



American Society of  
**Anesthesiologists™**

Central Line  
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VOICE OVER:

Welcome to ASA's Central Line, the official podcast series of the American Society of Anesthesiologists, edited by Dr. Adam Striker.

DR. ADAM STRIKER (HOST):

Welcome to Central Line. I'm your host and editor, Dr. Adam Striker. Today, I'm joined by Dr. Stacy Jones, co-editor in chief of ACE, which is Anesthesia Continuing Education. Dr. Jones is here today to talk to us about Alpha-Gal allergies, which is a topic I'm certainly looking forward to learning more about and provide a lot more information to those out there that have just heard of this on the fly. Welcome to the show, Dr. Jones.

DR. STACY JONES:

Oh, thank you, Dr. Striker. It's I'm happy to be here.

DR. STRIKER:

Before we get into the topic of the show, why don't you start out telling us a little bit about yourself and your role with ACE?

DR. JONES:

Okay. Well, I have been an anesthesiologist for over 25 years and I've been involved in anesthesia education for most of my career. So right now I am co-editor in chief of ACE, which is the anesthesia continuing education product produced by the ASA. I also have been writing questions for the written boards since 1998, and next year I'm going to chair the committee for the basic exam. So I've been involved in anesthesia education for a long time. I'm an adjunct associate professor at the University of Arkansas for Medical Sciences in Little Rock. And I was in private practice in Austin, Texas, for about 20 years before that. So that's me in a nutshell.

DR. STRIKER:

Okay, great. Well, we wanted you on the show today to talk about alpha-gal allergies, Alpha-gal syndrome, the difference, specifically because it's a topic addressed in the 19A volume of ACE. But before we get there, I did want to ask as a general question. When one is a topic of focus in an ACE issue, how much of the issue focuses on it and how are the topics decided upon?

DR. JONES:

Well, that's a good question. ACE comes out twice a year in October and in April. Each topic is a question and then there's a several paragraph discussion explaining the right answer and why the wrong answers were wrong. And there are ten editors on the editorial board, and we create all of the content. My other co-editor in chief, Dr. Joel Johnson at the University of Wisconsin, also writes questions. So even the editor in chiefs write questions for this. And we feel like people are more engaged if they pick the topic themselves. We encourage people to write outside of their area of expertise and to pick things from their clinical practice. But we'll think of something that maybe happened last week that you thought to yourself, Gee, I need to look that up again. I don't remember. Or, you know, that's kind of interesting. I haven't seen that very often. Maybe I should write an ACE question about that. And then the discussion will be two or three paragraphs really condensing that one single concept. I actually wrote this question in this volume of ACE about Alpha-gal because it was a pretty interesting concept and I thought that it actually has some bearing on your anesthesia planning that I hadn't thought about before.

DR. STRIKER:

Well, let's dig into this, because this is something I've heard about a little bit here and there over the last couple of years. I personally haven't had too much experience with this. Let's start out explaining what is Alpha Gal allergy and what's the difference between that Alpha gal syndrome? Let's just start with a little background on that.

DR. JONES:

Okay. So Alpha Gal is an abbreviation for Galactose Alpha one three Galactose, which is an oligosaccharide that's found on almost all mammalian cells except for humans and our closest relatives. So Catarina mammals like overall monkeys and apes and humans are the only mammals that don't have this oligosaccharides on their tissue cells. Even more interesting because we don't produce it, we have normal IgM and IgG antibodies

to Alpha Gal and that's actually the primary focus for acute rejection in xenotransplantation. So one of the prime reasons that xenotransplantation has failed so dramatically so early, is that this response to that one oligosaccharides.

So alpha gal allergy means that people have an IgE antibody against the alpha gal molecule and it causes an allergic reaction, which is sort of termed alpha gal syndrome. And that presents itself in a lot of interesting ways.

