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Alpha-Gal Allergy: Who's at Risk for Anaphylaxis?

**Dr. Buch:**
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. Joining us today to discuss alpha-gal allergy is Dr. Sarah McGill. Dr. McGill is an Associate Professor of Medicine at the University of North Carolina. Dr. McGill is passionate about getting the word out on alpha-gal allergies and has published "Suddenly Steakless: A Gastroenterologist's Guide to Managing Alpha-gal Allergy," which was published in the *American Journal of Gastroenterology* June 2022.

Welcome to the program, Dr. McGill.

**Dr. McGill:**
Thank you, Dr. Buch.

**Dr. Buch:**
It's a pleasure to have you here today. So, Dr. McGill, please describe the pathophysiology of alpha-gal allergy and why it is different from other food allergies.

**Dr. McGill:**
Right. Alpha-gal allergy is really interesting because it's a delayed allergy. This is an allergy to a sugar. It's the galactose-alpha-1,3-galactose sugar, and this sugar is present on all the cells of lower mammals, so that's your cows, pigs, deer, bunnies, everything like that, not on old-world primates, and our cells don't have alpha-gal sugar. It is delayed by a few hours. So usually, when you are exposed to an antigen—let's say, you eat a peanut and you have a peanut allergy—your symptoms are immediate, and that's why they call these types of allergies the IgE allergies, immediate hypersensitivity reactions. And the other difference is that most people have the allergy with exposure from eating the mammalian meat and mammalian organs, things like that. Most food allergies are to a protein, and this is to a sugar, which is also pretty unique.

It's our understanding that the Lone Star tick causes the sensitization to alpha-gal or your body to produce antibodies. So the Lone Star tick salivary glands have alpha-gal in them, we think probably from their prior feeding. Their main host animal is deer, so essentially, the understanding is that the deer has alpha-gal on all their cells, including their blood cells, and the ticks feed on the deer. Then the alpha-gal is in their salivary glands. When it bites the human being, that injects alpha-gal into the skin and into their body and then that person can react by mounting this IgE allergic antibody response.

**Dr. Buch:**
And how do we make the diagnosis? And what are the limitations of testing?

**Dr. McGill:**
The diagnosis is partly made by lab, but really, it's a clinical diagnosis. So the lab test is the IgE antibody to alpha-gal, and if you have those antibodies, then you are sensitized. You could have the allergy. Now, because GI symptoms and the GI symptoms of alpha-gal

can be really nonspecific—they're abdominal pain, nausea, vomiting, and diarrhea—and because a lot of things can cause that, just because you have the alpha-gal IgE antibody and those symptoms doesn't mean it's because of alpha-gal allergy. But at least in our studies, most of the patients who went on the alpha-gal avoidance diet did get better from their GI symptoms when they had those antibodies.

I think the limitations are that just because you have the IgE antibodies doesn't mean necessarily that you have the allergy. Then rarely, some people with the allergy who have been tested in a lab—they've eaten ice cream or they've eaten organ meats and had allergic symptoms—because of a history of what sounded like alpha-gal even though they didn't have the antibodies, so people can have the allergy without antibodies, but we think that's a little more rare.

**Dr. Buch:**
So for most clinicians out there, should they be testing, or should they just treat empirically?

**Dr. McGill:**
Well, I think they should be testing, and it also depends on where you're practicing. So if you're a GI practice in Alabama, North Carolina, or Virginia, certainly in rural areas where people are outdoors, then it makes more sense to be testing your patients; or, if your patients traveled in those areas or just took a camping trip in the Southeast, Mid-Atlantic, or Midwest, that's where alpha-gal is present because that's the range of the Lone Star tick.

**Dr. Buch:**
Thank you for that information. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Sarah McGill about alpha-gal allergy.

So moving on, how should we treat alpha-gal allergy?

**Dr. McGill:**
The treatment for alpha-gal syndrome or alpha-gal allergy is avoiding the antigen, essentially avoiding alpha-gal. There's a lot of alpha-gal in organ meat. Actually, one of the very first descriptions was people eating pork kidneys in Europe and having allergic reactions. Meat with more fat content tend to give more allergic reactions for some reason that we're not clear on. And then fatter dairy tends to have more alpha-gal or cause more allergies, like cream, ice cream, and soft cheeses, but there is some alpha-gal in all dairy. And then gelatin is made from the hooves of mammals, so there is some alpha-gal in gelatin.

**Dr. Buch:**
Perfect. Thank you. Which medications and devices provoke alpha-gal allergy?

**Dr. McGill:**
So the syndrome was actually first recognized in patients who anaphylaxed after infusion of cetuximab. Cetuximab is a chemotherapy agent for metastatic colon cancer, and in the clinical trials, there was very rare anaphylaxis, but what was happening in Missouri, North Carolina, and Tennessee in the 2000s is that when they started giving cetuximab IV infusions to their patients, about 1 in 5 patients were having severe anaphylactic reactions. And then they discovered that the alpha-gal was the problem. Cetuximab is from a mouse, a chimeric antibody, and so it was loaded with alpha-gal.

They have done ex vivo studies with pork valves and grafts made from mammals, and certainly, alpha-gal IgE for patients who are allergic to alpha-gal bind to those medical devices, so theoretically, that can cause early device failure. In people who have had cardiac devices, there have been some cases of anaphylaxis. It's not clear over time what that means to the alpha-gal patients who have these devices, but we can imagine it's not great for them.

**Dr. Buch:**

Thank you. And before we conclude, are there any other thoughts you would like to share with our audience today?

**Dr. McGill:**
I think I'd like to mention that alpha-gal allergy is an emerging syndrome, and for patients who have gastrointestinal manifestations with abdominal pain, diarrhea, nausea, and vomiting, we don't know so much about those patients yet because the studies are early. We think that alpha-gal antibody sensitization is largely unrecognized in kind of large database studies. We just kind of looked at serum that had been biobanked from a colonoscopy study in 400 patients who gave us very detailed descriptions of what they ate and their abdominal symptoms, and what we found was that sensitization, having the antibodies, was very common. It was in 30 percent of patients, but those patients weren't eating less mammalian meat than the patients without antibodies, and they actually didn't have more abdominal pain than patients without antibodies, which has been seen in other studies of GI conditions like H. pylori infection and celiac disease. Those conditions are also largely asymptomatic. We don't know yet the consequences of asymptomatic, unrecognized alpha-gal syndrome, but there are some studies that those patients may have increased risk of coronary artery disease because there are mast cells in the coronary arteries, so continued meat ingestion by these patients who have antibodies on those mast cells may be causing them to react.

**Dr. Buch:**
This was an important and informative discussion on alpha-gal allergy. I want to thank my guest, Dr. Sarah McGill, for sharing her insights. Dr. McGill, it was a pleasure having you on the program today.

**Dr. McGill:**
Thank you so much, Dr. Buch.

**Dr. Buch:**
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge. Thanks for listening, and see you next time.