

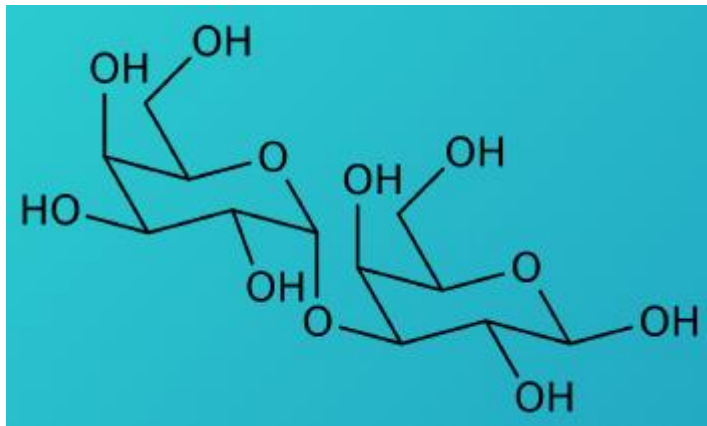
Alpha-gal Syndrome



Slides prepared by: Elena Diskin, MPH

What is alpha-gal?

- Carbohydrate named Galactose-alpha-1,3-galactose found in mammalian tissue
 - i.e., cattle, sheep, swine
- Humans, greater apes, old world monkeys, fish, birds, reptiles do not have this molecule



What is alpha-gal allergy?

Alpha-gal allergy is an allergy to the alpha-gal sugar molecule that is present in mammalian meat or mammalian derived products like...

- Red meat (beef, pork, venison)
- Gelatin
 - Vaccines made with gelatin (MMR, Rabies, Varicella, Yellow Fever, FluMist, Herpes zoster...)
- Carrageenan- made from red algae (common in cosmetics)
- Xenotransplantations (pork heart valves)
- Wool, leather, etc.
- Dairy
- Dog food
- Weird things- cane sugar, red wines, lip balm

What causes an alpha-gal allergy reaction?



Bite of a Lone Star Tick

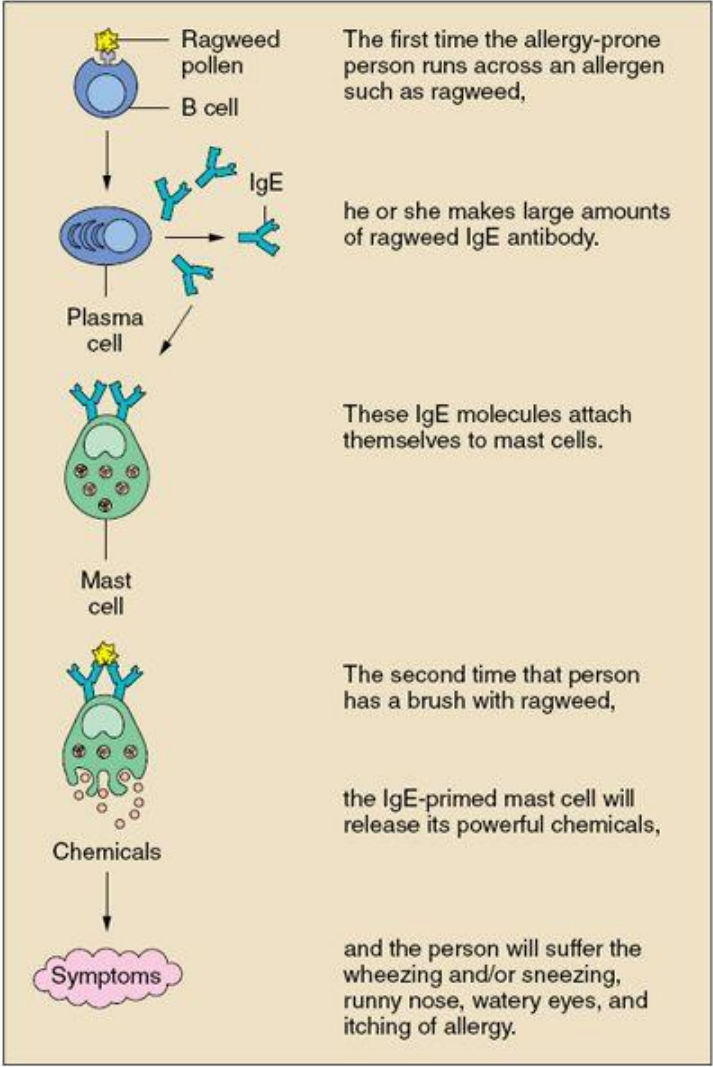
****exact mechanism unknown****

In some people the body makes IgE antibodies to alpha-gal sugar

****1-3 months after tick bite****

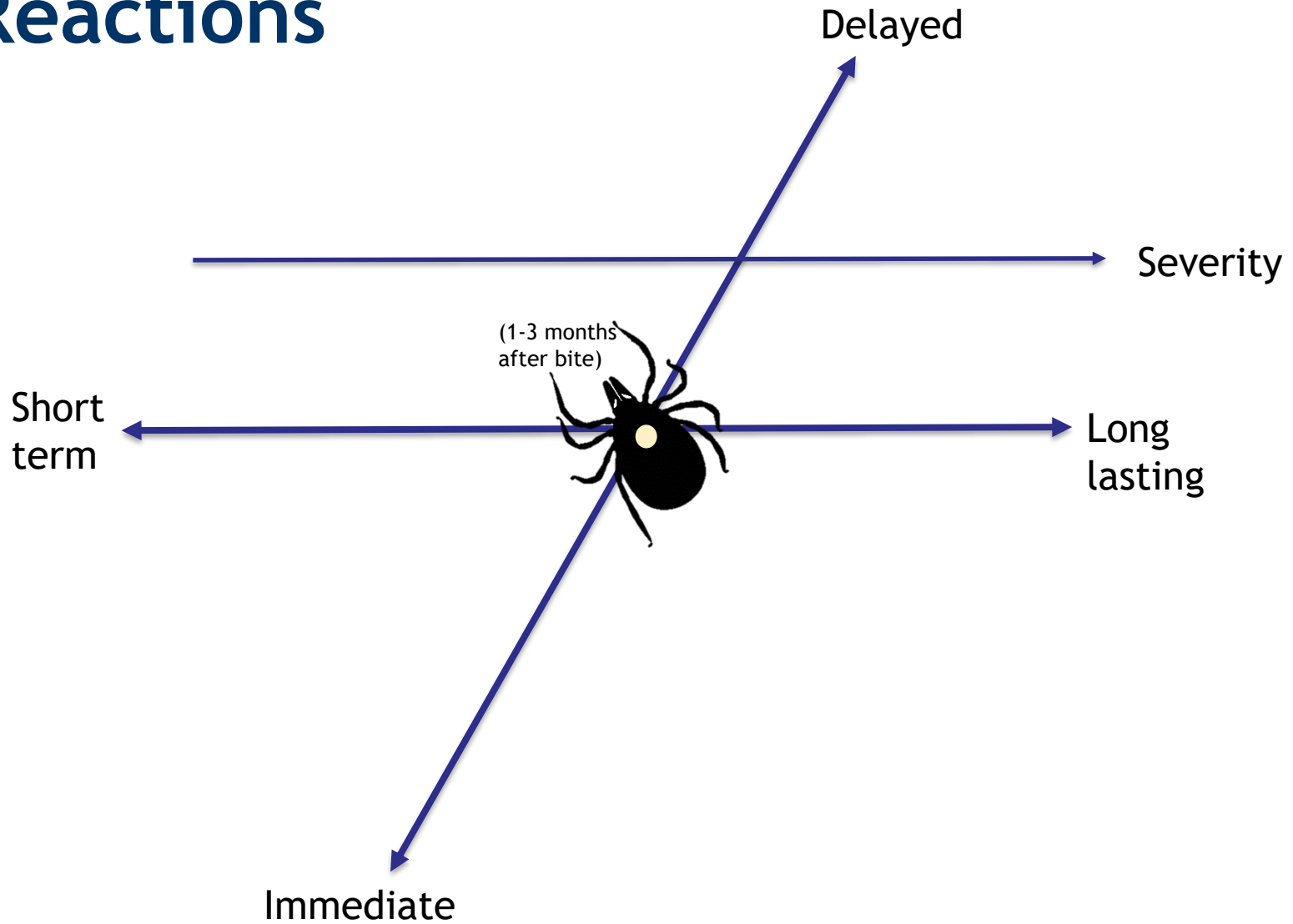
IgE antibodies attach to mast cells

When person consumes food containing alpha-gal or receives IV containing alpha-gal, mast cell releases histamines and other chemicals causing an allergic reaction of varying severity

