view is that epinephrine should be used earlier in order to prevent complications and the resulting fatalities.

Korenblat and colleagues carried out a retrospective study reviewing the number of epinephrine doses needed during treatment. The study looked at 105 episodes of anaphylaxis in 88 patients, approximately two-thirds following an allergic reaction and one-third following a live hymenopteran sting. Fifteen per cent of the patients were children under 12, the youngest of whom was four. The results showed that 35.5% of patients required more than a single dose of epinephrine.² Later substantiating studies, carried out by Wilford Hall Air Force Medical Center and William Beaumont Army Medical Center, have reported 21% and 31%³ of patients (retrospectively) needing more than one dose. In addition to these, a report by Varghese and Lieberman,⁴ which documented the use of automatic epinephrine injectors (AEIs), found that two injections of epinephrine were required, 30% when administered in the field and 50% when given in a hospital setting. The evidence seems to suggest that for patients who have had anaphylaxis in the past, or otherwise felt to be at risk for anaphylaxis, the availability of a second dose is important.

Management of Pediatric Anaphylaxis

Epinephrine Pens, Auto Injectors and Pediatric Use

In the US there are two choices of pre-loaded AEI: EpiPen® (Dey Pharmaceuticals) and Twin-Ject® (Verus Pharmaceuticals). While either of these devices can be used for the immediate treatment of anaphylaxis, they do have their drawbacks, essentially the limited lower doses for children. Both products provide 0.30mg per injection for children weighing 30kg or greater, and 0.15mg per injection for those weighing 15kg and greater. Both auto-injectors are available either as two

automatic epinephrines packaged as a ‘two pack’ or the Twin Jet which has a second non-automatic epinephrine injection as an attachment. However, there is an absence of a dose—in an autoinjector—for children weighing less than 15kg. The ‘time-honored’ accepted dose in a hospital setting is 0.01mg/kg. Suggestions for the lower dose to be available in a pen format can be supported by the observation that the median age onset for peanut allergy occurs at 14 months of age. Six per cent of children less than three years old have significant food allergies; however, this decreases over the first decade of life.

Contraindications to Epinephrine

The degree of cardiovascular and/or respiratory symptoms often trumps any possible contraindications for epinephrine. Caution is advised in adult patients for cases of pregnancy, hypertension, coronary artery disease (CAD), a history of cardiac rhythm difficulties, and any previous adverse episodes related to epinephrine. Pediatrics is one of the few circumstances where there is little or no contraindication for epinephrine. Children can have congenital cardiac abnormalities and this may be when it is not advised. Caution must be exercised if the patient is already taken certain medications (monoamine oxidase (MAO) inhibitors and tricyclic antidepressants), as this often can alter the response of the epinephrine, making it stronger than initially intended.

First-generation antihistamines have a time-honored role in the treatment of acute allergic reactions. Dr Korenblat says, “They allow medical staff to titrate the dose more closely, utilize the intravenous route of administration and provide repetitive doses at relatively short intervals because it has a shorter half-life than the longer acting second-generation antihistamines.” He continues, “I think for the first awareness of a reaction they can be the first medication given, but if that reaction starts to get a little out of hand, or you can tell it’s going to progress, then use epinephrine. If it is a severe reaction when you first spot it give the epinephrine first and the antihistamine becomes supportive.” Second-generation antihistamines do have their place in preventing difficulty, but the choice between the two, for the treatment of anaphylaxis, is very much a personal one and as of yet not evidence based. Intravenous fluid replacement must be considered very early when anaphylaxis is diagnosed since rapid loss of intravascular volume can occur and cause hypotension.

Living with the Threat of Anaphylaxis for the Pediatric Patient

It is of foremost importance to ensure that teachers and school personnel are aware that a child is food sensitive or

has a history of anaphylactic episodes when considering the speed of treating an episode. This would include having in place a written, pre-arranged emergency care action plan provided by a physician so as to avoid delays or improper treatment. As Korenblat explains, “Most reactions to food allergies occur away from the child’s home [and], this being the case, parents have a duty to inform the school and in turn the school should identify students at risk”. Trained staff should be immediately available to evaluate, treat and be able to follow the pre-arranged emergency action care plan when it arises that a student is having an allergic reaction. One step towards assisting all concerned, should an episode occur, is to allow students to carry their own inhalers and auto-injectors, and be fully knowledgeable of how to administer it at all times if requested by their physician. The US Congress acknowledged this in 2004 when they established the Asthmatic Schoolchildren’s Treatment and Health Management Act. “The bill mandates that students demonstrate the ability to give themselves medication, school healthcare officials must develop a written plan for managing students’ asthma or anaphylaxis episodes, and parents must give written consent.”⁵

Korenblat highlights the importance of all guardians and school personnel being informed and supported in caring for a child with a history of anaphylaxis or asthma, and stresses that no child is segregated or left out of activities that they are perfectly capable of doing. Sensitive to this the Food Allergy & Anaphylaxis Network (FAAN) has devised a program called ‘PALS’.⁶

The program is aimed at children with classmates or friends who have had an episode of anaphylaxis or asthma. It educates classmates about the awareness and issues of food allergy in a fellow student. This lessens the embarrassment for the student and includes the classmates in helping to protect the student. In addition to this particular program in the US, there is an extensive food allergy network that provides support and education, as well as regular communication concerning food product dangers. Such organisations include: Asthma and Allergy Foundation of America and Allergy & Asthma Network: Mothers of Asthmatics.

Conclusion

In terms of treating anaphylaxis the priority is very much on the speed of treatment. Quick administration of the initial treatment, ideally epinephrine, can prevent cardiovascular and respiratory distress and prolonged episodes (and thus the worsening of symptoms) but, most importantly, reduce potential fatalities. The convenience of pen injector systems to administer epinephrine, and often the much-needed second dose, have proved themselves vital, particularly for the treatment of pediatric patients, especially when reactions occur outside of the home or hospital settings. Children are able to continue living a healthy life with the vigilance of their guardians and school staff, the education of their peers in the classroom and by taking responsibility for their own medication in the event of an anaphylactic episode. ■

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