

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



USDA/FSIS Undeclared Allergen Public Meeting

March 16, 2017

Scott P. Commins, MD, PhD
Associate Professor



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

CONTRIBUTORS

Tom Platts-Mills

Tina Merritt

Lisa Workman

Alex Schuyler

Maya Jerath

Shailesh Choudhary

Onyinye Iweala

Shahid Karim

Gary Crispell

Anubha Tripathi

Loren Erickson

Kelly Cox

Walter Oliveira

Josh Kennedy

Hayley James

Whitney Stevens

Shama Satinover

Libby Kelly

Kiho Lee

Rob Rhoads

Samer El-Kadi

Cate Beach

Scott Boyd

Tho Pham

Barrett Lewis

Michael Land

Joey Lane

Gary Rakes

Erin McGintee

Luis Matos

Saju Eapen

Dane McBride

Overview · Tuesday, January 1, 2008

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.



[Click to read photo caption.](#) Photo by Jason Smith; ©2008 Endeavors.

But at Carolina's Lineberger Comprehensive Cancer Center, the first three patients who received the drug had



Regarding cetuximab HSR:

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.

From "A Mysterious Allergy Afflicts the South" by Sheila Read in *Endeavors*, 24:2, 2-3, 2008.

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,^a Shama M. Satinover, MS,^a Jacob Hosen, BS,^a Jonathan Mozena, MD,^b Larry Borish, MD,^a Barrett D. Lewis, MD,^c Judith A. Woodfolk, MBChB, PhD,^a and Thomas A. E. Platts-Mills, MD, PhD^a *Charlottesville and Fredericksburg, Va, and Springfield, Mo*