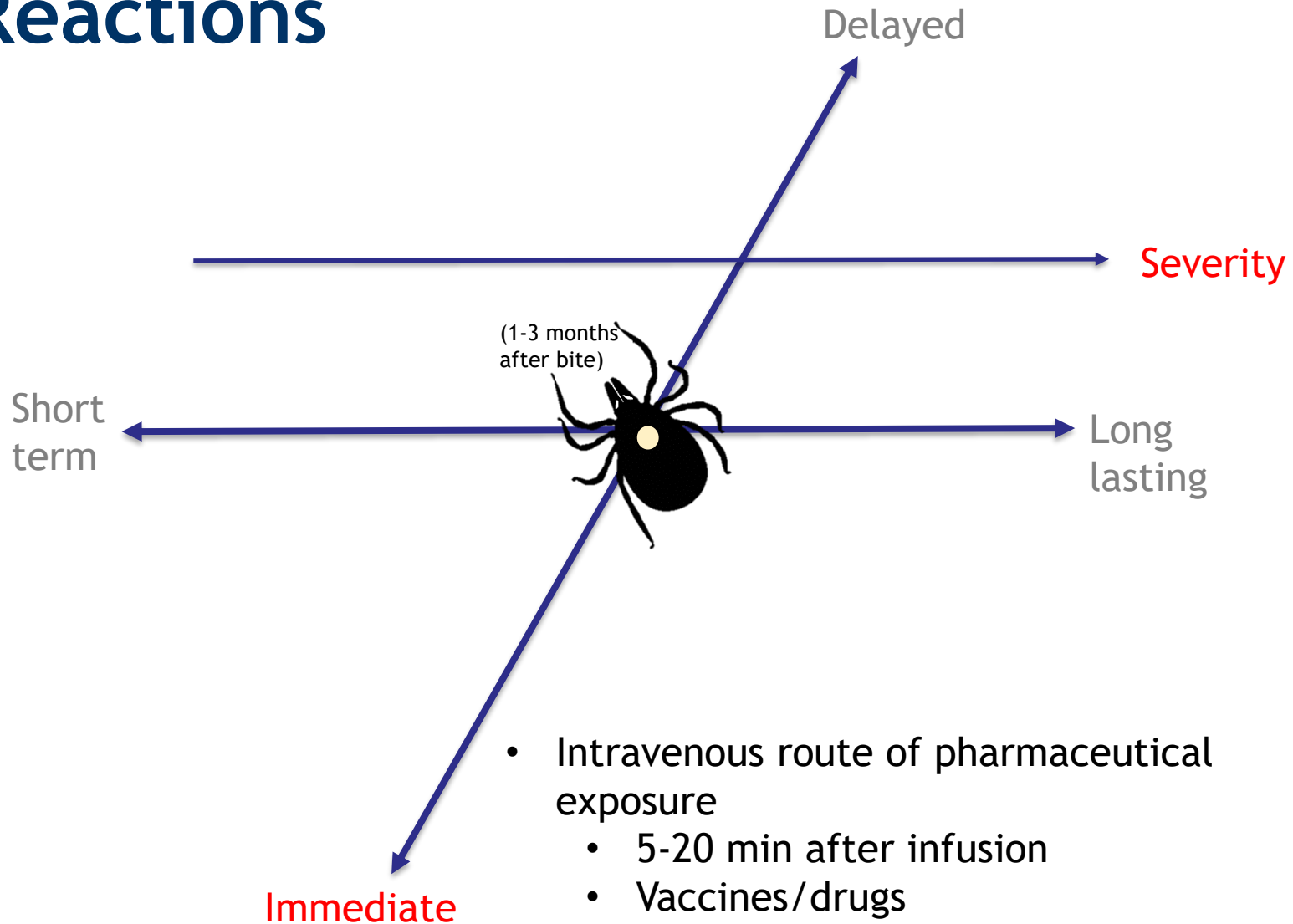


http://www.imgt.org/IMGTEducation/Tutorials/ImmuneSystem/UK/the_immune_system.pdf

