



Anaphylaxis

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Anaphylaxis is the medical terminology for the ultimate in allergic reactions where in addition to hives, some other organ system will be involved in the allergic reaction. This can be important, because if serious enough and the involved system is the cardiovascular or respiratory system, the outcome could be fatal. Having said that, one should also know that nationwide in a given year only 500 to 1000 patients will succumb to a fatal allergic (anaphylaxis) reaction where the allergen is of a food source. So, these other symptoms of serious allergic reactions by organ system include:

Respiratory: Lip or tongue swelling, sneezing, watery or itchy nose, hoarseness, coughing, trouble breathing, wheezing or a "tight chest"

Gastrointestinal: Nausea, abdominal pain, vomiting, cramps and diarrhea

Skin: Hives and swelling (angioedema)

Cardiovascular: Low blood pressure, light headedness, fainting, loss of consciousness, "sense of impending doom"

Food allergens are one of the principal antigens (substances) to produce anaphylaxis as a response. To experience one of these potentially serious anaphylaxis reactions, the food must be ingested, reach a mucus membrane or the blood stream. Inhaling the aroma of the food or being in the room with the food will not produce this sort of response. Getting the food on your intact skin may produce local irritation, but unless there is a breach in the skin that allows access to the blood stream, anaphylaxis will not be the outcome. So if you have a ten-year-old and a twelve-year-old children and one is peanut allergic, the other child could be eating a PB&J and the allergic child is at no risk because he'd know not to ingest the peanut butter. Now if the siblings are two and four-year-old children, all bets are off given the naiveté of that age and the probability that unintentional sharing could take place. You'll get to be the judge and plan accordingly in your family. At some point as they evolve, the child patient will understand the risks and potential consequences and liberalization of the environment can take place. Actually, across the child and adolescent spectrum, the teenager and young adult is at risk for bad outcomes more than children to unanticipated food allergen contact and anaphylaxis. This has nothing to do with the allergens. It has much more to do with reckless behavior and the reality that injectable epinephrine, though prescribed, is often not carried by this "bullet proof" age group. This is an unfortunate reality indeed. So parental coaching may have a biphasic greater need for the youngest and oldest of your children.

One more point to be made about those youngest children. The babies with atopic dermatitis (eczema) who've reached four or more months of age are ready to consider the introduction of "complementary foods" (spoon foods). After four months, the AAP opinion opens the flood gates to the rest of a healthy and balanced diet with very few exceptions. The perspective that withholding foods to six months and beyond is more than under fire and is no longer ratified in contemporary advice. These proteins are reflected in breast milk and avoidance is a flawed concept for a breast



feeding mother. The most evaluated of the proteins is peanut protein because it stands at the top of the problematic five principal food allergens (legumes: peanut/soy, dairy, eggs, tree nuts, and shell fish) who by themselves are the causative food allergen in ninety-five percent of food induced allergy reactions. So in cultures (Israel is the best example) where the peanut protein is introduced early and maintained in the feeding culture, peanut protein allergy is far less a problem than in the United States where peanut protein has been avoided for medical reasons that were not driven by reliable data. Though this opinion is softened in recent years and even more so in recent months, the angst about peanut has a lingering impact. If you have a baby or child who has been eating peanut protein without apparent difficulty and whose eczema is not improved much despite all your efforts at the skin level and you are tempted to remove peanut protein for a period of time to see if this will help, think about some things first. Eczema is a skin disorder of babies and young children with a waxing and waning severity that over the long haul improves in the clear majority of children over time (months to years). Conventional dermatological care advice will center much more on care of the skin than removal of suspected foods for which the baby has apparent tolerance. So, removal of peanut protein proceeds for a period of several to many months and either the skin is improved or not. At the end of the experiment, it remains completely uncertain if there is an association and peanut protein is reintroduced. It now is an unfortunate reality that the response to this secondary peanut challenge may be a bonified food allergy with hives and perhaps more. The science in this tiny area is evolving, but for my money, I'd continue the peanut protein unless considerable medical evidence argues against that on an individual basis. Perhaps skin or blood testing for peanut allergy before a removal "experiment" is conducted to improve eczema would be a more reasonable approach.

So far this has been quite dire. There is good news though that one single and available medication halts the allergic release of histamine and helps to stabilize the potentially fatal cardiovascular and respiratory consequences in anaphylaxis. That medication is injectable epinephrine and is for the most part is sold in pre-measured auto injecting devices marketed as Epi-pen, Epi-pen junior, Adrenaclick (two sizes also) and generics (two sizes) made by Adrenaclick that with some learning can be quite simple and effective to use. All of the mentioned above are effective and the decision about which to use is often times driven by the insurance company. Regardless of which product you have, learn how to give a dose (or two in some instances) and be prepared to use it effectively if the need arrives. Doses are given in the anterolateral thigh (the front of and to the outside of the middle of the thigh). Hold the device like a pen, remove the safety cap (blue in Epi-pen/Epi-pen junior) press the "business-end" (orange in Epi-pen/Epi-pen junior) of the device against the skin and press the triggering device that was under the blue safety cap. Hold in place for ten seconds. The actual dose is given in two seconds, but to avoid incomplete dosing in a moment of nervousness, plan to hold in place for the full ten seconds. All of the products are sold in a two pack partly so that if a dose is wasted by nerves or inexperience, a second dose is available.

