

“Where’s the Beef?”:

Alpha-Gal Syndrome Identification and Risk Management in the Perioperative Setting

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Disclosure Statement

2024 VANA Winter Workshop

Shannon R. Noffsinger, DNAP, CRNA

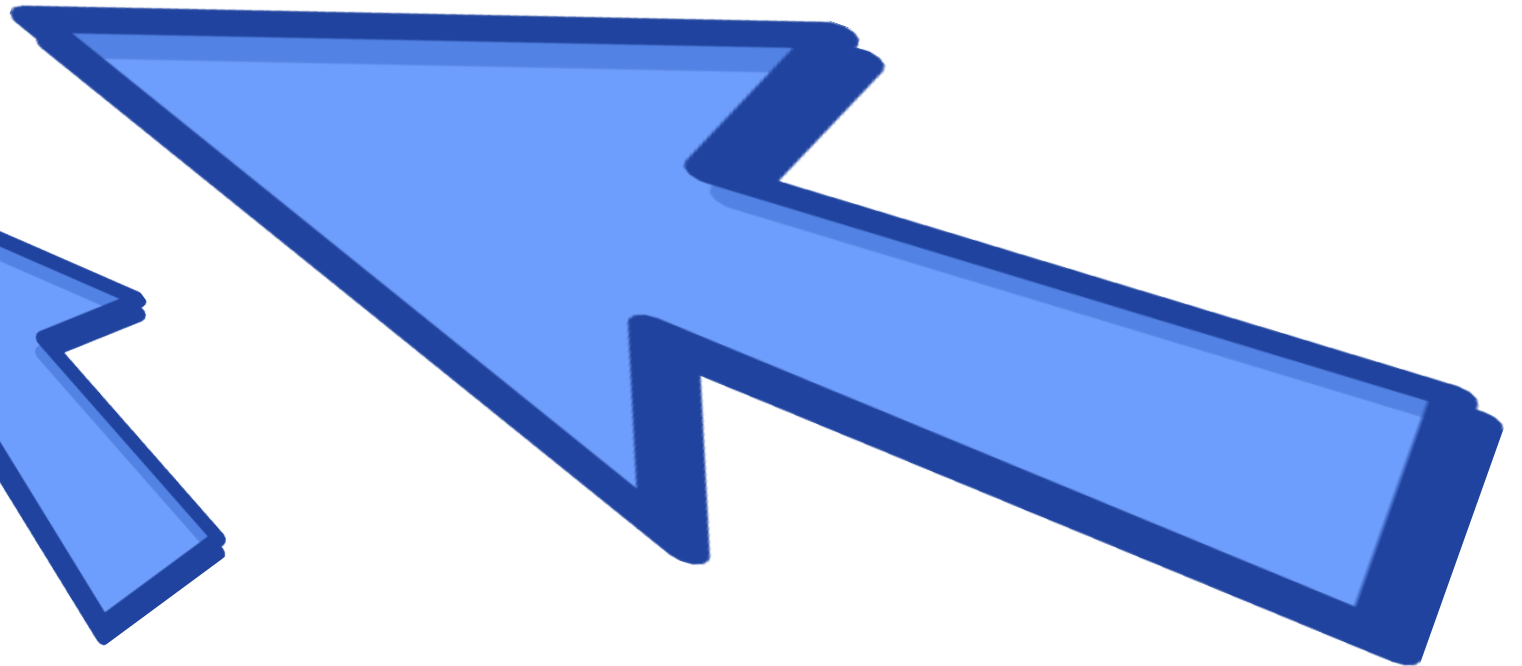
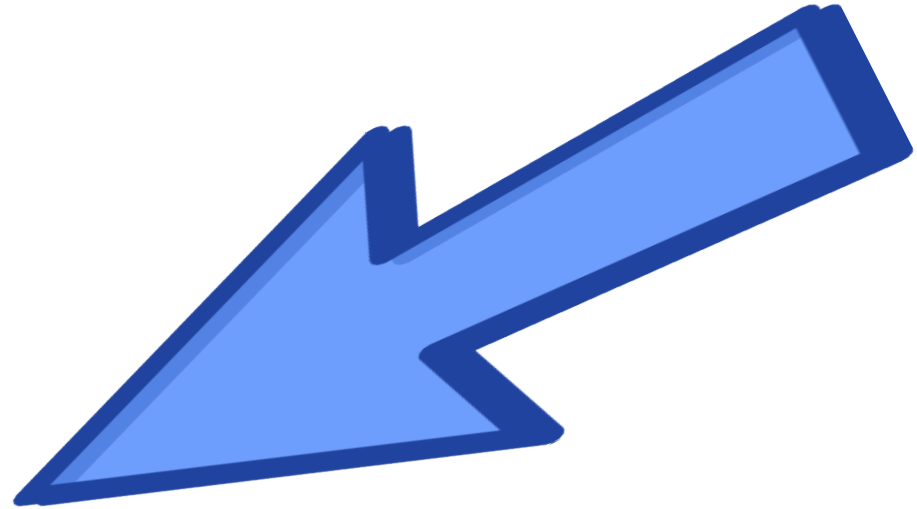
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Learner Outcomes