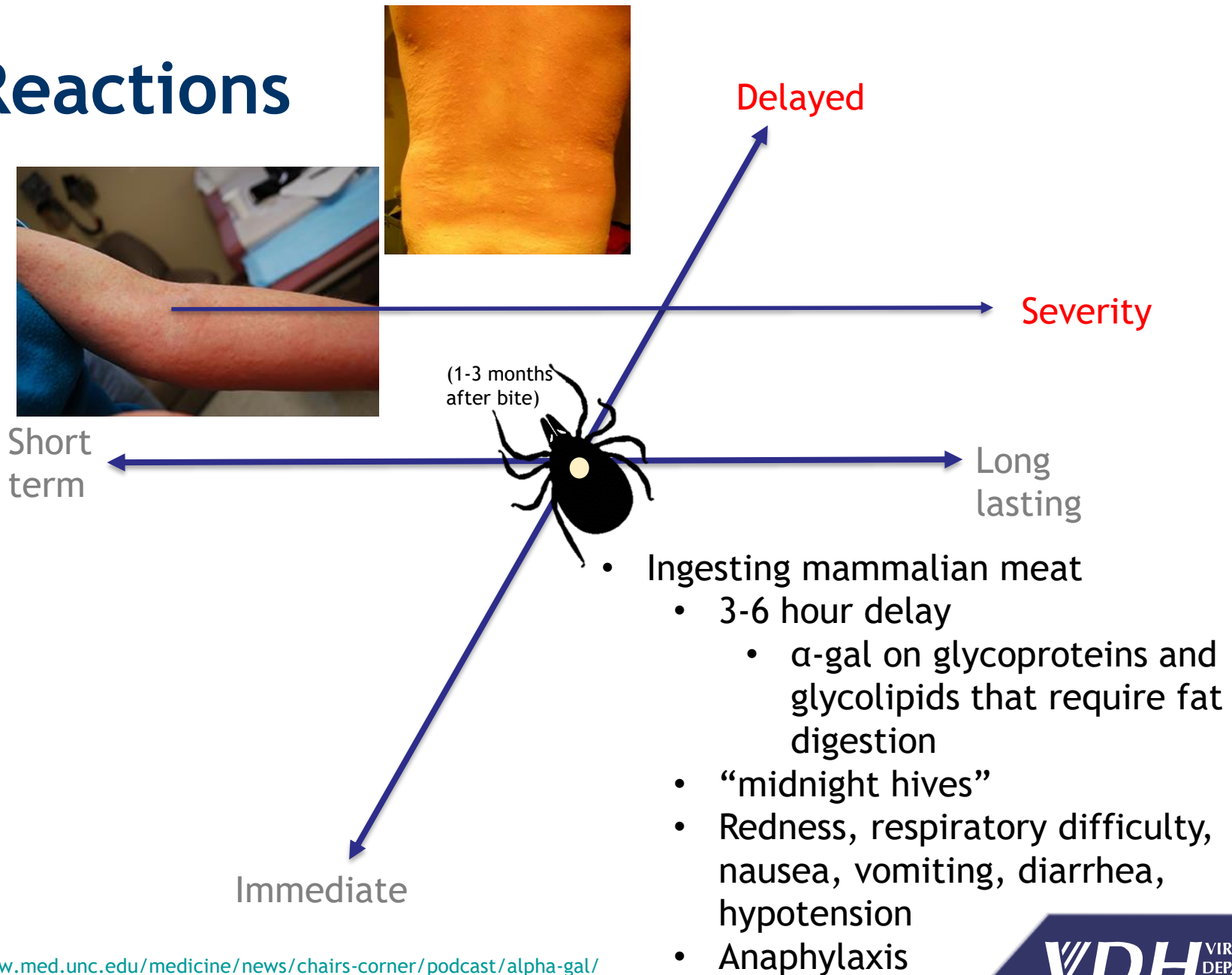
Reactions



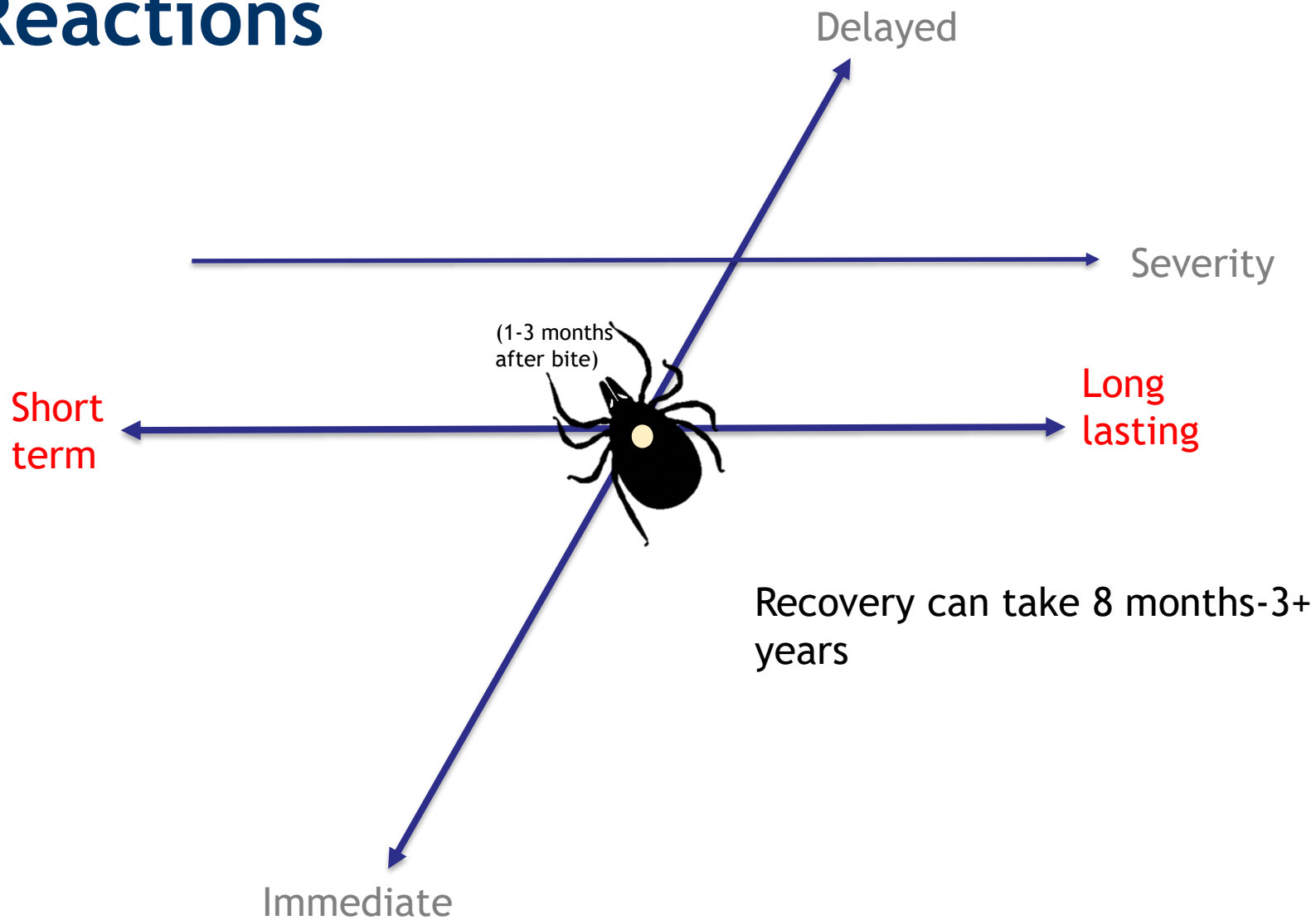
Reactions



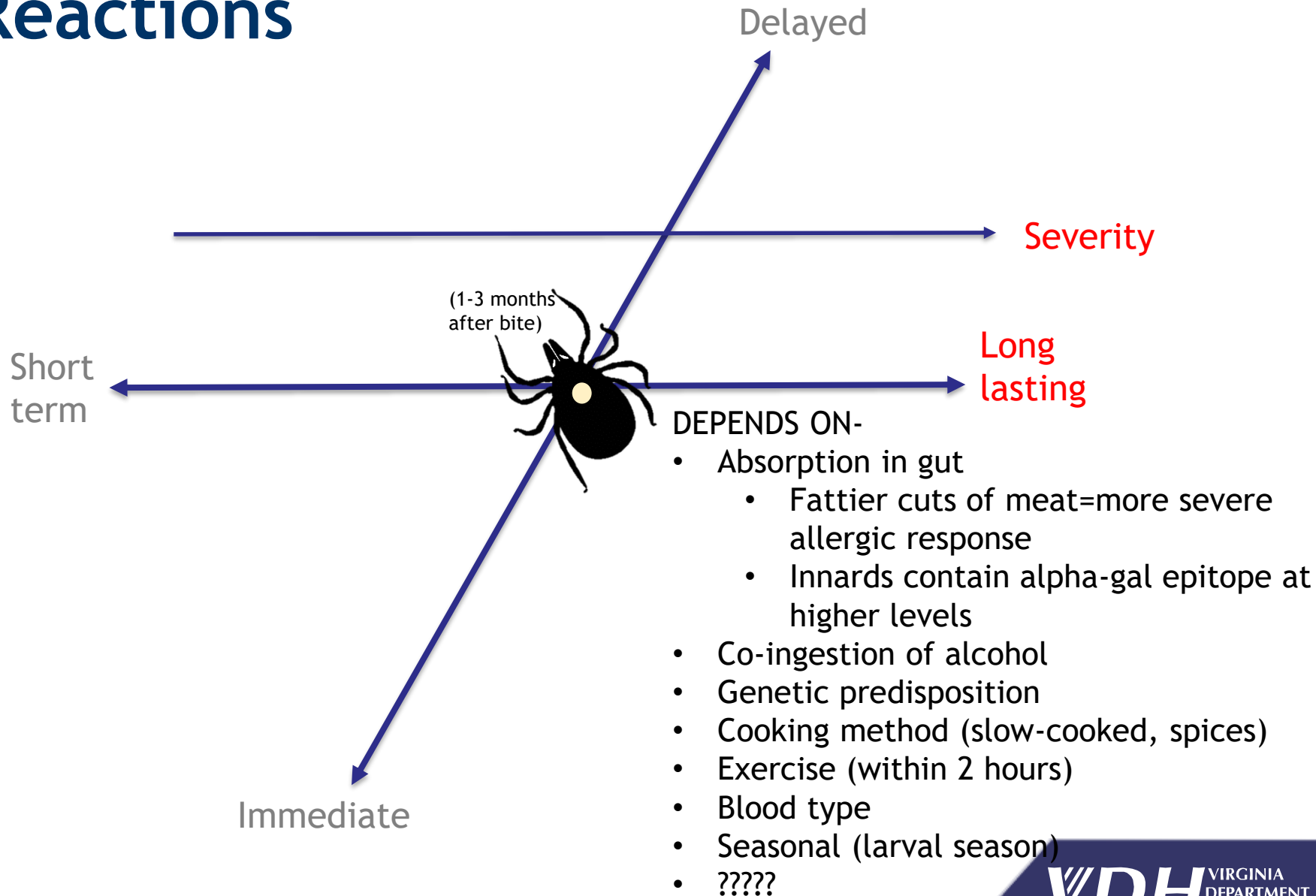
Reactions



Reactions



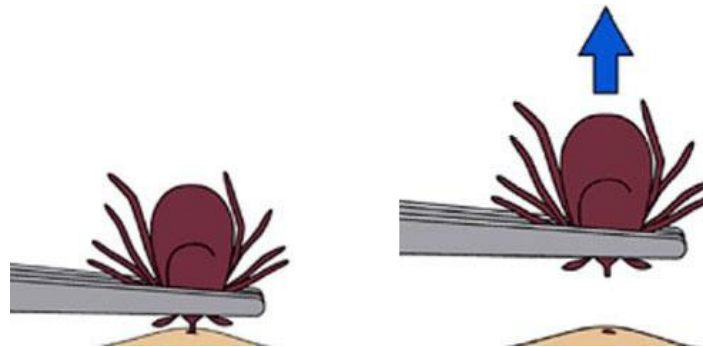
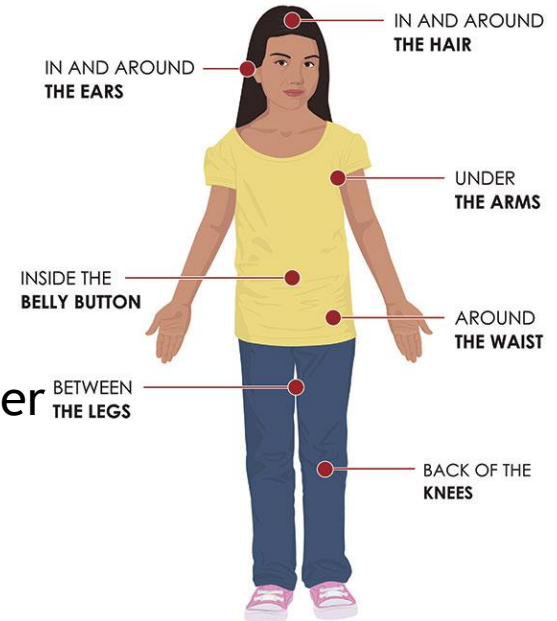
Reactions