In up to twenty percent of cases, a second (biphasic) reaction will occur with return of anaphylaxis symptoms hours after an initial good epinephrine response. That second injector could be used for a biphasic reaction or can be repeated in as little as five to fifteen minutes after the first dose if the patient is not improving. Failure to improve the initial dose will occur in up to twenty percent of patients. Response should be rapid, with the onset of improvement measured in minutes. The typical consequence of giving a dose or a second dose will be an acceleration in heart rate. In children who typically have healthy coronary arteries, this will be of no consequence unless there is some exceedingly rare pre-existing cardiac condition that increases risk. However, if anaphylaxis is in



progress, the eventual outcome will possibly be death, so no matter the risk, risk of anaphylaxis likely "trumps" that and the required dose or doses of epinephrine should be given. If there is to be a serious or fatal consequence in anaphylaxis, it is usually linked to the reluctance to administer the epinephrine dose and resultant delay, allowing the allergic cascade to become more established and harder to treat. If a food ingestion occurs and prior ingestions of that food allergen have produced only hives in the past, then dosing with the prescribed antihistamine and closely observing the patient for involvement of a second organ system (respiratory/gastrointestinal/cardiovascular) would be warranted. In this limited situation, waiting to give the epinephrine would be acceptable. Having said that, with the least additional provocation, the epinephrine should be given and no criticism of that decision would be medically warranted. Antihistamines treat hives. Epinephrine treats anaphylaxis and antihistamines are relegated to a supporting role ONLY in treating anaphylaxis.

WHEN IN DOUBT, GIVE THE EPINEPHRINE, ASK QUESTIONS LATER.

So, back to the "biphasic" reactions. They can be of the same, lesser or greater intensity than the first reaction. As a consequence, the universal advice if the reaction was judged to be serious enough to warrant one or more doses of epinephrine, is that the patient should next go to the emergency room for observation for a biphasic reaction. Hopefully one will not occur and even if having to sit in the emergency waiting room for quite a while, you'll be in the right place if a second reaction takes place. The biphasic reaction is less likely if the original reaction was not severe, was not prolonged, if epinephrine, antihistamines and corticosteroids were given early in the care of the initial anaphylaxis reaction. The biphasic reaction can occur in as little as two or as much as thirty-eight hours after the first reaction. Most emergency rooms will have a protocol regarding the recommended period of observation that will take into account the severity of the reaction. Honestly, if the patient nearly died, the inconvenience of as much as more than a day of observation will be, and will seem to be, a prudent choice.

There is at least one more caveat to consider in food allergy and anaphylaxis. The coexistence of asthma and food allergy is "mutually-exacerbating". Food allergy makes the likelihood that an asthma exacerbation will be severe, more likely. Asthma makes the likelihood that a food allergen induced anaphylaxis will be severe, more likely. If you have both conditions, respect this association and be all the more prepared to treat either or both conditions aggressively. One caveat here also. If you have both asthma and food allergy and an unintentional food allergen ingestion occurs and obvious wheezing is the result. This is anaphylaxis first and asthma secondarily. This needs to be treated with epinephrine first. If wheezing persists, a second dose of epinephrine should be given, hospital emergency based care sought and then approach symptoms with rescue doses of albuterol and steroids. In this scenario, it can be a huge problem to start and stay with repeated albuterol doses and ignore the therapy of the anaphylaxis. Remember, even if you were wrong, giving epinephrine has virtually no significant consequences other than raising the heart rate.

Now one more quirky food related allergy diagnosis to discuss. Oral allergy syndrome is a circumstance where a patient with seasonal allergy (pollens-can be pretty mild) has itching inside the mouth in response to eating one or more fresh fruits or vegetables. No other discernible changes are noted, but the response persists over time and occurs with each exposure. There is no swelling in the mouth/tongue, no vomiting, no cramps, no diarrhea, and no involvement with anaphylaxis symptoms of other organ systems. Consider apples as an example, a bite of a raw apple or apple slice is repeatedly met with this symptom only. Even more curiously, this patient eats apple pie repeatedly



and never has any symptoms. Two things are operative here. One, the patient has some degree of seasonal allergy, though these symptoms can be very mild. Secondly, the offending food allergen has to be heat sensitive and is denatured (changed) by heating so it no longer represents an allergen and thus no symptoms occur while eating the cooked fruit (apple pie in this example). If you meet this strict definition, it is current expectation that virtually no risk exists to progress beyond this to more significant allergic syndromes. If there are more symptoms, such as tongue swelling, sneezing, chest tightness or difficulty swallowing, you do not fit this tiny niche and a conversation with your physician before continued exposure would be wise.