1. Review Alpha-Gal Syndrome (AGS) from a historical and epidemiological perspective.
2. Understand AGS transmission, incidence, risk factors, and pathogenicity.
3. Understand common triggers for AGS in the perioperative environment.
4. Understand methods for identifying undiagnosed AGS in patients and be able to develop a safe anesthetic plan for this patient population through a discussion of current evidence and recent case studies.



Where's
the
Beef?

Case Study

69 y.o. F with severe MR


- Scheduled for elective MVR with bioprosthetic valve with CPB
- 23 allergies listed on anesthesia preoperative evaluation
 - *Allergy to Pork*





Ughhhhhhh,
Now What?

Is this a real allergy?

- Like, a really real allergy?
 - Can I use heparin?
 - What's the dose of bivalirudin?
 - But there's heparin in the CPB circuit, right?
 - What medications are OK and not OK to give?
 - Heart valve is bovine, *phew!*
- 

Preoperative Assessment on DOS

“Actually I’m allergic to anything that’s got four legs. I have alpha-gal syndrome.”

Pop Quiz!



Historical Background

Late 1990s-early 2000s

- ImClone + Bristol Myers Squibb
- Drugs for metastatic colon cancer
 - Monoclonal antibody: **Cetuximab**
 - Epidermal Growth Factor Receptor Inhibitor
 - Genetically engineered from mice

Historical Background

In earliest trials, 1-2 of every 100 cancer patients experienced an allergic reaction

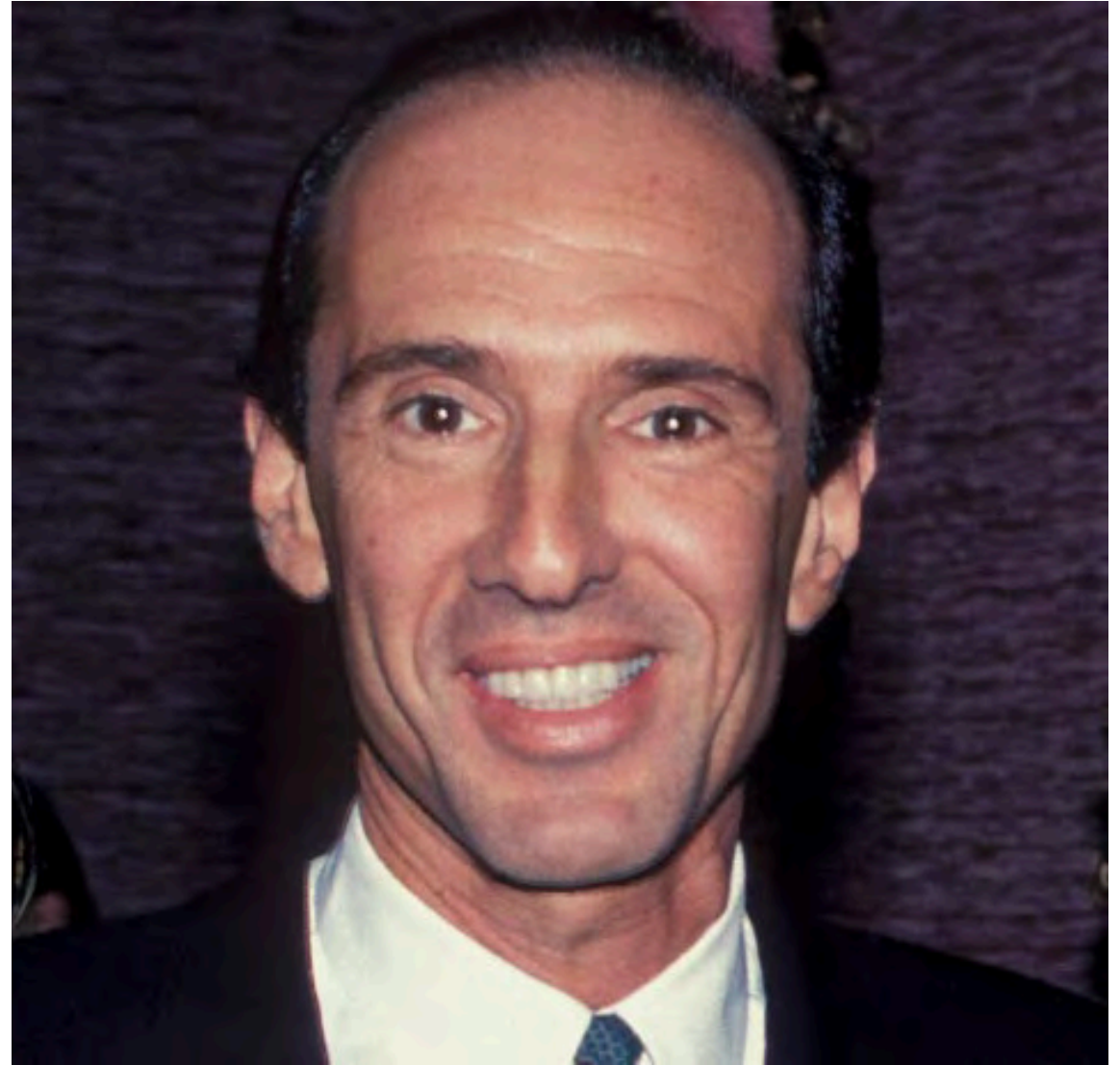
- Hypersensitivity or anaphylaxis
- 1-2% reaction rate remained consistent in larger and larger groups