JACI, February 2009

- 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 $<4\text{mm}$ SPT



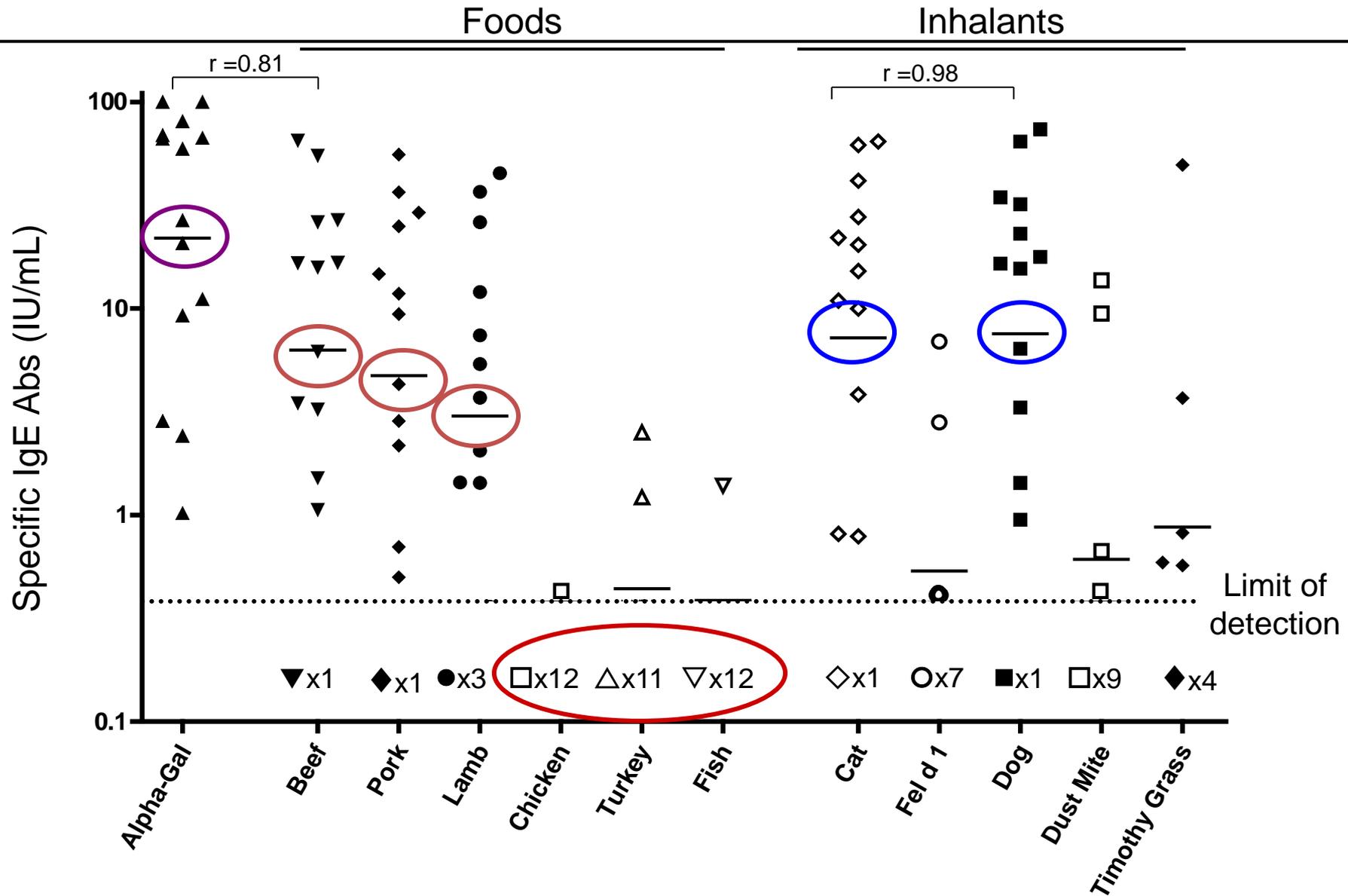
PRICK TEST



INTRADERMAL

Prick test performed using lancette and intradermal testing with 25 gauge needle in the same patient on a single clinic visit.