Thus far, we've considered anaphylaxis only in response to food allergens, but let's move on and discuss stinging insects. Despite the interest and in some cases, dread of these flying venom bearers, only about one hundred people die of envenomation anaphylaxis in a given year. You know the offenders already. They include the Hymenoptera order and the various families in that order:

Apids: Honey bees, bumble bees, "Africanized" honey bees

Vespids: Yellow jackets, yellow hornets, white-faced hornets, wasps

Formicids: "Imported" fire ants

Though they are different insects and the venoms are slightly different, the responses to those venoms and the medical advice regarding the avoidance of and the "after-care" of being stung is quite similar. Clearly, most patients who are stung will be free of medical consequence other than the pain and limited local inflammation and swelling around the "sting". Apids will leave a stinger and venom sack behind and removal of the stinger is warranted. The degree of reaction is volume of venom dependent and as such, removal of the stinger and venom sac is warranted. Debate as to the proper technique (scraping with a credit card or pulling out with one's fingers) is not necessary as the two techniques are of near equal effectiveness. What is certain, is that time to removal is more important than technique, so get busy with one of the techniques. Vespids will leave behind a part of the stinger only if the stinger was "broken-off" during the envenomation, but a venom sac will not be attached and removal is less important than with Apids. Cooling, oral antihistamines and topical steroids can be helpful with the limited local inflammation, pain and swelling. Be cautious not to injure with prolonged exposure to ice, especially on the smallest parts of the smallest patients.

A small percentage of patients will experience hives as an "allergic response" to being stung. This is an immediate response and will occur in minutes up to as much as an hour after exposure. True allergic response will not take place hours and days later, so just that first hour or so needs your closer observation. A very small percentage of patients will have other systemic symptoms. So review the symptom list for anaphylaxis above and judiciously try to determine if one of these other symptoms evolved as part of the response. This is an important differentiation because anticipatory care differs greatly. If the patient only had hives in response to a sting and there were no other symptoms of anaphylaxis (cough, hoarseness, throat or chest "tightness", wheezing, dizziness, fainting, loss of consciousness, low blood pressure, "sense of impending doom", repeated vomiting, nausea, diarrhea, cramps), then this patient is likely to repeat with a hive response with the next envenomation and need only local care and an oral antihistamine. These "hive-only" responses are no more likely than the general population (one percent) to proceed to a life threatening response. As a result, planned avoidance of future stings is less important. Care of an allergist, immunotherapy and injectable epinephrine likely will not be needed. So, as you can see, the patient who responds with hives to a



Hymenoptera envenomation should be observed with a critical eye, if not yours, then that of a judicious physician.

Of those patients who respond with anaphylaxis to a Hymenoptera sting, about sixty percent will repeat with anaphylaxis at the next occurrence. Unlike food induced anaphylaxis, where the severity can be less, similar or worse at the next episode, the tendency for sting induced anaphylaxis is not to worsen. So if you had mild anaphylaxis symptoms, this may give you a sense of comfort. Nonetheless, the standard of care would be the full spectrum of anaphylaxis preparedness including planned avoidance, injectable epinephrine, oral antihistamines, systemic steroids, allergy evaluation and probable immunotherapy.

If you've been stung and had no response other than a limited local response, you may be one of us who's proactive and wants to get skin tested and see if you're at risk. Sorry, this plan will bear no "usable fruit". About one percent of the population will have an anaphylaxis response to Hymenoptera venom, but fifteen percent of the population will have a positive skin test but not be at risk for these severe responses. The mental anguish and "medical-dollar" expenditure would be considerable and to no purpose and hence should not be pursued. This is not a familial condition, so the fact that another close family member has this problem would also not be justification for a preemptive evaluation and therapy.

One last category of response to Hymenoptera stings should be discussed. If you are one who has had a huge local reaction (usually takes hours to days to fully evolve) with swelling, redness, itching, pain (because of the magnitude of the swelling) that lasted for days before gradually improving with or without medical care, you may wonder what your risks are. For the most part, the news is good for you. This patient is at no greater risk than the general population of progressing to anaphylaxis and risk of death. So the risk of anaphylaxis is what it is for all of us, about one percent. It could therefore be argued that the full spectrum of medical options is not needed. What we do know is that in children, the next envenomation is likely to result in a similar large local response but nothing more. If repeated envenomation is likely, then there is the choice to implement immunotherapy ("allergy shots") for Hymenoptera. It will be effective at reducing the severity of local reactions and the time/cost expenditure may well be worth the improvement derived. A typical immunotherapy plan for Hymenoptera (anaphylaxis reactions or large local reactions) would reach maintenance levels of allergen in six weeks. The continued therapy plan would be:

- Year one: injections at four week intervals
- Year two: injections at six week intervals
- Year three: injections at eight week intervals

In seasonal/pollen allergies, the immunotherapy plan is usually for stoppage after five years with the expectation that most patients will be cured for the long term or a lifetime. If symptoms do begin to recur, the sneezing and runny nose will certainly be a problem, but not one that could be considered life threatening. Hymenoptera immunotherapy would likely produce a similar period of response protection. However, since return of symptoms, if immunotherapy was stopped, could be life threatening (if it was life threatening initially), most should plan to continue immunotherapy for the long haul. Actually, one thirty-gauge needle injection at eight week intervals is a small price to pay considering the bleakest of the potential outcomes should life threatening Hymenoptera anaphylaxis return at some point if immunotherapy was discontinued.