Then Phase I & II trials expanded into more clinics...

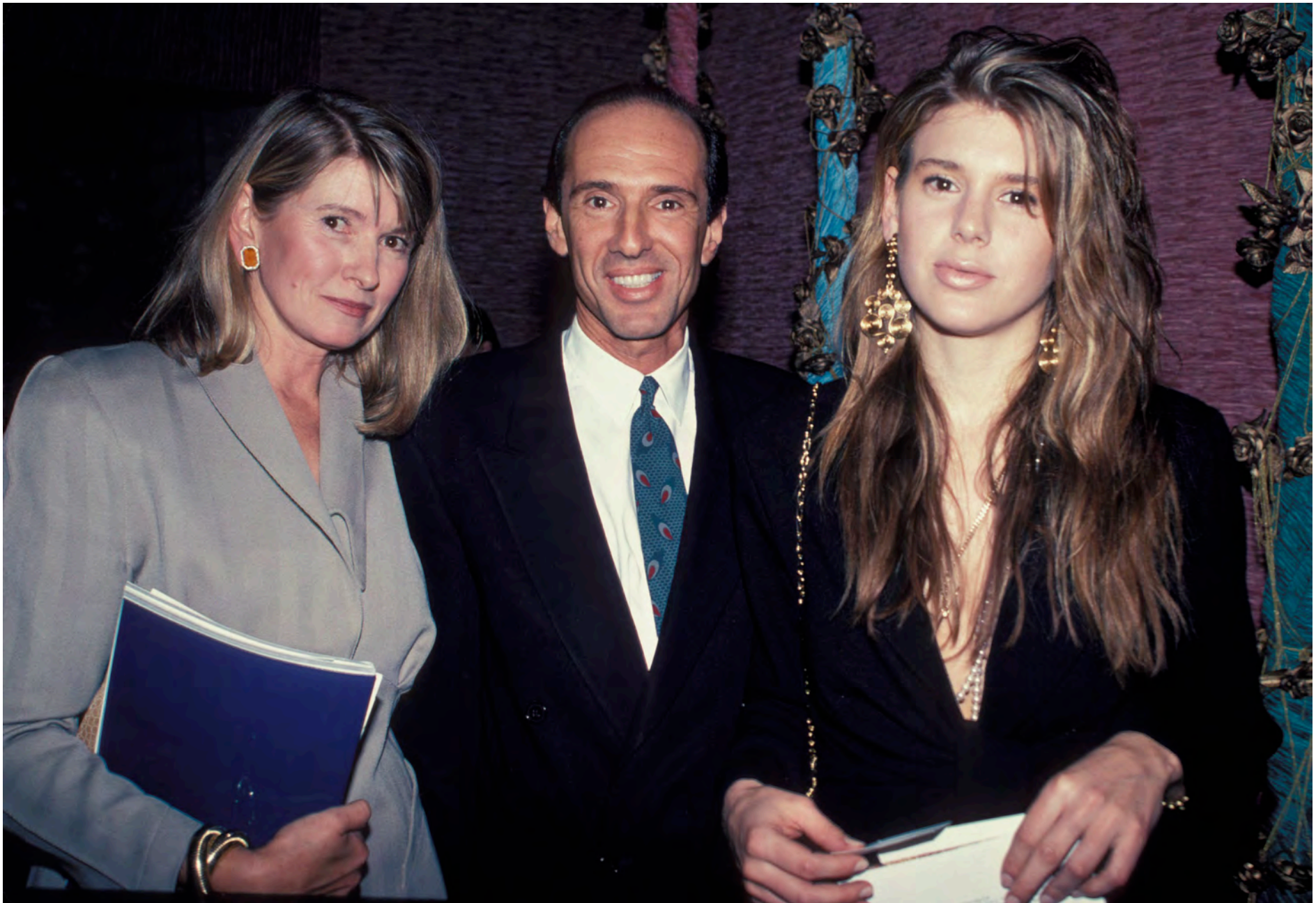
- Delayed hypersensitivity reactions and frank anaphylaxis in 25% of participants
- Several deaths