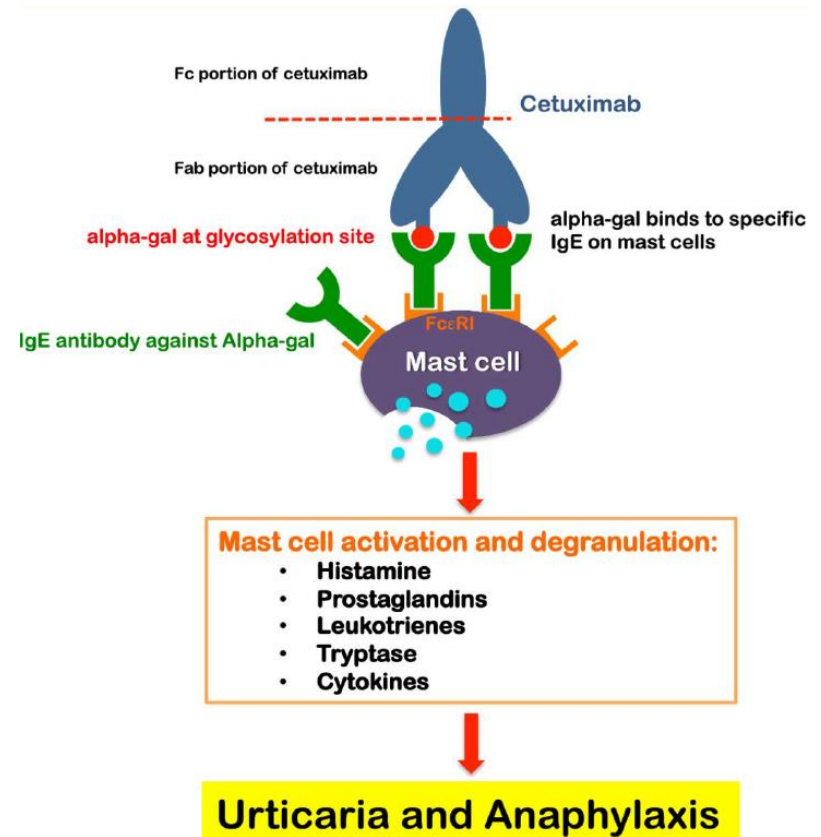
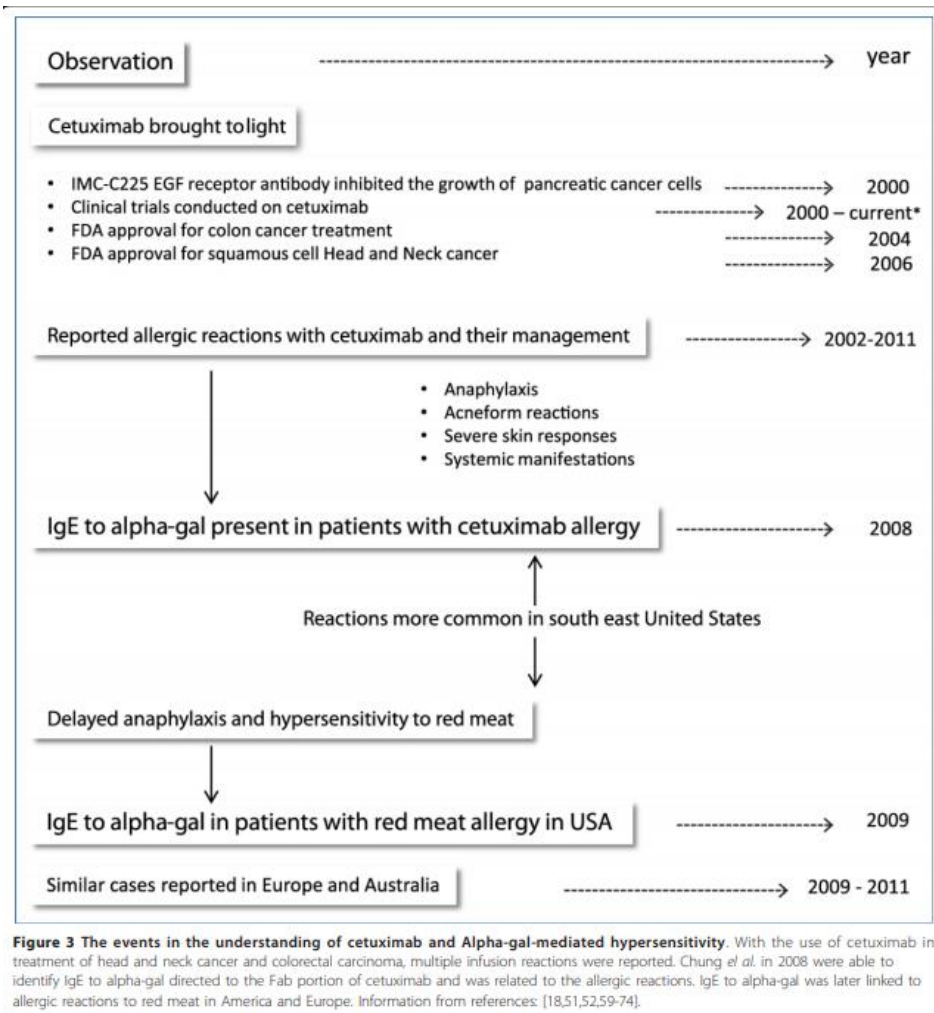
Prevention

Standard tick prevention

- Treat clothing/gear with permethrin
- Tuck pant-legs into socks
- Avoid wooded and brushy areas & walk in center of trails
- Check for ticks after outdoor activity
 - On you
 - On others
 - On your pet
 - On your gear
- If found, remove properly as soon as possible
 - Save for ID



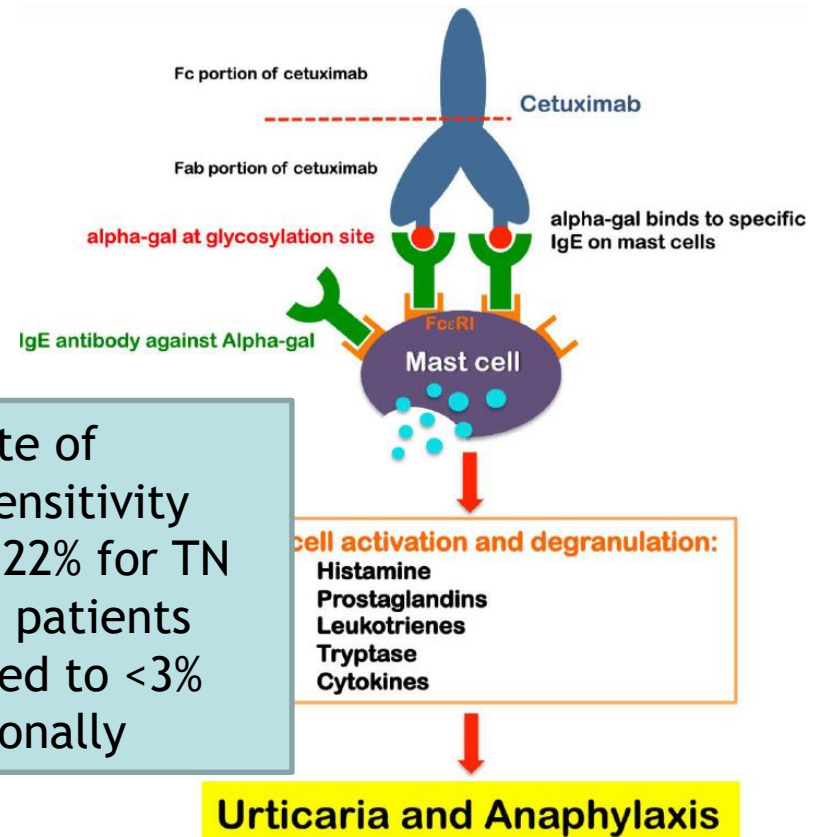
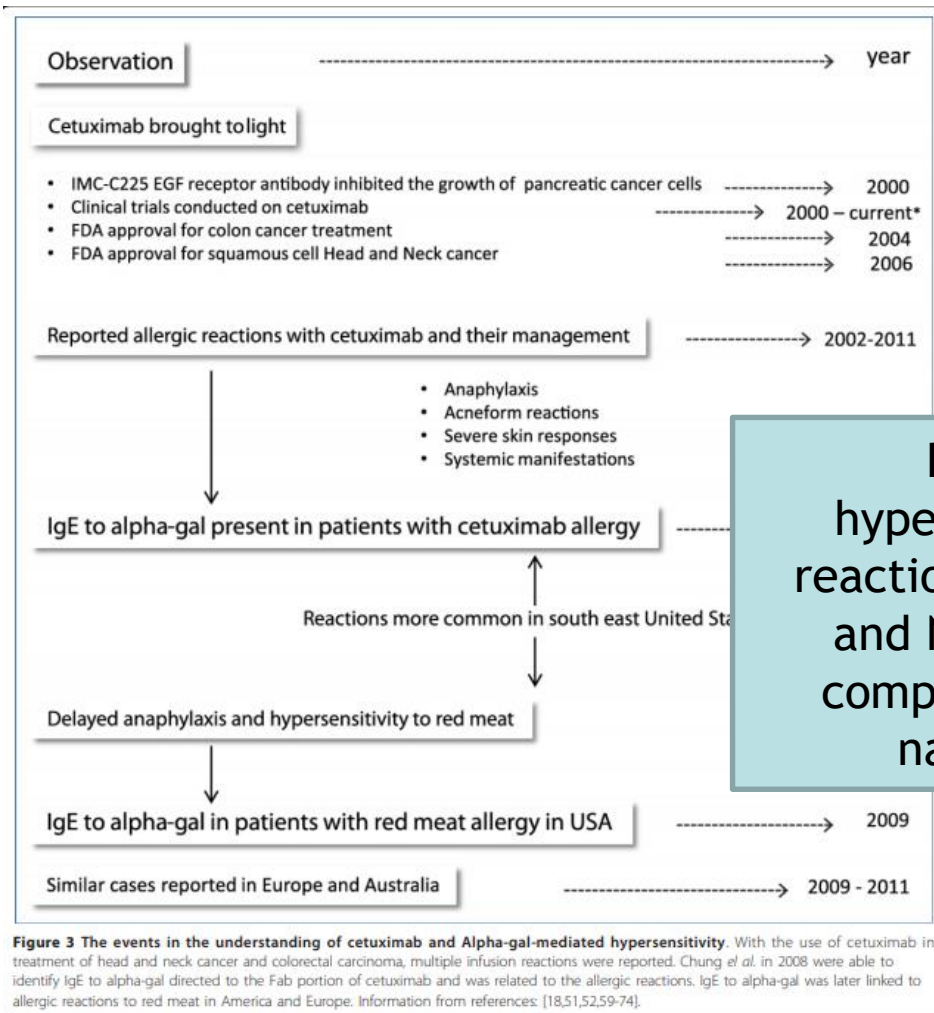
How was this discovered?



