Delayed allergic reactions to mammalian meat induced by tick bites: a brief history of “alpha-gal allergy”

USDA/FSIS Undeclared Allergen Public Meeting

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A Mysterious Allergy Afflicts The South

by Jason Smith

When Bert O’Neil began giving Erbitux to colon-cancer patients in clinical trials, he had no reason to be wary. After all, the drug had already been tested and was FDA-approved for use in colon cancer.

But at Carolina’s Lineberger Comprehensive Cancer Center, the first three patients who received the drug had
The story got stranger as O’Neil talked to more oncologists. He heard that a colleague in Nashville, Tennessee, was finding the same problem. But when O’Neil spoke to oncologists from other areas of the country, they didn’t know what he was talking about. A prominent colorectal oncologist in New York “thought we were lying or crazy,” O’Neil recalls.

IgE to alpha-gal: a (very) brief history

O’Neil et al, JCO 2007

Dark blue = human
Light blue = murine
What is alpha-gal?

- Carbohydrate synthesized by the glycosylation enzyme alpha-1,3-galactosyltransferase

- **Alpha-gal is present on the tissues and cells of all lower mammals**

- Humans and apes, however, do not have alpha-gal due to an inactive gene product
II. Defining a “new” food allergy
Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-α-1,3-galactose

Scott P. Commins, MD, PhD, Shama M. Satinover, MS, Jacob Hosen, BS, Jonathan Mozena, MD, Larry Borish, MD, Barrett D. Lewis, MD, Judith A. Woodfolk, MBChB, PhD, and Thomas A. E. Platts-Mills, MD, PhD

Original articles

24 patients
Virginia & Missouri
- Symptoms delayed 3-6 hours after eating mammalian meat
- Prick skin test often less than 4mm
- Intradermal skin test positive
Skin Testing Results: Often <4mm SPT

Prick test performed using lancette and intradermal testing with 25 gauge needle in the same patient on a single clinic visit.
Immuoassay of Specific IgE Abs in Patients with anti-Gal IgE
Subject #FC-07: sIgE to alpha-gal = 9.3 IU/mL; Total IgE = 204

Whole blood was collected, fixed & stained

6 hours after consuming 56g of pork sausage, subject released with (disappointing) mild itch and single hive
Approximately 7.5 hours after eating sausage
Approximately 8.25 hours after eating sausage
Mammalian meat challenge
Subject #FC-08: sIgE to alpha-gal = 30.3 IU/mL; total IgE = 146

Before 3hrs 45min after pork sausage
Diffuse urticaria appeared at 4hrs 15min after pork sausage (left arm shown here)
Mammalian meat challenge
Subject #FC-10: sIgE to alpha-gal = 29.1 IU/mL; total IgE = 201

4hrs 25min after eating pork sausage: pruritus followed by urticaria on right flank
• Avoidance diet:
  - Mammalian meat, esp fatty cuts (ice cream)
  - Dairy and cheese usually tolerated

• Caution re: exercise, alcohol, recent tick bites

• Counsel re: bioprosthetics (valve, ligaments, etc) and vaccines (Zostavax, ?MMR)

• For some patients, other foods and products become an issue…
Gelatin

Strip can contain lanolin
Does “Natural Beef Flavor” create a risk for patients allergic to alpha-gal?
IV. TICKS. REALLY?
Geographical distribution of cetuximab hypersensitivity reactions

As reported by O’Neil et al, JCO 2007
Geographical Incidence of Rocky Mountain Spotted Fever

Data from CDC website for 2009; accessed 2/2011
Total IgE versus IgE to Alpha-Gal

R = 0.78
P < 0.001

- Report tick or chigger bite(s)
- No history obtained for tick bite(s)
- Specifically deny tick bite(s)
Distribution of known cases of delayed anaphylaxis to mammalian meat

Commins SP, James HR, Kelly LA...Platts-Mills TAE. The relevance of tick bites to the production of IgE ab to the mammalian oligosaccharide galactose-α-1,3-galactose. J Allergy Clin Immunol 2011
Geographical range of *Amblyomma americanum* population

Data from CDC website; accessed 10/2010
Geographical range of *Amblyomma americanum* population

Data from CDC website; accessed 9/2012
IgE to Alpha-gal and Total IgE Rise Following Tick Bites

- IgE to Alpha-gal and Total IgE
- Rise Following Tick Bites

Graph:
- IgE (IU/mL) on the y-axis:
  - July 10
  - Sept 7
  - Sept 21
  - Oct 5
  - Oct 19
- Alpha-gal sIgE
- Total IgE

Data points:
- July 10: Total IgE
- Sept 7: Total IgE
- Sept 21: Total IgE
- Oct 5: Total IgE
- Oct 19: Total IgE

Graph comparison:
- Alpha-gal sIgE
- Total IgE
Tracking IgE to Alpha-gal and Total IgE over Time (E202)

Red bars = episodes of multiple tick bites
Tracking IgE to Alpha-gal and Total IgE over Time (E202)
Early and Late Response to Tick Bite in Patient with IgE Ab to alpha-Gal
Skin testing with 1:100 dilution of 1mg/mL Lone Star tick extracts
SUMMARY

• We have described an entirely new form of food allergy that can break well-established oral tolerance

• Evidence suggests that tick bites can affect total and specific IgE levels in some patients

• Additional tick bites may lead to more significant increases in the IgE response

• Preliminary data show the alpha-gal response to ticks can be replicated using a mouse model
JAPANESE FOOD

Jellyfish Stings Might Make You Allergic to Natto

ALEX SWERDLOFF
MAY 27 2015, 2:30PM