Immunoassay 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



Subject #FC-08: Mammalian meat challenge

**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: bioprosthesis (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?



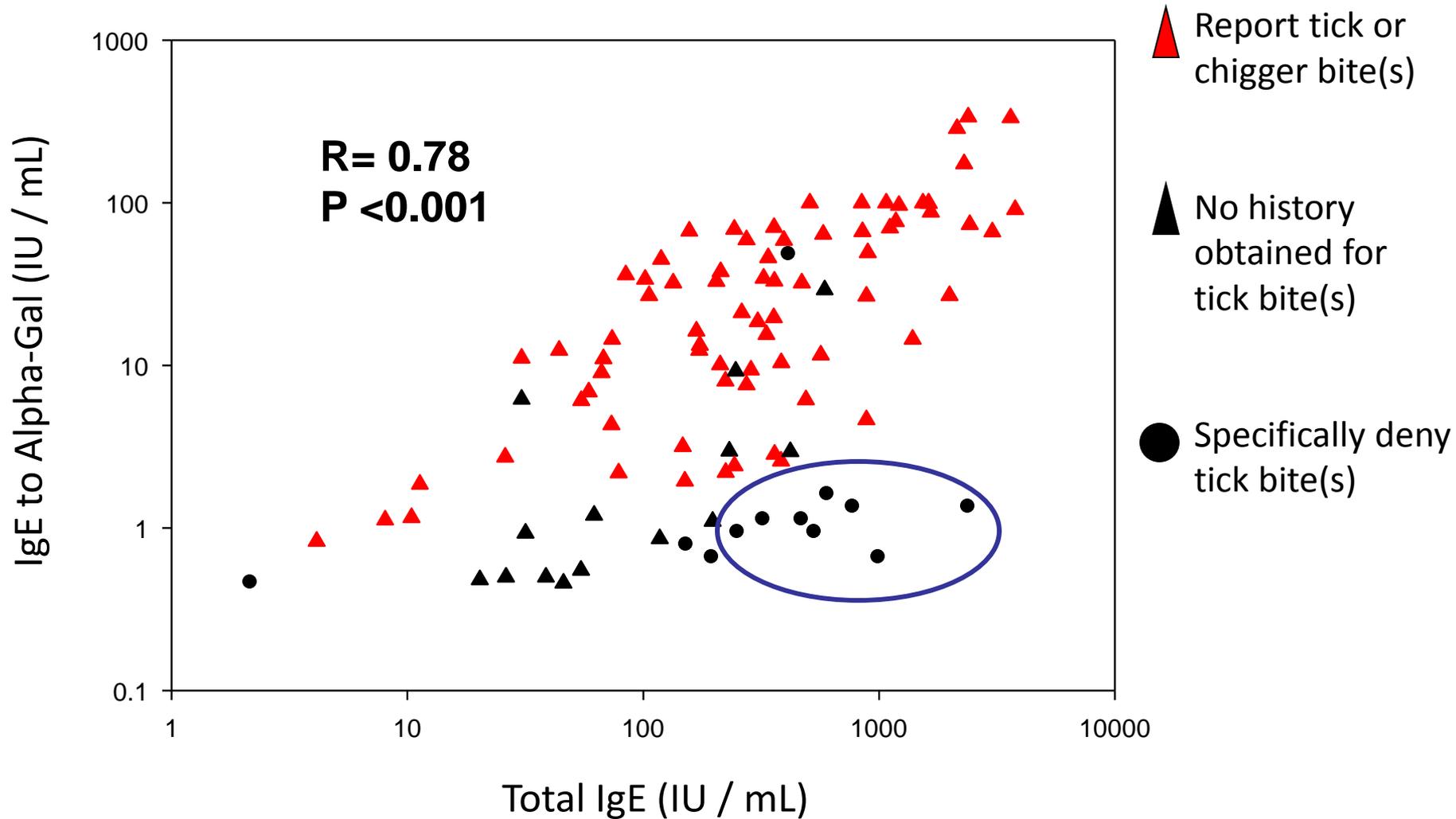
IV. TICKS. REALLY?