Saleh et al. (2012) Anaphylactic reactions to oligosaccharides in red meat: a syndrome in evolution. Clin. Mol. Allergy 10: 5. (11 pp.)

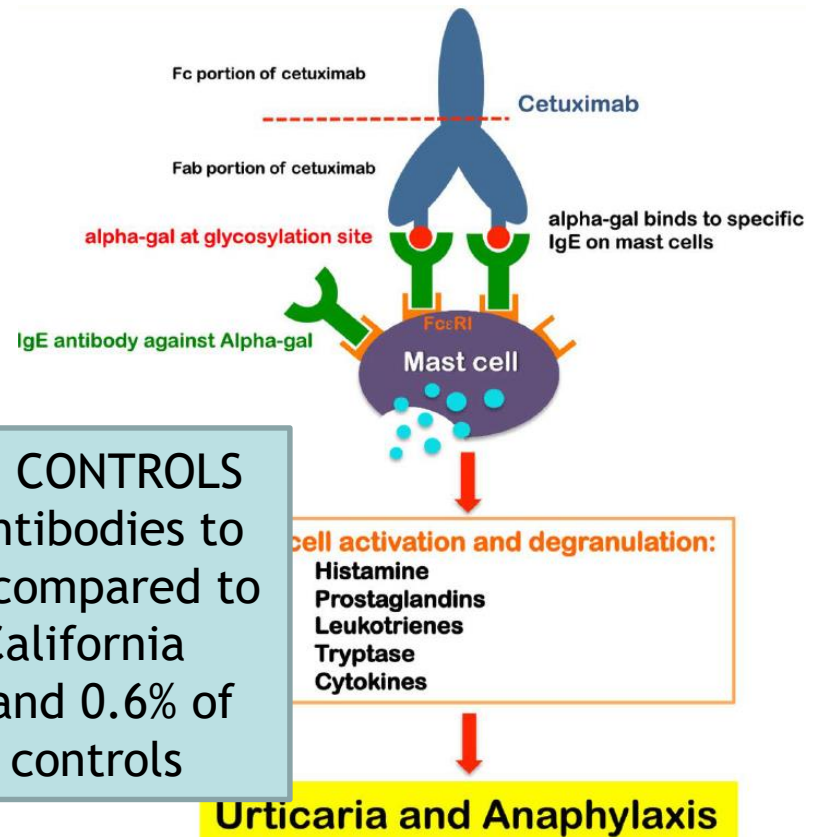
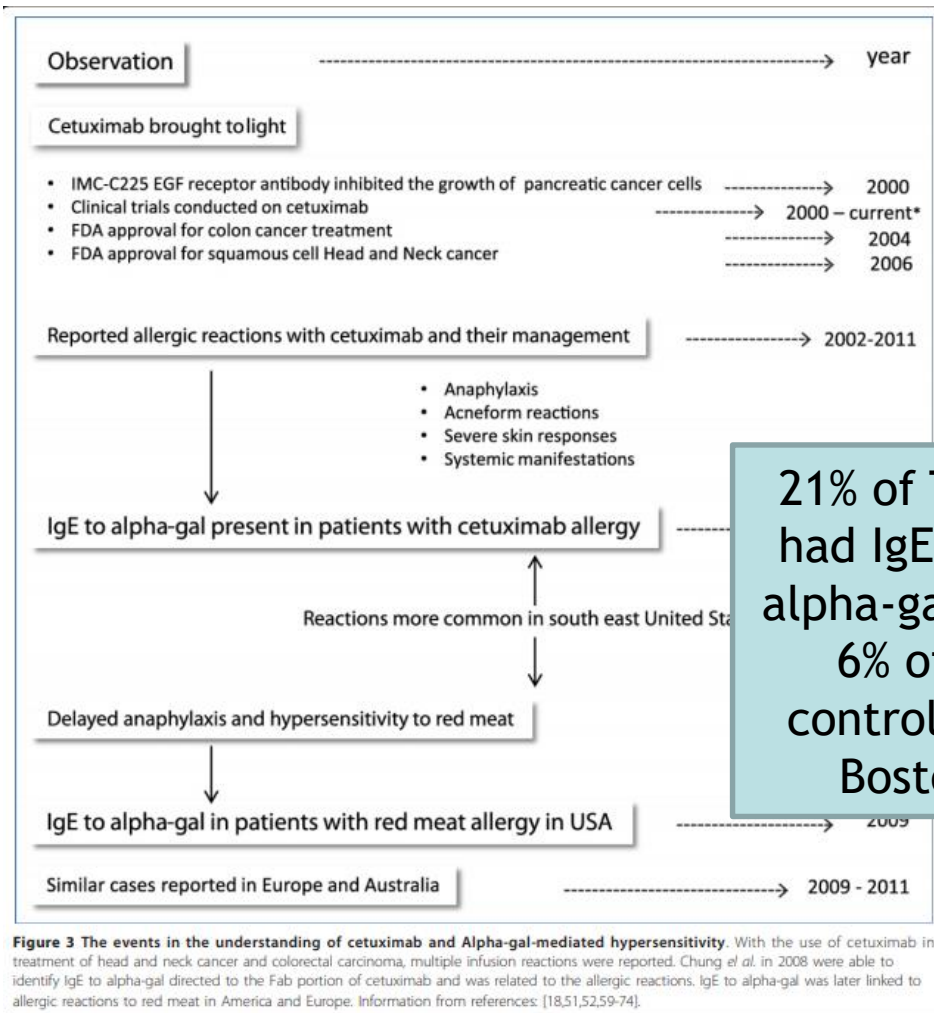
O'Neil et al. (2007) High incidence of cetuximab-related infusion reactions in Tennessee and North Carolina and the association with atopic history. J. Clin. Oncol. 25: 3644-3648.

How was this discovered?