And I have to give a little history. In the early 2000, 2006 to about 2009, there started being reports, some early in Australia, of patients that had allergies to red meat and also had histories of tick bites. But in the US it sort of presented a little differently. In 2006, Cetuximab became clinically available and it is for the treatment of metastatic colorectal cancer and some types of head and neck cancer. It's a recombinant human protein that's created using other mammalian cells. And so there were areas in the southeastern United States -- Virginia, Tennessee, North Carolina -- where there was an unusual, very strangely high percentage of anaphylaxis on the first administration of this drug. It was pretty regionally isolated, and they started looking for antibodies to that particular drug that they were administering and found that Alpha Gal is on the surface of that. People had IgG antibodies to it. And something like 20% of patients in those southeastern areas had IgE antibodies to Alpha Gal, whereas maybe one or 2% in the Northeast. Because there had been some connection between the tick bite. Then we started looking at the distribution of a particular tick in the US. Apparently this occurs all over the world, but the vector is different. It's a different species. And fortunately for us, the the nasty bug that that carries Lyme disease is not associated with the triggering of this allergy. Tick bites apparently are very immunogenic and they believe that there is alpha gal or a similar molecule on tick saliva, and they believe that it is a tick bite that sets up and causes the IgE response to Alpha Gal. And then those people had anaphylaxis and there were even some deaths at the first administration of Cetuximab. And then they also noticed that these people had a history of red meat allergy. And it's interesting because you have to ingest the red meat. It usually occurs 3 to 6 hours after ingestion of red meat, of pork, beef, lamb, beef being the most frequent. And people had complained of nausea, diarrhea, but all the way to anaphylaxis, the whole spectrum that you see in allergic reactions. That so called constellation is really what's I think termed Alpha Gal Syndrome.

So it does two things the allergy to Cetuximab that can be very dramatic. And then this allergy to red meat. Where this becomes a problem for us as anesthesiologists, is that some of the drugs we administer are recombinant human proteins and they were grown in cell culture from other mammals. And so the potential for this particular oligosaccharides to be present is pretty high. And also things like gelatins, stearic acid, lactic acid and magnesium steroid are also things that can be used as binders or as

coatings on different capsules or pills or formulations of drugs as inactive ingredients. And these all have the derivatives of some sort of mammalian protein and can precipitate anaphylaxis in some people. And it's hard to know in the drugs that were administering people what the actual inactive ingredients are in which we're plant derived or animal derived.

DR. STRIKER:

So just to review, in the US at least allergic reactions on the initial dose of Cetuximab , through back tracing, then found out it was due to tick bite. That was the initial, the initial itus for the IgG antibody, correct?

DR. JONES:

Yes.

DR. STRIKER:

Now the red meat allergy, then if you get the tick bite, you can be allergic to red meat without having had that medication, correct?

DR. JONES:

Yes. Yes. And in the allergy to red meat, interestingly, typically occurred later in life when you'd be more likely to be exposed to tick bites. It's not something that people are necessarily experienced when they're very young. But the IgE to Alpha Gal is what causes all of this. And again, the very dramatic Cetuximab allergy, but then also the red meat allergy. And again, that it's a delayed allergic reaction, and we're not really sure why, but it has something to do with the digestion of the red meat. And that reaction occurs somewhere between 3 and 6 hours after ingestion. So it's not immediate. Like like you think of peanut allergies, for example.

DR. STRIKER:

Mm hmm. That's interesting. But it is found more later in life because of susceptibility to tick bites. In other words, younger individuals don't tend to get the red meat allergy per se, or don't end up developing the alpha gal allergy.

DR. JONES:

Yeah. And again, this is most of it's speculative because it's all been put together using past history and what people remember or don't remember. But in in toddlers, for example, you know, you just don't you don't see as many red meat allergies like this that occur, you know, 3 to 6 hours later because they're less likely to have the inciting agent.

DR. STRIKER:

Okay. So older, you mean just adults, correct? Not necessarily older in age, like.

DR. JONES:

No, just somebody who might have been wandering around in the woods.

DR. STRIKER:

Gotcha. Okay. All right. But it's. But it's still [00:10:00] confined primarily to southeastern us.

DR. JONES:

Well, it's the nasty bug that does it in the US is the Lone Star tick, which being from Texas, I thought it was a Texas tick, but it's not. It has like a little white spot on its body. So they call it the Lone Star tick. And, you know, because the association between tick bites and red meat allergies had already been made, they started looking at the distribution and the distribution of the allergies to Cetuximab were literally in the southeastern United States. And they were looked at the distribution of ticks that went along that same distribution. You don't see the tick that causes Lyme disease doing this. It's this one particular tick in the US. It's a different tick in Australia.

DR. STRIKER:

Interesting. Now, with regard to the red meat allergy, is this something that's so far life long?

DR. JONES:

Seems to be. And you know, the presentation can depend on your IgE titers. How much of the alpha gal you're exposed to? But as far as we know, it seems to be lifelong. I suspect, like so [many other allergens, it's worse early on.

DR. STRIKER:

Gotcha. Well, I. More questions for you. We'll just going to take a very brief patient safety to break.