Geographical distribution of cetuximab hypersensitivity reactions



As reported by O'Neil et al, JCO 2007

Total IgE versus IgE to Alpha-Gal

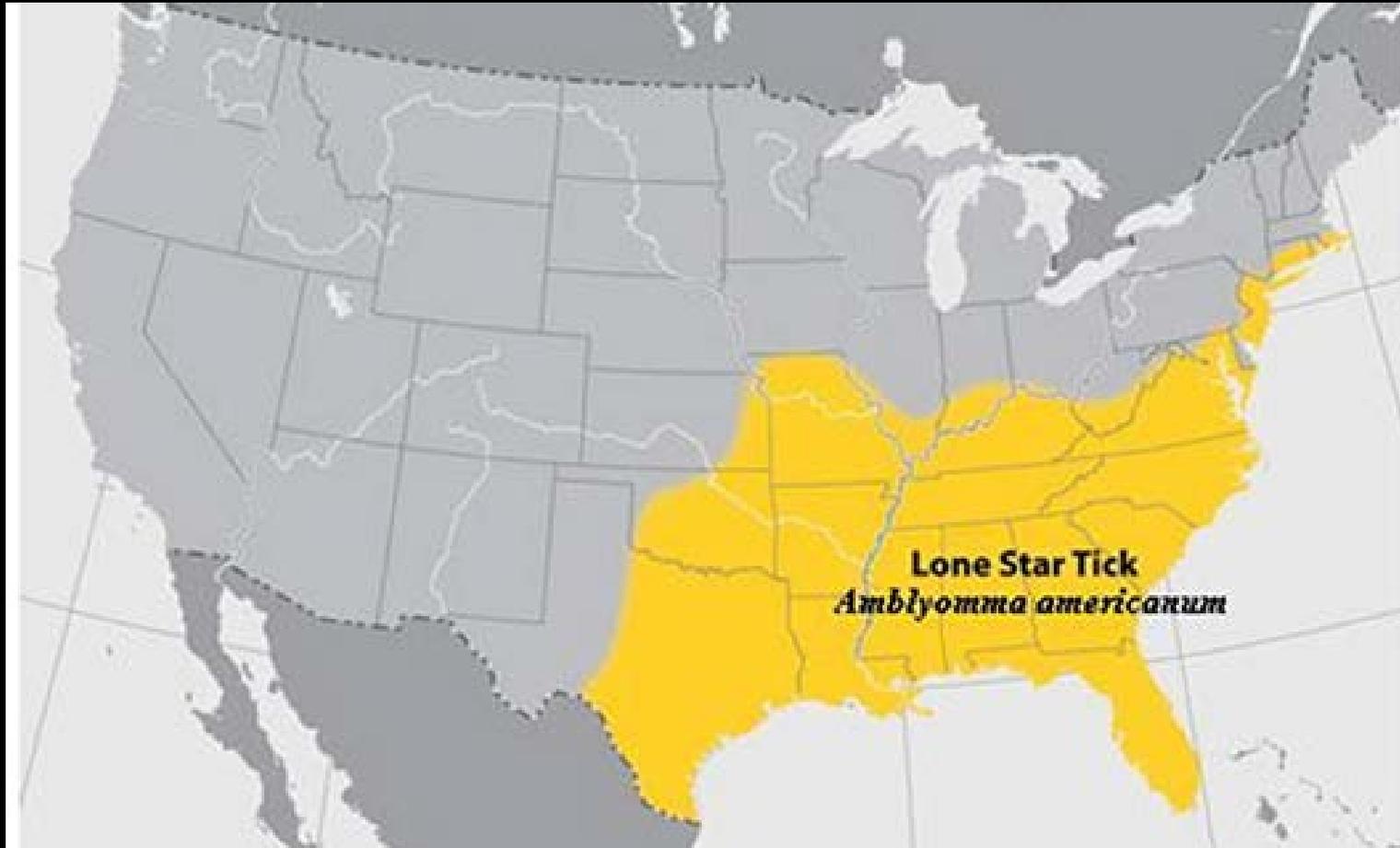


Distribution of known cases of delayed anaphylaxis to mammalian meat