Rate of hypersensitivity reaction 22% for TN and NC patients compared to <3% nationally

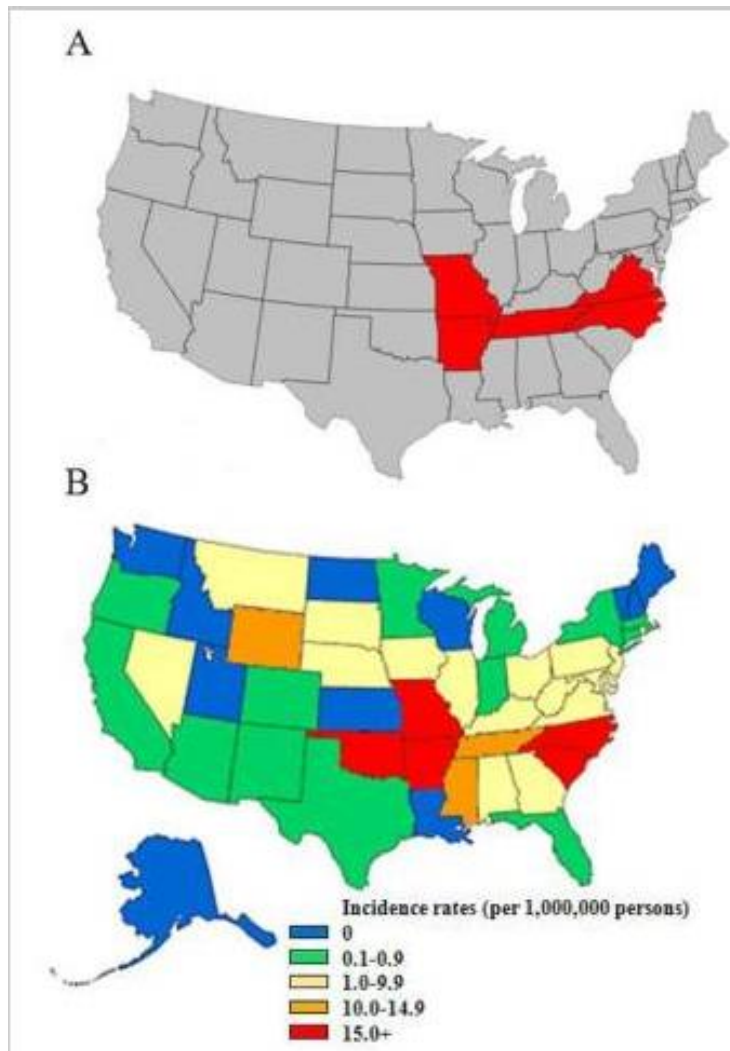
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Association of ticks with mammalian meat allergy



A) Distribution of cetuximab hypersensitivity

B) Incidence map of RMSF in the USA
(Vectored by Lone star tick, American dog tick, Brown dog tick)

Association of ticks with mammalian meat allergy

C



A) States with red meat allergies identified

(65 cases AR, 14 GA, 8 MD, 5 MS, 30 MO, 35 NC, 25 OK, 40 TN, **>200 VA**)

D



B) Distribution of *Amblyomma americanum* (Lone Star Tick) in US

Association of ticks with mammalian meat allergy

C



A) States with red meat allergies identified

(65 cases AR, 14 GA, 8 MD, 5 MS, 30 MO, 35 NC, 25 OK, 40 TN, **>200 VA**)

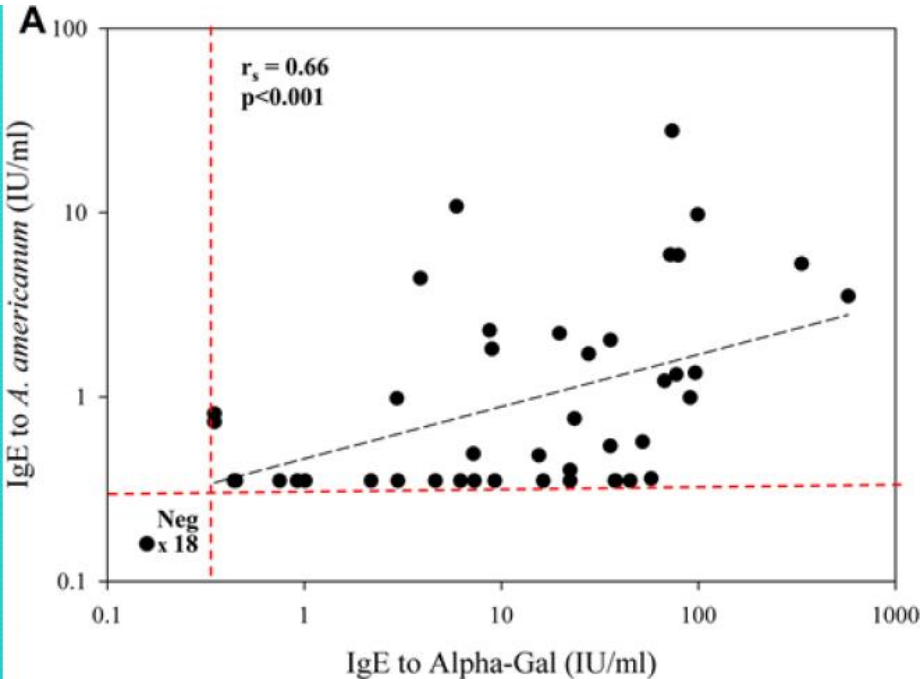
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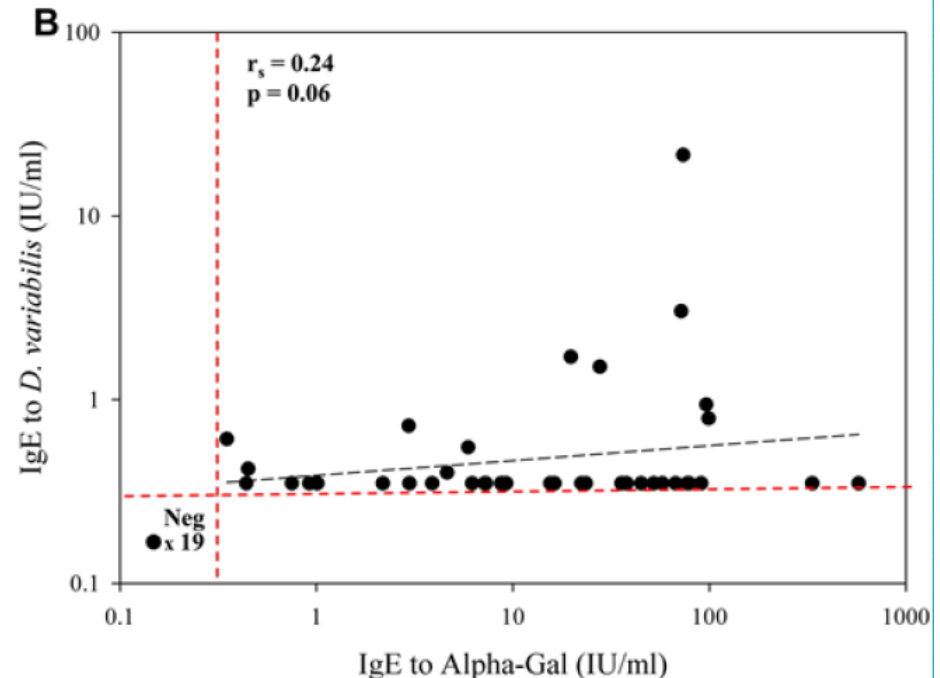
B) Distribution of *Amblyomma americanum* (Lone Star Tick) in US



Association of ticks with mammalian meat allergy



Amblyomma americanum
Lone star tick



Dermacentor variabilis
American Dog tick

US Burden

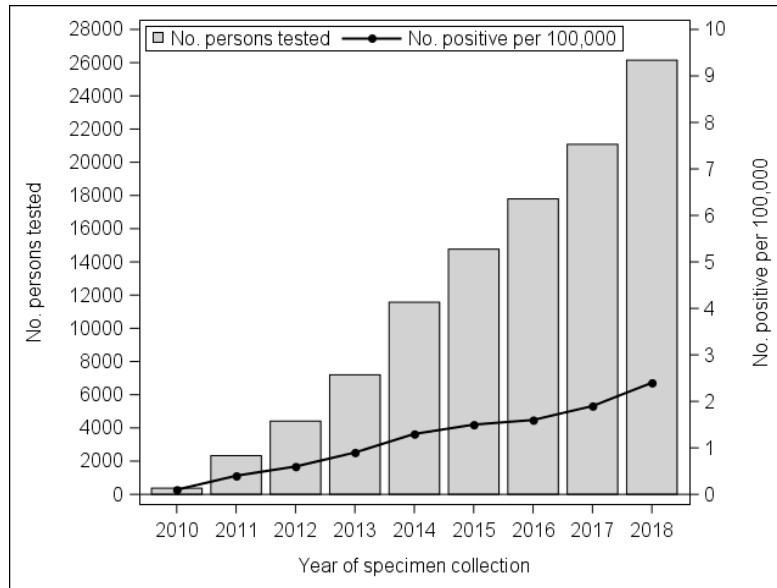


Patient reported incidence of alpha-gal (Zee Maps, 2017)