Historical Sidenote

Samuel Waksal, CEO of ImClone









GUILTY!
GOOSE COOKED: MARTHA FACES PRISON

YANKEES DREAM TEAM
to Japan to see
in opener PAGE 18

NEWS

MARTHA GUILTY ON ALL COUNTS
CURTAINS



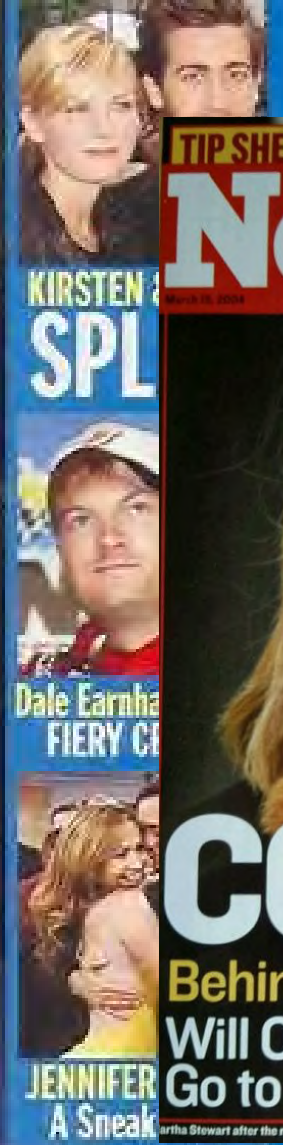
FULL COVERAGE
BEGINS ON PAGES 2-3

People

Martha Stewart

Ready for Jail?

Martha Stewart summons her strength, slims down and launches her comeback. But can she handle life on the inside?



KIRSTEN
SPL

Dale Earnhardt
FIERY C

JENNIFER
A Sneak

TIP SHEET SPECIAL: PAYING FOR YOUR RETIREMENT

Newsweek



COOKED

Behind the Verdict
Will Other CEOs
Go to Prison?

Martha Stewart after the ruling

So What Happened?

- Drug ingredients?
- Cleanliness of manufacturing plants?
- Questionable practices at the trial clinics where cetuximab was administered?
- Some sort of allergy to mice?

Bert O'Neil, MD



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TREATMENT-RELATED COMPLICATIONS

High Incidence of Cetuximab-Related Infusion Reactions in Tennessee and North Carolina and the Association With Atopic History

[Bert H. O'Neil](#) , [Robert Allen](#) , [David R. Spigel](#) , [Thomas E. Stinchcombe](#) , [Dominic T. Moore](#) , [Jordan D. Berlin](#)...

The First Coincidence

- Oncology clinic in Bentonville, Arkansas
 - One of the first anaphylactic deaths from cetuximab clinical trials
- Dr. Tina Hatley, private practice immunologist in Bentonville
 - Postgraduate training at UVA
 - Dr. Thomas Platts-Mills



- **Prior sensitization**
 - Serum IgE antibodies
 - Sugar molecule present in muscle tissue of non-primate mammals