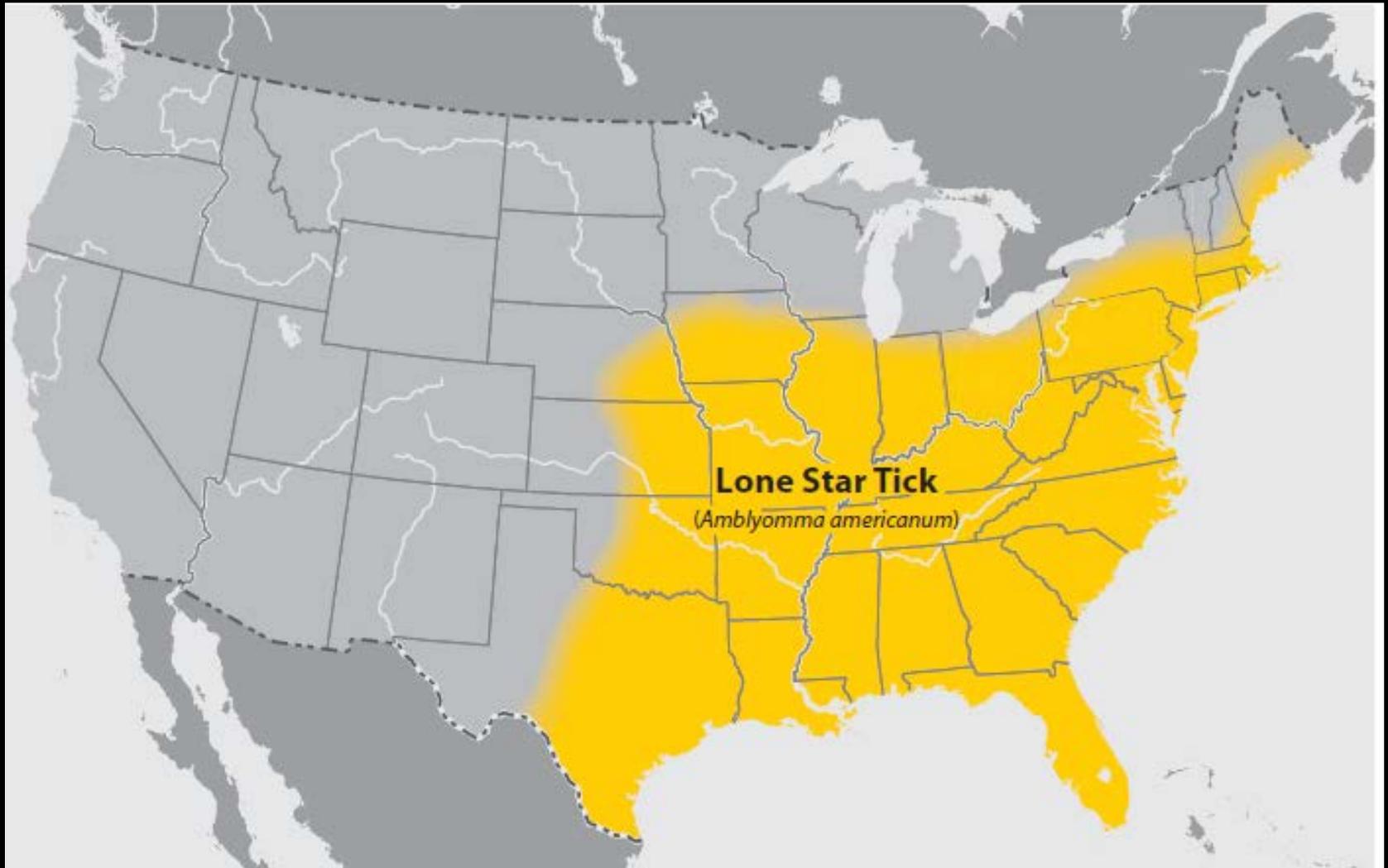
Commins SP, James HR, Kelly LA...Platts-Mills TAE. The relevance of tick bites to the production of IgE ab to the mammalian oligosaccharide galactose- α -1,3-galactose. *J Allergy Clin Immunol* 2011