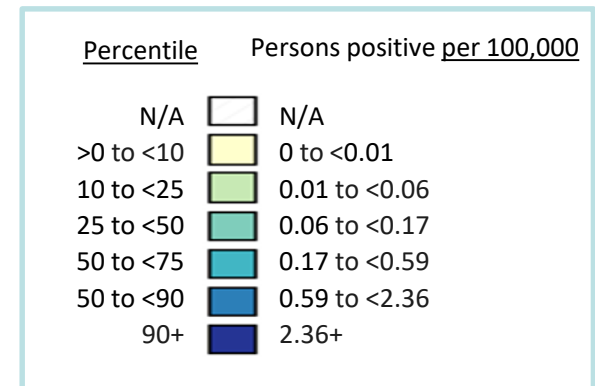
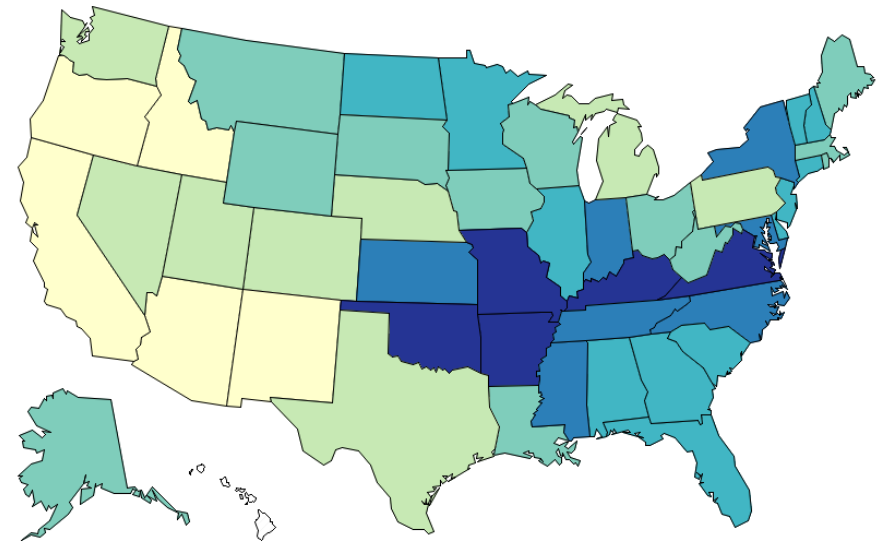
Persons positive per 100,000 population by state, 2010-2018 (n=15,091)

US Burden

No. persons tested and percent positive annually, 2010-2018



- **No. persons tested:**
 - 2010: 372
 - 2018: 26,148 (70-fold increase)
- **No. persons positive:**
 - 2010: 0.07 per 100,000
 - 2018: 2.39 per 100,000



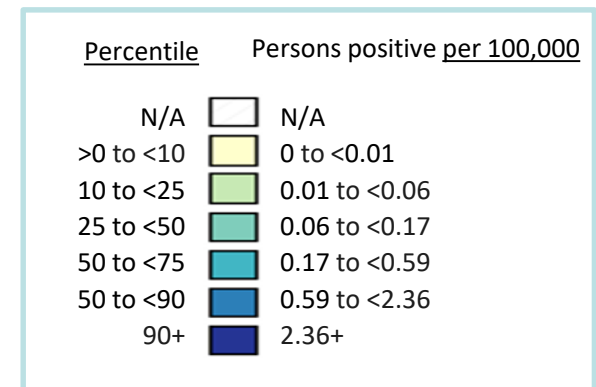
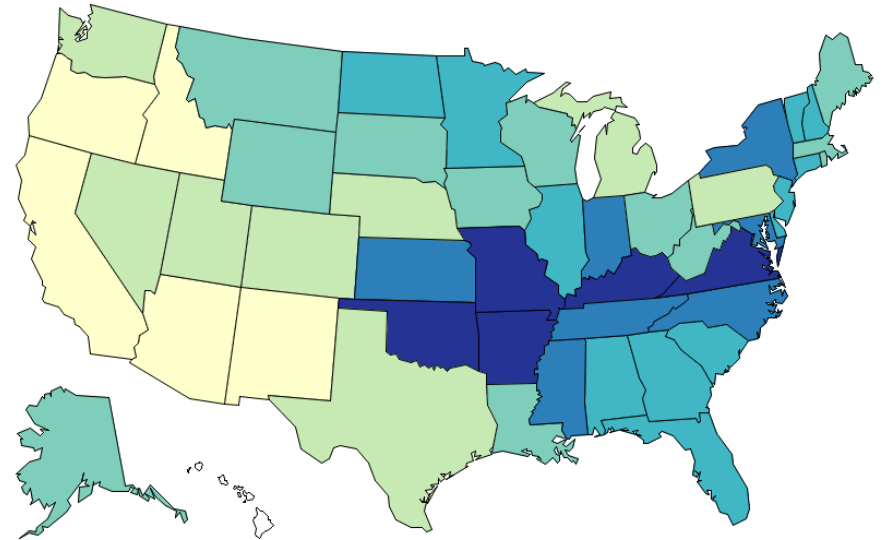
Data from Viracor analysis by Ally Binder & Paige Armstrong, CDC

Persons positive per 100,000 population by state, 2010-2018 (n=15,091)

US Burden

Demographics

- **Average age:**
 - 47 years old
- **No. persons positive:**
 - **50% female**
 - **50% male**



US Burden

- Estimated US burden is ~5,000 cases since 2013 (Platts-Mills and Commins)
- Virginia has estimated 13/100,000 incidence (Fisher et. al. 2016)

****CSTE CASE DEFINITION IN DEVELOPMENT****

Position statement to be submitted for June 2020 meeting for standardized case reporting and surveillance

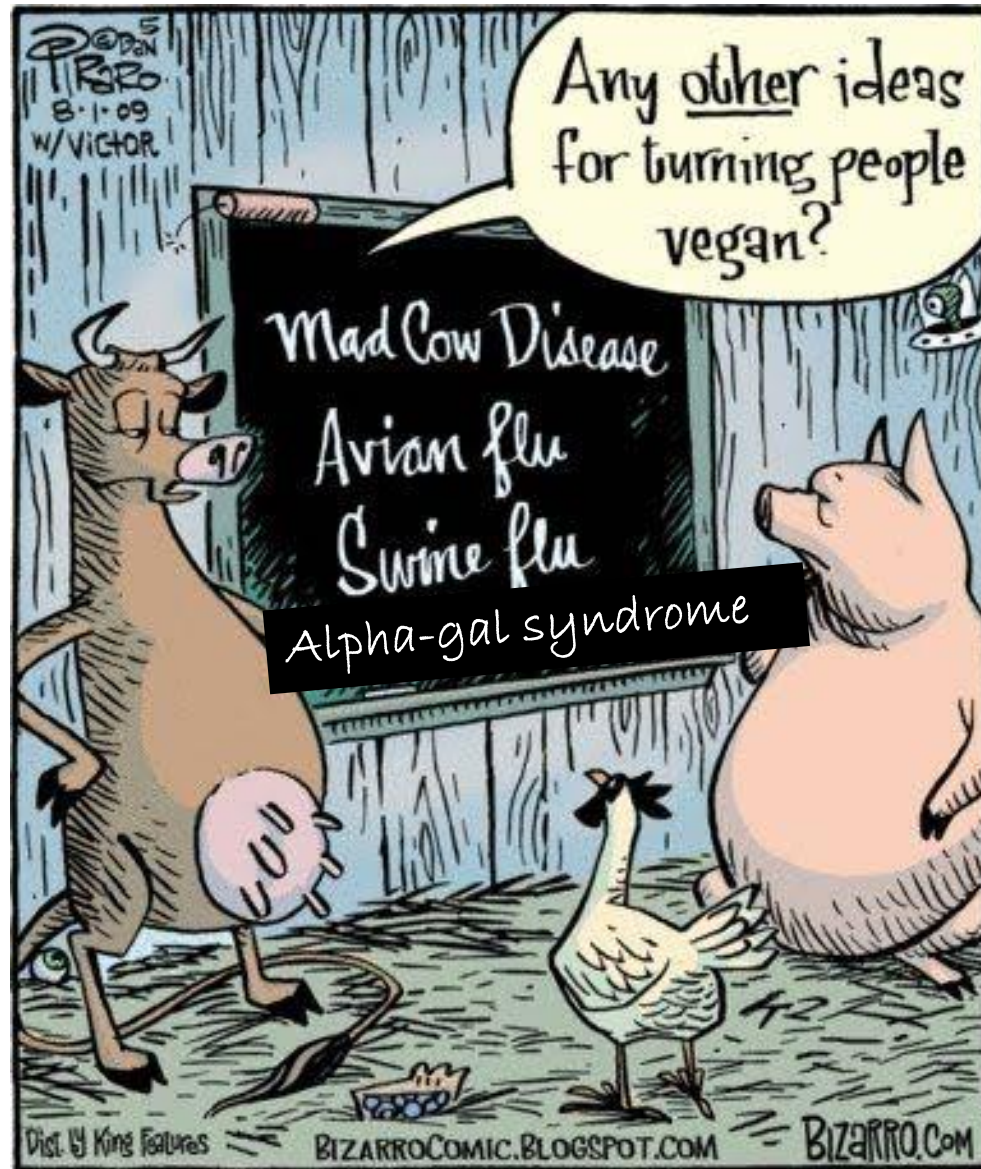
Worldwide Burden

- Worldwide (6 continents & 17 countries) reports of tick-induced mammalian meat allergy!
 - Tick species vary worldwide-
 - *Amblyomma americanun*
 - *Amblyomma cajennense*
 - *Amblyomma sculptum*
 - *Amblyomma testudinarium*
 - *Amblyomma variegatum*
 - *Ixodes ricinus*
 - *Ixodes nipponensis*
 - *Ixodes austaliensis*
 - *Ixodes holocyclus*
 - *****Haemaphysalis longicornis* (Asian Longhorned Tick) indicated in Asia!****

Acknowledgements

- William L. Nicholson, PhD CDC Rickettsial Branch
- Amy Peterson, CDC Rickettsial Branch
- Allison Janes, CDC EIS
- Ally Binder, CDC
- Kristen Nichols Heitman, CDC
- Paige Armstrong, CDC

Questions?