(SOUNDBITE OF MUSIC)

DR. JEFF GREEN:

Hi, this is Dr. Jeff Green with the ASA Patient Safety Editorial Board. The intra hospital transport of patients can be risky, but most complications are avoidable with planning, preparation and safety checks. Ensure an anesthesia face mask is available and be prepared for the possibility of manual ventilation during transport by threading the oxygen tubing through the hole in the mask to ensure it is included during transport of an intubated patient. Should an inadvertent exacerbation occur, and assuming the patient is an easy mask, it might be preferable to mask ventilate the patient with 100% oxygen until conditions are appropriate for urgent re intubation. Some even consider having a supraglottic airway device and keeping emergency medications readily available. Don't forget a mask before embarking on transport. This simple tip may save your patient's life.

VOICE OVER:

For more information on patient safety visit [asahq.org/patientsafety22](http://asahq.org/patientsafety22).

DR. STRIKER:

Well, we're back. Okay. Well, let's say a patient comes in with this history, as anesthesiologists, what do we need to know?

DR. JONES:

Well, I think that if someone comes in with an allergy to cetuximab, that should be your big red flag. But also, I mean, it's kind of easy to discount an allergy to red meat as something that's really not all that important or maybe just sort of a food intolerance. But if a patient comes in with a history of allergy to red meat or specifically, you know, I had anaphylaxis to cetuximab, then you need to think, well, it may be Alpha Gal Syndrome. And exposing these people to other drugs or formulations of drugs that were produced using mammal derived proteins could trigger an anaphylactic reaction.

DR. STRIKER:

As anesthesiologists, there's nothing specific we need to avoid. It's the general awareness of the potential for anaphylaxis to anything we do.

DR. JONES:

Well, I think there are things that we use every day or we encounter in the O.R. that you don't necessarily think are mammalian derived. Right? There is one study that found a high percentage of patients with IgG antibodies to Alpha Gal in people that had reactions to a factor seven. So activated factor seven is a recombinant human protein that is actually grown in a culture of, I kid you not, baby hamster kidney cells. All right. So being a non catalan mammal, baby hamster, kidneys, kidney cells are going to express alpha gal on all their surfaces. So that particular drug has a possibility of causing anaphylaxis in these people. There's a lot of talk about heparin because heparin is derived either from, you know, bovine or porcine sources. Heparin is so ubiquitous and we use it in such great amounts that we haven't really identified that as an allergy to heparin, but it's a potential concern. And surgicel, the hemostatic agents that they use by gallons in the spine room, right, that sort of thing, those are derived using other mammal proteins. And so anaphylaxis to the hemostatic agents, to some recombinant drugs that we use. There even been people that reacted to the gelatin coating on acetaminophen tablets because sometimes that gelatin is animal derived rather than plant derived. Magnesium spirit is in a lot of things. It's in a lot of suspensions of some drugs. Stearic acid is in a lot of tablets. Oxycodone and lactic acid is an injectable hydromorphone and injectable haloperidol. So some drugs have these inactive ingredients in them that can trigger this allergy.

DR. STRIKER:

Okay so, you know, we're practicing and we deal with this all the time. You have a patient that may have a reaction to something and we've given a number of medications, or it's at some point during the surgery where we're not exactly sure what the trigger was, and we have our big ticket items that we think of: antibiotics, muscle relaxants, what have you. And many times, if we don't know for sure, it may just be assumed that one of these things, or perhaps latex or something like that, was a cause. How does the practitioner go about delineating all this?

DR. JONES:

Well, if you have a patient that comes in with an allergy to red meat, you need to keep in the back of your mind that you could potentially have anaphylaxis to one of the drugs you're giving them. And just be aware of things that that, you know, that were produced

by with animal proteins. Now, there's a wonderful article, I think it's November 2019 in Anesthesia and Analgesia that was written by some folks at Duke. And they actually went so far as to have their pharmacists create a list of drugs you need to avoid in patients with suspected Alpha Gal syndrome. And what they determined was it was actually kind of hard to do outside of the biggest, you know, cetuximab recombinant proteins, topical thermostatic agents. Except for those, it's really hard to tell because the inactive ingredients don't necessarily have to be reported in a lot of things. But they spent an enormous amount of time creating this kind of list. And some people recommend pre treating with H one and H2 blockers and steroids prior to administering some of these drugs and people with alpha gal allergy.

DR. STRIKER:

But is there evidence out there that we can hang our hat on with regard to associations with patients that do have this allergy and specific medication?