Geographical range of *Amblyomma americanum* population



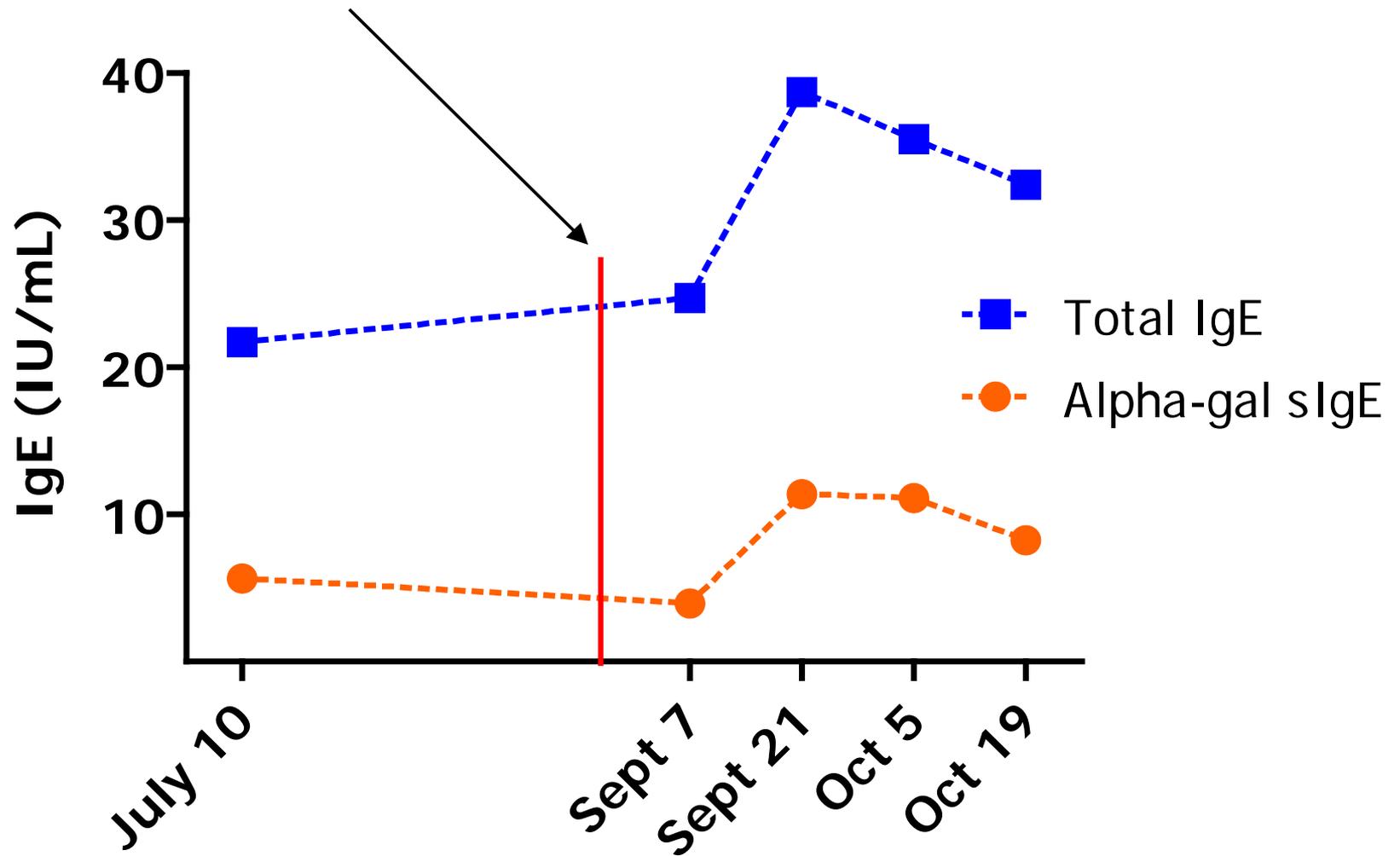
Data from CDC website; accessed 10/2010

Geographical range of *Amblyomma americanum* population