Galactose-Alpha-1,3-Galactose

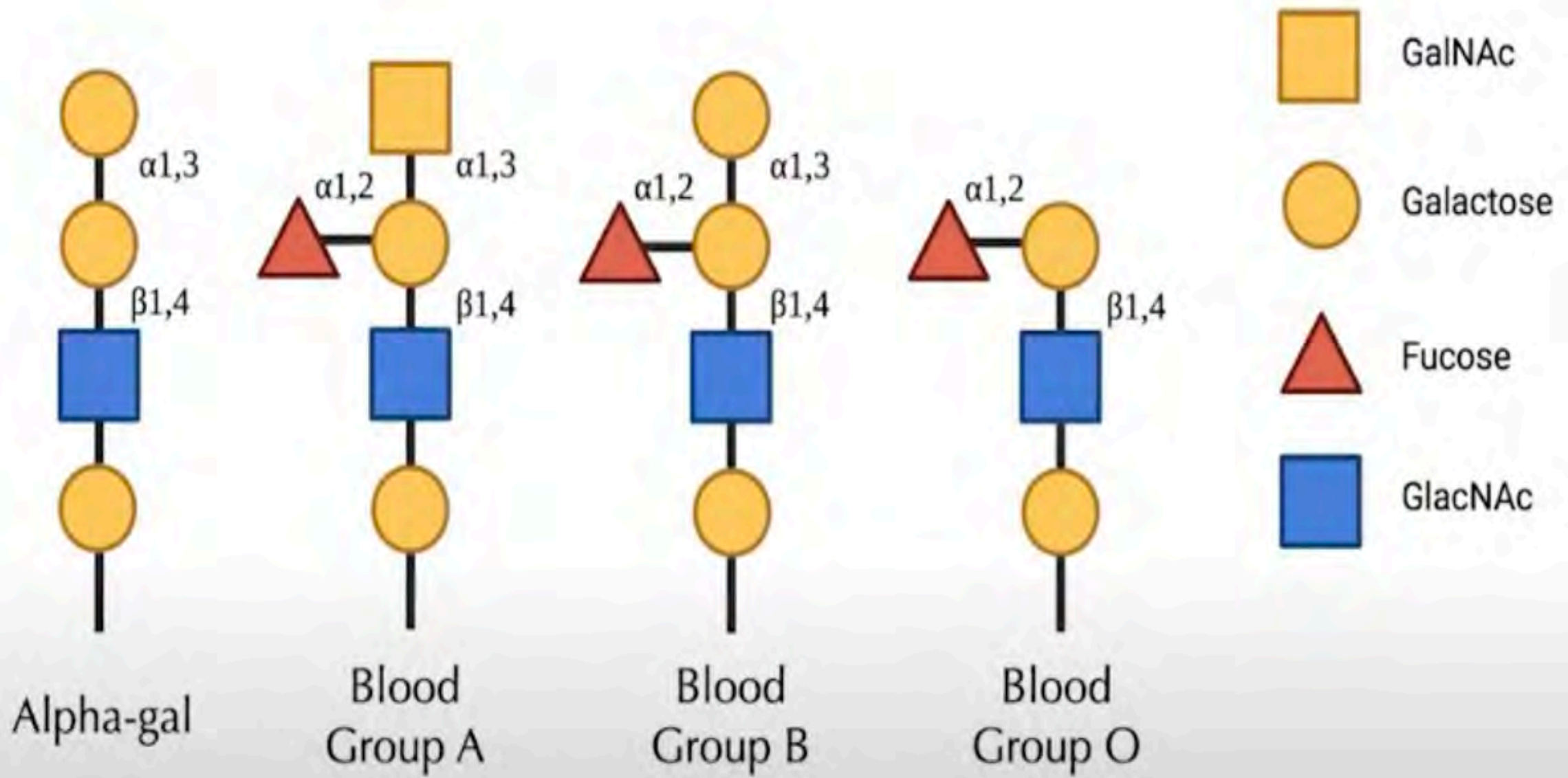
Alpha-Gal

Historical Perspective

Dr. Karl Landsteiner, MD

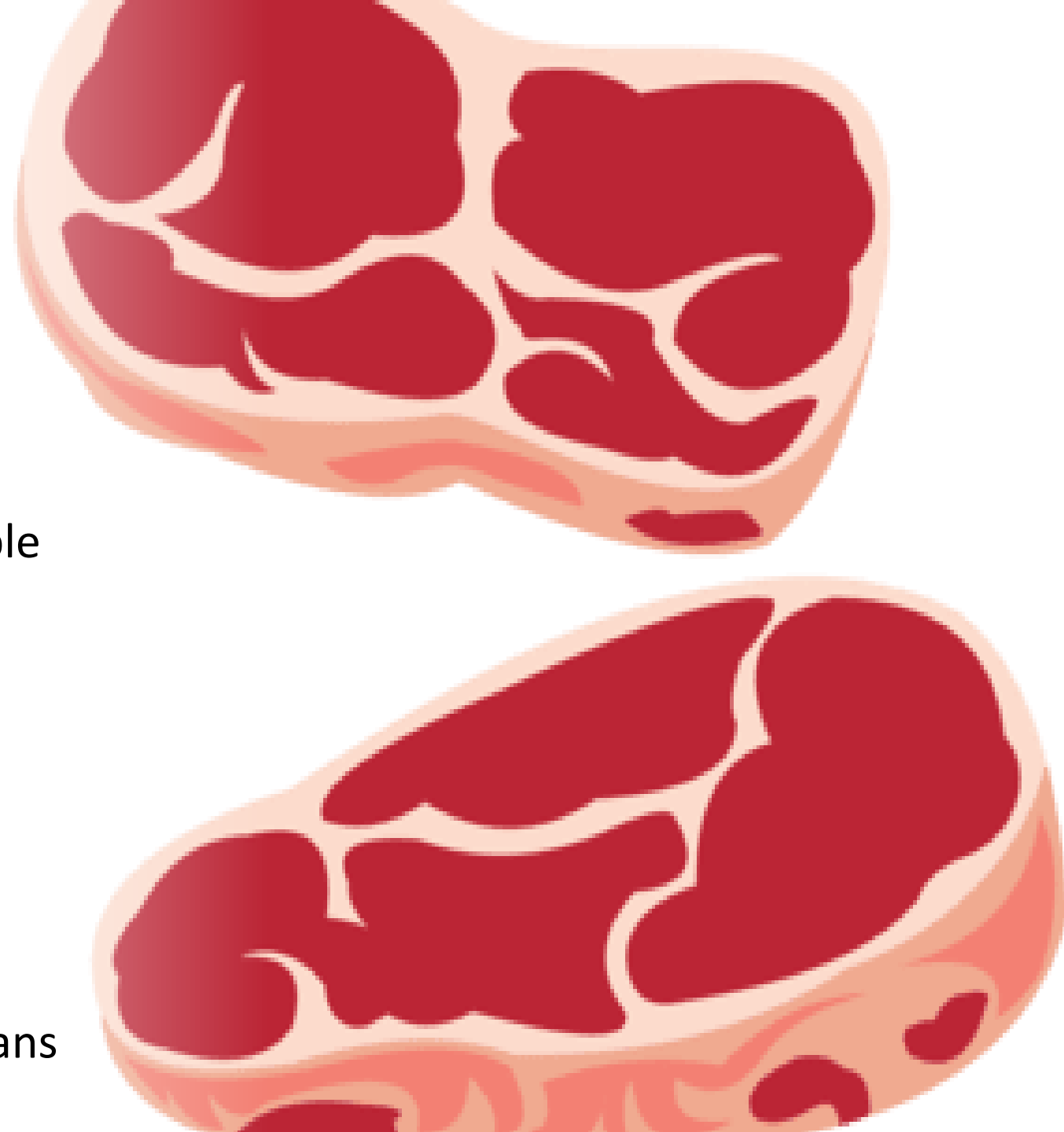
- 1930 Nobel Prize in Physiology/Medicine
- Discovery of A, B, O, AB blood types and antigens preventing transfusions across species
 - “B-like oligosaccharides”
 - Now known as “**alpha-gal**”





The Red Meat Connection

- Oligosaccharides are found in all non-primate mammals
 - Oligosaccharides = saccharide polymer containing a few monosaccharides (simple sugars)
- Requires gene encoding alpha-1,3-galactosyltransferase
- Gene is non-functional in primates
 - Humans, chimpanzees, gorillas, orangutans



The Red Meat Connection



- Humans therefore cannot produce alpha-gal
- We form IgG/IgA antibodies to alpha-gal upon exposure
- This is the main reason xenotransplantation has been unsuccessful





So how were the Cetuximab trial participants already sensitized to alpha-gal?

The Red Meat Connection

UVA researchers scrutinized affected patients and their families for any possible links or patterns...