DR. JONES:

Not particularly. The article from Duke talked a lot about concerns with heparin, but they really couldn't back that up much more than opinion. A lot of what you read is partly opinion, you know, and potentials for for allergies. Again, except in the case of Cetuximab. The Recombinant Factor seven argument was pretty strong in people that had Alpha Gal syndrome. And this one particular study of very high percentage of them, more than 50% of them, also reacted to recombinant factor seven if they did the allergy testing. And the other thing that makes this hard is that there's not an FDA approved allergy test for this. Right. So there is one there's one available, but it's not specifically FDA approved. So that makes it a little bit harder.

But I think from the average anesthesiologist, if someone has a red meat allergy, don't chalk it up to just indigestion. You know, I think maybe we need to be careful with drugs that I know could contain animal proteins. Now, albumin is fine. The albumin that we use clinically is human derived.

DR. STRIKER:

Okay, that's good to know.

DR. JONES:

So it's not a problem, but gelatin is and it makes you think, you know, I am mostly a cardiac anesthesiologist and we think about volume expanders all the time, right?

DR. STRIKER:

Sure.

DR. JONES:

We don't use the gelatin in this country, partly because of the very high incidence of allergic reactions. And I think that would actually make it even worse.

DR. STRIKER:

Yeah.

DR. JONES:

And I was thinking maybe maybe this is anaphylaxis. Now because the blood pressure drops. Look hinky. I'm thinking maybe. Well, maybe anaphylaxis just needs to be higher on my list when I run through my list of why are things going south?

DR. STRIKER:

Yeah. No, absolutely. Would you say a couple takeaway key points here are, number one, don't dismiss a red meat allergy as something that, just don't dismiss it outright, treat it as a potential true allergy. And then, number two, keep the substances in mind that that could trigger it so that your awareness is higher. And just be more aware and on your toes to treat anaphylaxis as it as it potentially rears its head during it during a case.

DR. JONES:

And the other thing is we're using more and more recombinant drugs or monoclonal antibody derived drugs that were produced that way. And so whereas historically, for example, when people took growth hormone, they actually got human growth hormone. Well, nowadays, I think you're giving a recombinant drug in place of that. And we're seeing more and more those types of drugs being produced compared to when I first started back in the Dark Ages. And so I think we need to be aware, I think a little bit about any drug that has MAB at the end of it is a monoclonal antibody. Right. And so it very potentially could have been derived from something that could precipitate an alpha gal allergy.

DR. STRIKER:

Well, before I let you go, is there anything more you'd like to tell our listeners about the 1980 volume of ACE, the issue, anything other topics that are highlighted or anything you want to discuss?

DR. JONES:

Well, one thing we go very carefully through ACE and try to identify, you know, different states have different licensing requirements. You know, Texas requires medical ethics and identification of human trafficking. New Mexico requires administration and chronic pain treatment CME for your license. And so in every volume of ACE will identify the questions that would help meet those criteria. And also, we've been awarded some patient safety credits. So each volume of ACE will be reviewed and they'll determine which questions would actually qualify as patient safety for MOCA. That'll be in the first part of the book. It'll probably vary from issue to issue, but you'll be able to pick up some patient safety credits doing ACE, and that's always been hard, at least for me to get all my patient safety credits in. But my my push for ACE, it comes out twice a year. It's each volume has 100 questions. Question, answer. And there are wonderful discussions. I think the strength of ACE is the material in the discussions. And there will be some beautiful color images. And the editorial board, we try to keep it balanced. We have chronic pain specialists, we have OB specialists, we have a couple of PD people, so and several cardiac and critical care. So we cross the board and we try to keep it as evenly distributed as we can. It's not a test. It's not like a high stakes exam. It's just the question is the hook to get you to read the discussion. And we hope it will be fun and interesting. And each volume qualifies for up to 30 Category one AMA credits. So if you do both volumes every year, you've got 60 credits.

DR. STRIKER:

Yeah, absolutely. It's the times I've done ACE I've I found it convenient, valuable, interesting. Personally, I have found it to be a really, really valuable tool to not only get your credits, but just as a general convenient overview and review of of a lot of different topics that we deal with in anesthesia. And so it's a I think it's a great program.

DR. JONES:

Well, thank you. Obviously, I do, too. And it's something that is is truly a labor of love for this editorial board.

DR. STRIKER:

Well, Dr. Jones, thanks so much for joining us, talking about this topic and also ACE in general. Really appreciate your time.

DR. JONES:

Thank you Dr. Striker, it's been wonderful.

DR. STRIKER:

I just want to put a thanks out to our listeners for tuning in and certainly tell other people about it and please tune in again next time to Central Line.

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