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Bring On the Peanuts: Food Allergy Therapies Move Closer to Approval

Fifteen years after an experimental peanut allergy shot killed one patient, researchers have ramped up the science to find alternative treatments, including protein powders and herbal mixtures

By Katherine Harmon | Thursday, June 30, 2011 | 4 comments

The tableau is common enough these days: after a miscalculated meal, snack or sip, a parent rummages frantically for an EpiPen or antihistamine as a swollen-mouthed child sits, frightened, possibly gasping for breath.

The prevalence of food allergies has shot up in recent years and now affects some 8 percent of children in the U.S. And of the approximately six million kids who have food allergies in this country, more than a third (38.7 percent) have severe reactions. These responses, triggered by an immune system over-reaction, can lead to anaphylaxis, a systemic response that, if untreated, can be fatal.

With so many people just a bite or a drop away from a potentially deadly allergic reaction—and the cost of treatment for these allergies spiraling to about half a billion dollars in 2007—scientists have cast a wide net in the search for new and more effective ways to eliminate food allergies and have pulled in some promising approaches. Potential therapies—including peanut protein powders and mixes of traditional Chinese herbs—are moving quickly through clinical trials, and some might be ready for regulatory evaluation within a year.

Pin it

SPOONFUL OF DANGER?: Experimental therapies are helping many children with severe food allergies eat peanut butter or milk without getting sick. But are the treatments ready for the millions of eager, allergic patients?
Image: iStockphoto/Fertnig

Down the hatch and under the tongue

Shots for pollen and other airborne allergens have been around for decades. So, as food allergy rates started to rise a couple of decades ago, researchers got to work adapting this principle for the new set of patients. In 1996 12 people with severe peanut allergies entered a clinical trial studying an injectable vaccine. One child in the study, however, had a severe reaction to the shot and died, making many people wary of the field altogether.

But the growing number of people with food allergies has been reigniting interest. Newer research has moved on to therapies that adults and kids can take orally—many as a powder that can be mixed into juice or a snack, such as applesauce. Other candidates include drops that are placed under the tongue (and held there for a couple minutes before being swallowed).

The principle is simple enough: slowly acclimate the immune system to the offending protein starting with minute doses. The very first dose of an experimental oral peanut allergy therapy, for example, might include about one one-thousandth the amount of peanut protein as is found in a whole nut.

Over weeks and months, the quantity of the protein is slowly ramped up. "With the

repeated administration of the dosing, your immune system begins to change," explains Wesley Burks, the chief of Pediatric Allergy and Immunology at Duke University. For most people in the trials (which have each generally enrolled fewer than 30 subjects so far), their immune system starts to accept larger and larger quantities of the noxious protein. And after several months many previously allergic kids can eat a tablespoon of peanut butter without ill effect.

These oral-base therapies hold the most promise, says Robert Wood, chief of Allergy and Immunology at Johns Hopkins Children's Center. He notes that a return to the injectable vaccine is still tentative (even though many speculate that the previous fatality was likely the result of a dosing error). Wood's research has focused on milk allergies and has had especially promising results from powder formulas—in large part because of the administration route. He and his team have been able to work subjects up to as many as 2,000 milligrams of milk protein via that method, whereas the below-the-tongue approach has only reached about seven milligrams of the extract. (As he points out: "you can only put so much liquid under a person's tongue and have them hold it there.")

The body allergic

Just how the oral approach works is still somewhat of a puzzle for researchers, especially when compared with shots. Allergy injections introduce low levels of the offending protein (called an antigen) in the neighborhood of 10 to 100 micrograms to acclimate the body to the antigen's presence.

But for the oral therapies in development for peanut, milk and other food allergies, doses are higher, with as much as whole grams of an antigen in them. So in the body's response to them, "It's possible that the mechanisms are different," explains Dale Umetsu of the Children's Hospital Boston and Harvard Medical School's Division of Immunology. In mouse studies higher doses of antigen seem to actually trigger eventual deletions or reductions of the immune cells that target the antigen. After an initial rise the antigens linked to the protein slowly starts to decrease, lessening the chances of an over-reaction. "So there's definitely immunological changes, but exactly how this works is not clear," he says.

Another question is whether adults and children will respond differently over time to immunotherapies. Most of the studies so far have specifically enrolled children with food allergies, but research has shown that whether people are 60 or six, their immune systems seem to behave the same way. "Adults can get as much benefit as the children—and the results are very similar," says Kari Nadeau, director of allergy research at Stanford Medical Center.