Pattern #1:

- Patients seemed to spend a significant amount of time outdoors

Pattern #2:

- Patients experienced hypersensitivity 3-5 hours after consuming red meat

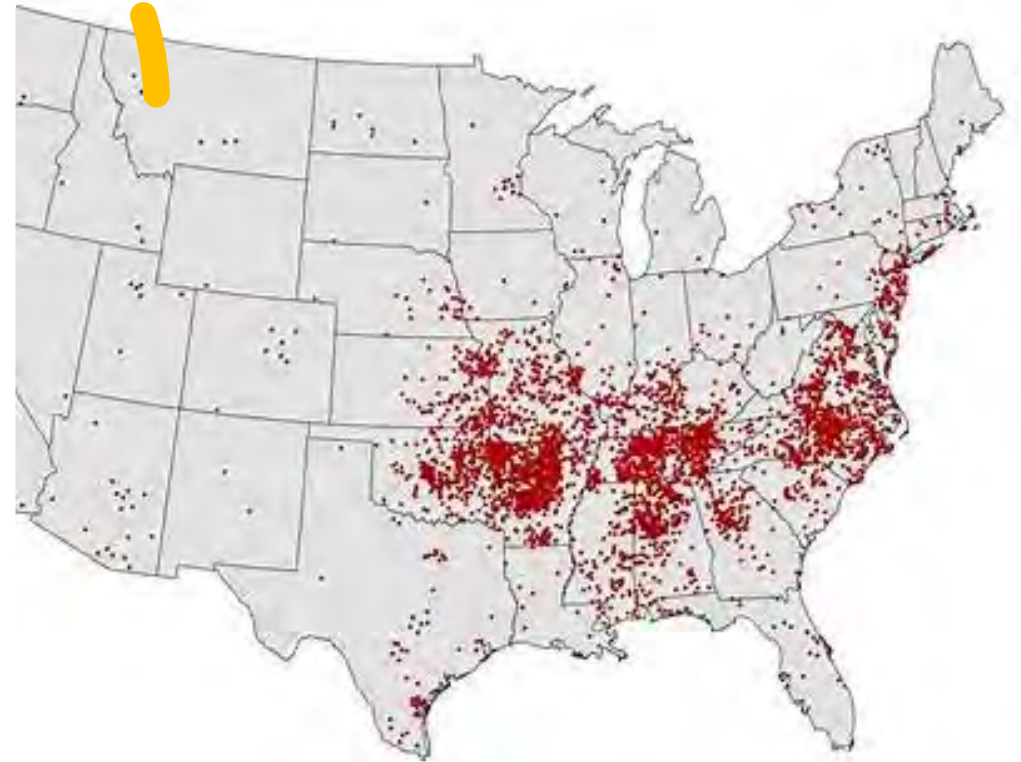
Pattern #3:

- Hypersensitivity/anaphylactic reactions appeared to be regional
 - North Carolina, Tennessee, Arkansas

The Second Coincidence

Dr. Jacob Hosen

- Researcher in Dr. Platts-Mills's lab
- Came across CDC map showing prevalence of Rocky Mountain spotted fever



The Lone Star Tick

Amblyomma Americanum

- One of the most common ticks in the south-eastern U.S.



The Hypothesis

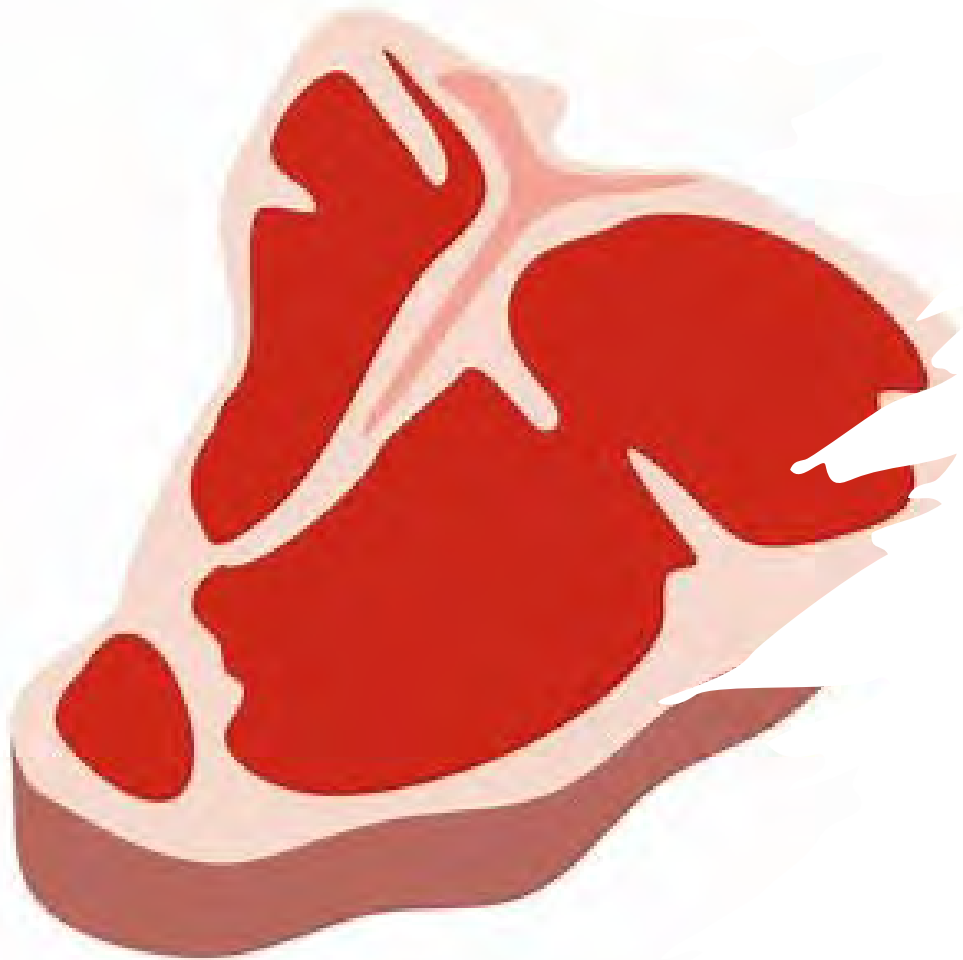
A decorative yellow dashed arc is positioned in the upper right corner of the slide.