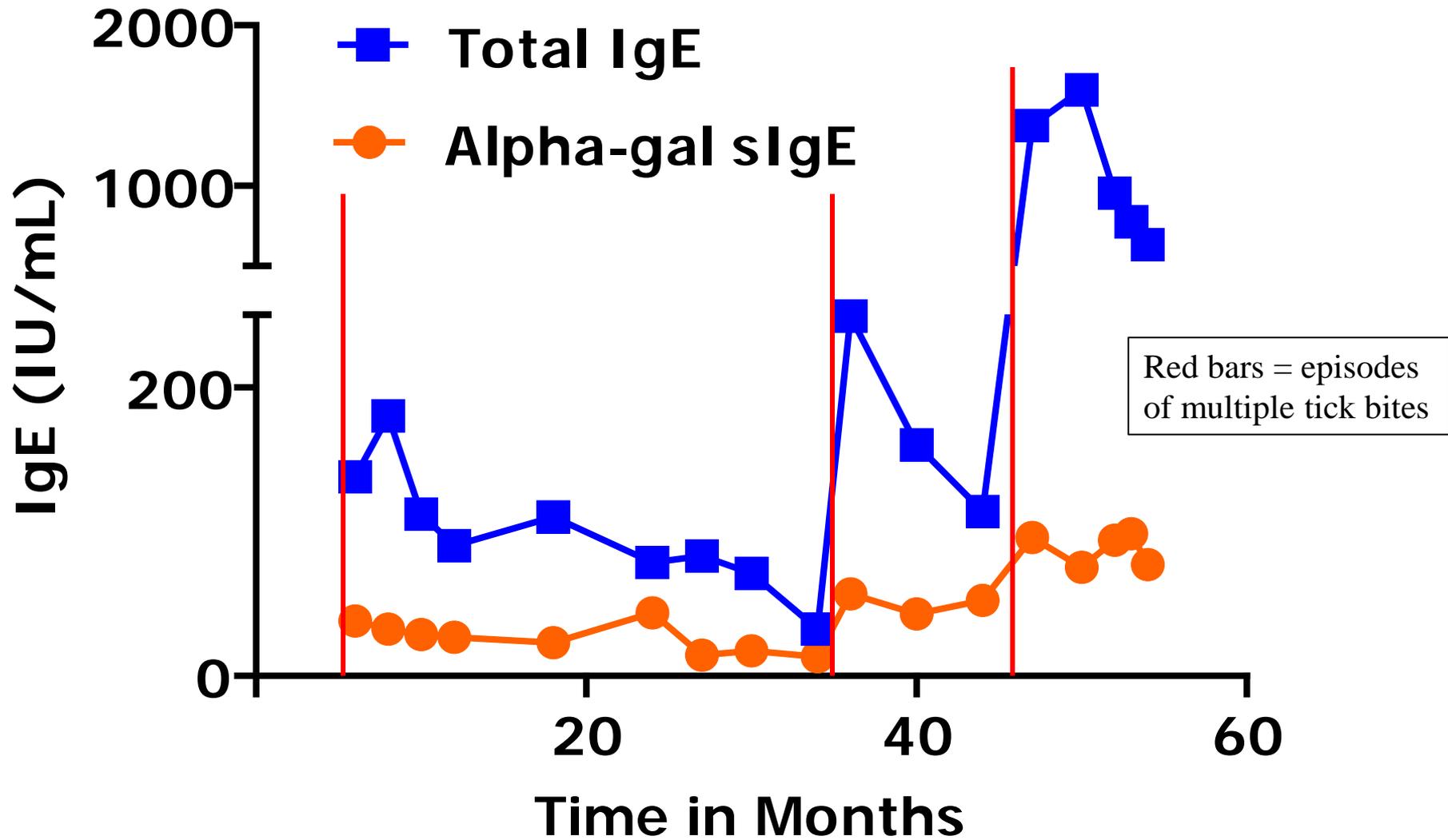


Data from CDC website; accessed 9/2012

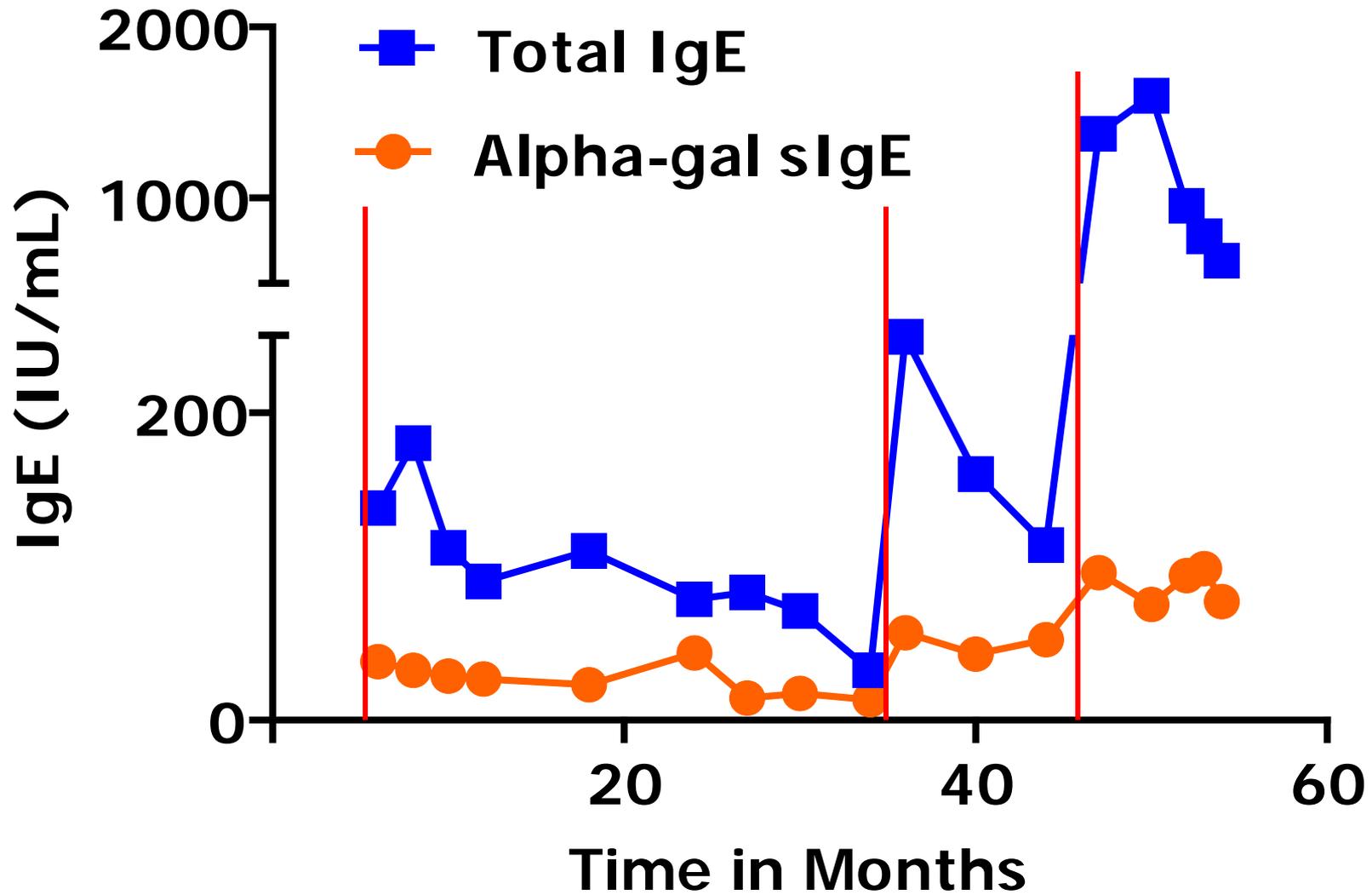
IgE to Alpha-gal and Total IgE Rise Following Tick Bites