Spoonful of herbs

Like the food allergens themselves, the oral treatment—even in the smallest doses—can cause the immune system to lash out with a stomachache, an itchy mouth, hives or more severe systemic reactions. And for 10 to 20 percent of people these symptoms are bad enough to make them drop out of the trials. Especially for children, getting through an uncomfortable reaction from the therapy is tough. "When you're a five-year-old kid, you're worried about your tummy pain *now*" more than decreased risks later, Nadeau says.

One possible way to get patients to stay with the program is to dampen their immune systems before they get the dose of allergens. So-called monoclonal antibody drugs, such as Omalizumab (Xolair), approved for asthma, could be the answer. They inhibit an antibody type known as immunoglobulin E (IgE), which is elevated in people who have the more severe allergic reactions. "IgE is kind of the match that lights the fire behind allergies," Nadeau explains. "So if you don't have the match, you won't have the fire." The suppressor drugs work "like a protective cover" for the immune system by binding to IgEs and blocking them, Nadeau says.

Researchers based in part at the Mount Sinai Medical Center in New York City are taking a more unconventional approach. They are investigating the use of a blend of Chinese herbs to disarm the body's response to food allergens. The formula that is currently in clinical trials is thought to work on a similar principle as the monoclonal antibody drugs. FAFH-2, as it is currently known, combines medicinal

herbs from *ling zhi*—a blend used to reduce allergies and inflammation—and *wu mei wan*—a treatment for gastrointestinal problems.

With these mitigation approaches, Umetsu says, "we may be able to treat more of the patients—and do it more rapidly."

Close to a cure?

As long as people can tolerate the treatment, therapy seems to go over well, increasing exponentially the amount of a previously dangerous food that a patient can consume. But what happens when people stop taking the frequent doses currently required to boost immunity? "That's the next big question in this research: When can you get off this food therapy," Nadeau asks.

Even for approved allergy treatments, such as those for bee stings, the notion of indefinite protection remains controversial. After years of desensitization and maintenance shots for bee sting allergy some individuals might still revert to being allergic if they go off the therapy, Umetsu says. And the same could very well be true with food allergies.

In his group's milk allergy studies, he says, most of his patients are drinking milk and eating cheese and ice cream. But the research is still too new to determine if the subjects are *cured*—or if continued treatment will be needed to maintain their tolerance. About 10 to 20 percent of patients who have gone off the milk allergy therapy for a couple weeks or months had allergic reactions after ingesting milk proteins. "I don't think anyone would venture to say that we've cured anybody," Umetsu says.

So instead of a cure, "another goal is to get a patient to tolerate more of the food," he notes. As Burks points out, "for many parents, that's what they want"—just to know that an accidental dusting of peanut protein in a granola bar or bake sale cookie is not going to send their child to the emergency room. "They don't want the fear that one bite will kill them."

The peanut model

Much of the research so far has focused on the two most common food allergens: the dreaded peanut and dastardly milk. Peanuts are responsible for a quarter of all childhood food allergies, followed by milk at 21 percent (and shellfish at 17 percent). But the good news is that most specific food allergies seem to work in basically the same way.

"The peanut is basically a prototype by which we're going to use the same methodology to solve other foods," Nadeau says. So if a peanut prophylaxis proves effective, those for other foods might quickly follow.

But, Wood points out, the major food allergy categories have some key differences. For example, nut and shellfish allergies turn out to be rather diverse fields that reflect the relationships of the foods themselves. Walnuts and cashews are quite different nuts, evolutionarily speaking—just as lobsters (crustaceans) and mussels (mollusks) are fairly far apart on the marine phylogenic charts. So trying to treat entire categories is "going to be considerably more complex," Wood says.

Parsing out that problem has already begun. If researchers can isolate the peptides of each allergen's noxious protein, they might be able to make treatments targeted to individual patients' allergy profiles. But right now, scientists are still unsure what components of peanut, milk or fish proteins that upset so many people's immune systems. Studies are underway to test various possible peptides in mice that have been made allergic to some of these problematic foods.

And if scientists can isolate these food peptides, they might be able to combine them for more comprehensive treatments for people who have allergies to multiple food categories—much like the current customized allergy shots for people who have more than one airborne allergy. In the June *Pediatrics* study 30.4 percent of children with food allergies had reactions to more than one subset of food.

For now, however, all of the food allergy therapies remain in research labs. "The early results are promising, but they're really [just] studies right now," Burks says. And as much as parents are anxious to start their children on them, he adds, "they're not ready for clinical practice." But if the work continue to go well, he says, some of the oral therapies might reach the U.S. Food and Drug Administration for approval as soon as 2012.