IgE Antibodies to Cetuximab found in 21% of samples from TN controls, 6% CA controls, 0.6% Boston controls

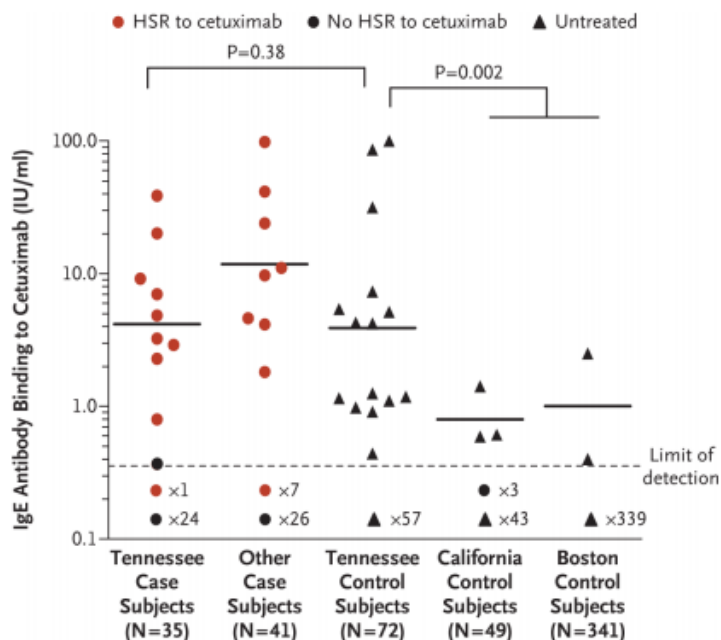
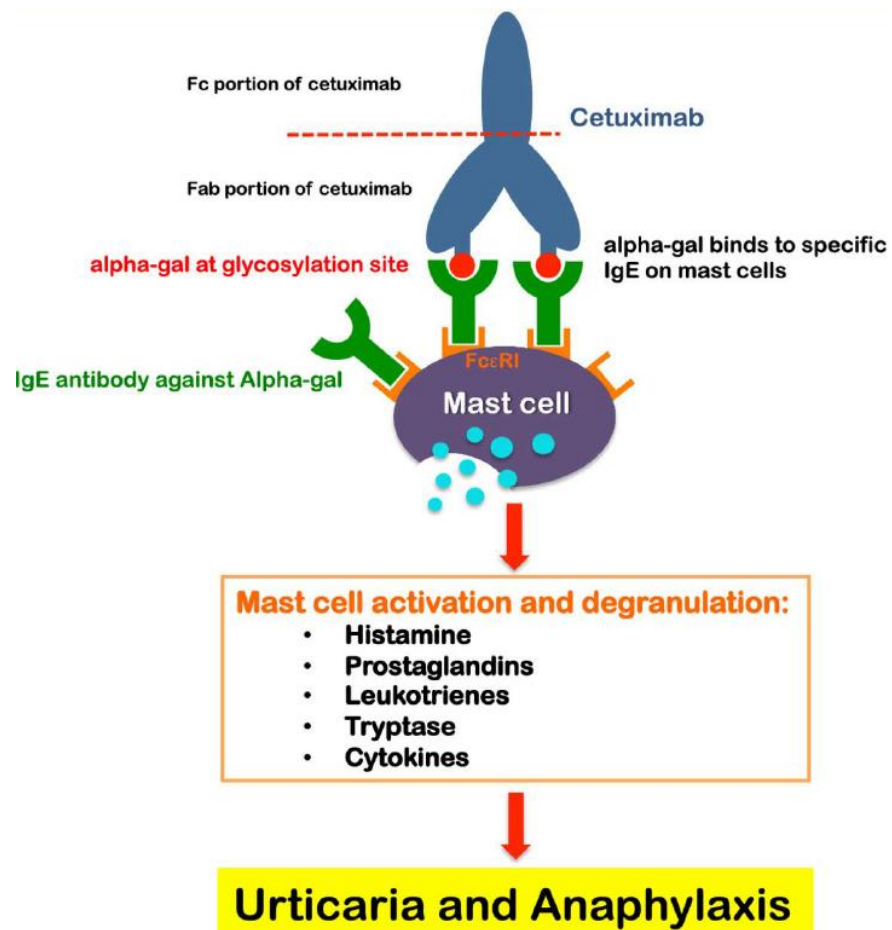
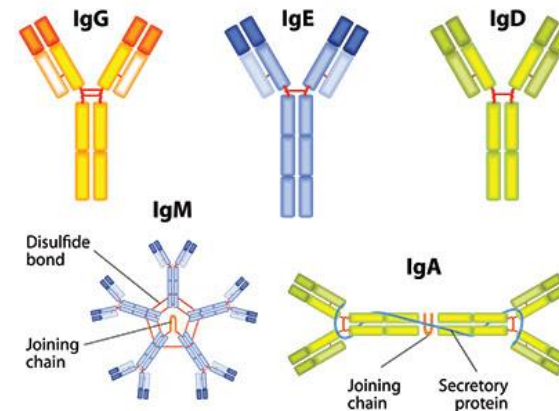
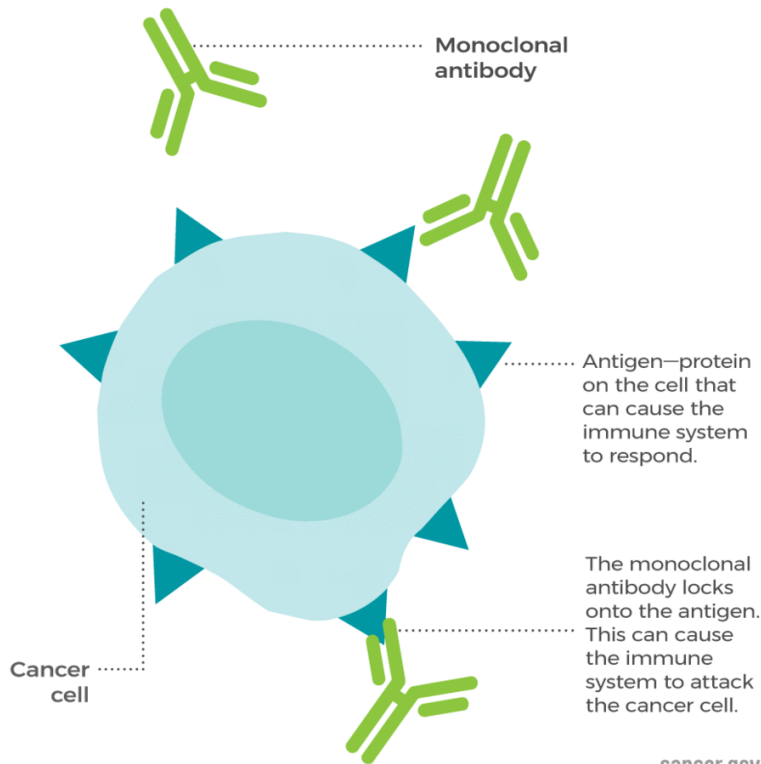


Figure 1. IgE Antibodies Binding to Cetuximab in Serum Samples from 76 Case Subjects and 462 Control Subjects

Results are shown according to whether the treating physician reported a hypersensitivity reaction (HSR) to cetuximab or no HSR reaction. Results are also shown for pretreatment serum samples from control subjects and from subjects who had not received cetuximab. The horizontal lines indicate geometric mean values for the positive results. Values with multiplication signs indicate the number of negative values for each symbol.



Immune Response- Antibodies



<https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/monoclonal-antibodies>