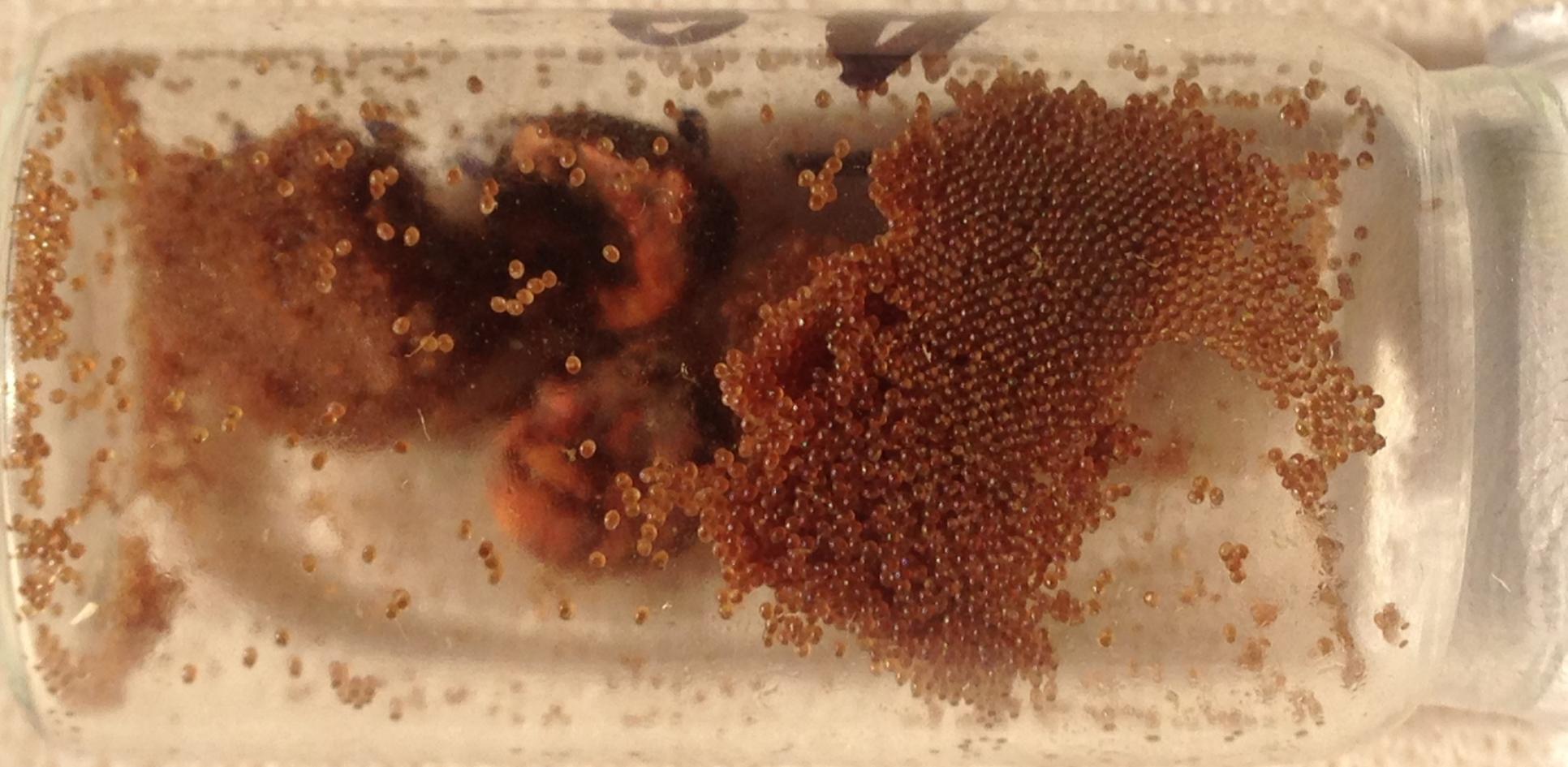
Tracking IgE to Alpha-gal and Total IgE over Time (E202)



Tracking IgE to Alpha-gal and Total IgE over Time (E202)



LONE STAR TICKS: EGG CLUSTERS







Deer tick nymphs



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

AS

ALEX SWERDLOFF
MAY 27 2015, 2:30PM

