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Fighting food allergies on all fronts

No one should have to be afraid of their food. But for eight percent of children and about two percent of adults, only fear, or at least hyper-vigilance, will prevent a violent or even fatal allergic reaction to certain foods. Whether it’s peanuts, eggs, or wheat, or a combination of several foods, people with food allergies must watch every bite and even avoid contact with objects and surfaces that might have food allergens on them.

Food allergies are on the rise nationwide, for reasons that aren’t well understood. The U-M Division of Allergy & Clinical Immunology is at the forefront of helping patients recognize and cope with allergies of all kinds, and studying allergies at both the molecular and societal levels in order to improve diagnosis, treatment, and awareness.

This year, the division opened its new Allergy Specialty & Food Allergy Clinic at Domino’s Farms, which includes space devoted specifically to a Food Allergy Service that sees thousands of patients each year.

Two rooms are devoted to performing “food challenges” that evaluate a patient’s response to a specific food, with the help of a nearby kitchen. Most patients have one of the “big eight” food allergies, which together account for about 90 percent of all food allergies nationwide: milk, tree nuts, peanuts, shellfish, eggs, soy, wheat, and fish.

In the clinic, allergy faculty and fellows evaluate patients from all over the region to identify their specific allergies and assist families in understanding the severity and provide education to help them adjust to the diagnosis. Resources available to families include an educator, registered dietician, social workers, and nursing support. Each family is provided with a specific food allergy action plan and a food allergy education binder which contains additional information and resources for the family.

In the case of children, the team may work with parents on ways to educate schools, daycare centers, family, and friends to the dangers of an allergic reaction and steps that everyone can take to protect the child. For patients whose reactions to allergens might be severe, resulting in a significant reaction called anaphylaxis that could potentially be fatal, the physicians prescribe an EpiPen or Twinject, or self-injectable epinephrine (SIE), that can be carried at all times.

This year, in fact, the team presented results of a survey of school principals across Michigan, about the use of SIE in school. The survey, which was completed by 541 school administrators, reveals that a 2004 Michigan House bill allowing food-allergic children over age eight to carry SIE at all times has had a positive impact, but not a complete one.

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For example, only 32 percent of the principals said they allow students to carry SIE, compared with 17 percent when the survey was last done in 1999. And a majority said they kept SIE in the school’s front office, and had school secretaries, administrators, or teachers who were trained to administer an epinephrine injection in a child who was having a violent allergic reaction. But the researchers, led by Allergy fellow Darlene Kassab, MD, and Food Allergy Service Director, Marc McMorris MD (right), say their findings show there is a long way to go before schools are truly ready to deal quickly with a serious allergic reaction in a child. Dr. McMorris in conjunction with Allergy fellow Matt Greenhawt, MD, with support from the Food Allergy and Anaphylaxis Network, launched a national survey to assess the situation on a broader scale, by asking food-allergic people about their exposure to peanut and tree nut residue in public places.

Meanwhile, another study led by Dr. Greenhawt tackled the issue of food allergies among college students—by surveying hundreds of students who are among the first generation to be raised with a broad awareness of food allergies in themselves or others.

In the study, a sizable percentage of the students surveyed said they had been diagnosed by a physician as having a food allergy. But of those, just 22 percent said they owned an epinephrine injection device—a sign that their allergy was considered severe—and just 17 percent of those students said they carried the injection with them all the time.

This year, the Allergy clinical team also turned its attention to a little-known form of food allergy that may be under-diagnosed because it does not present itself through hives, wheezing, or anaphylaxis.

Eosinophilic esophagitis (EE) is a form of allergic response characterized by an overwhelming number of eosinophils, a type of white blood cell, which leads to swelling of the esophagus—the “food pipe” that connects the throat to the stomach. Especially in men and boys, EE can cause heartburn and severe reflux, difficulty swallowing, food impaction, nausea, vomiting, and a “failure to thrive” in infants.

Testing for EE involves not only standard food allergy skin prick tests and RAST studies, but also the application of food-specific patch tests that allow for evaluation of a delayed response to specific foods. Patients can then be advised as to which foods need to be eliminated from their diet, and are then managed by both an allergist and a gastroenterologist. We expect patients to come from throughout the region for this extensive evaluation.
Even as the clinical side of food allergy had an active year, the basic and translational side was busy too.

Limited information exists about the effects of foods on direct mast cell activation. Allergy fellow Miguel Wolbert, MD, and Cem Akin, MD, PhD (below), examined the effects of food extracts on direct non-IgE mediated activation of human mast cells and compared the results with those of dust mite and hymenoptera (flying insect) venom proteins. To do this, they used aqueous and lyophilized protein extracts for selected food allergens, dust mites, and venoms.

They found that food extracts and dust mites did not cause significant degranulation (release of immune-response particles) from non-sensitized mast cells at the concentrations tested, but the hymenoptera venoms each caused significant histamine release from the mast cells.

After winning a grant from the Food Allergy Initiative nonprofit group, a team led by Dr. Akin is preparing to launch a clinical trial to find out why people who are allergic to the same food can have such different levels of allergic response.

The study will test the blood and urine of dozens of food-allergic patients to look for markers that might be associated with the severity of their allergic response. Some patients will be chosen because they have experienced a life-threatening anaphylaxis episode in response to a food allergen, while others will be chosen because they have had less-severe responses.

Depending on what they find, the U-M researchers may be able to develop a way to predict which new patients will have a very strong reaction to the trace levels of allergens used in food-allergy testing, and which ones are at highest risk of a life-threatening response to an accidental exposure to their allergens.

The research will search for markers associated with mast cells—the immune response cells that are the “first responders” when the body detects the presence of an allergen. Mast cells bind to the immunoglobulin E (IgE) molecules that bind to allergens, and the resulting cascade of signals released by the mast cells brings in the inflammatory cells that lead to symptoms.

Currently, some patients are tested for food allergies using a blood test called RAST that measures their specific food IgE levels after exposure to the allergen. But this test only detects the presence of IgE to a specific food, and not the severity of response to an accidental exposure.

Dr. Akin, an expert in a severe mast cell disorder called mastocytosis, has studied abnormalities in mast cells with colleagues at the University of Michigan and the National Institutes of Health. This year, for example, they published evidence that a genetic mutation in a gene called cKIT is associated with unexplained anaphylaxis. That paper, in the journal *Blood*, gives important new evidence that a single genetic mutation can lead patients to suffer severe allergic reactions outside the setting of mastocytosis.

Other genetic abnormalities, some of which might lead to the production of abnormal proteins on the surface of mast cells or in the mix of signals released by mast cells, could become useful in the fight against food allergy. The U-M research, which will be conducted together with colleagues in England and Virginia, will look for markers related to abnormal activation or survival of mast cells.

If successful, the research may do more than allow some patients the peace of mind of knowing they’re not likely to suffer anaphylaxis, while warning others that they’re in danger of severe, life-threatening reactions from a trace of peanut butter. The study may help in the development of drugs to target allergic reactions, and to prevent the development of allergies.

And for patients and their families who live in fear of an accidental brush with a dangerous food, that day couldn’t come soon enough.

Left: Drs. Susan Hungness and Cem Akin with Yibin Jiang of the Akin lab