If the mystery reactions shared a footprint with a known tick-borne disease, could ticks be linked to these reactions too?





The Red Meat Connection



Dr. Scott Commins

- Post-graduate fellow in Platts-Mills
- Called every new patient to ask about tick bite exposure

“I think 94.6% of them answered affirmatively and the other few would say, ‘You know, I’m outdoors all the time. I can’t remember an actual tick that was attached, but I know I’d get bites.’”



The Final Coincidence





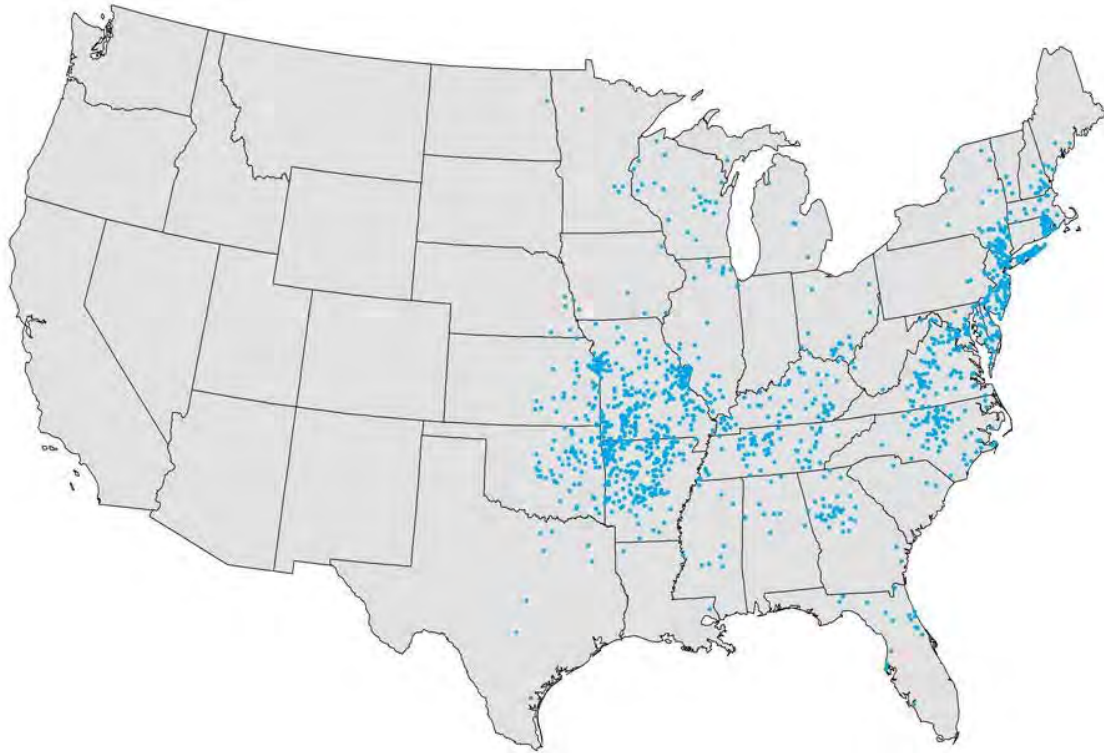


The Lone Star Tick

- Does NOT transmit Lyme Disease
- A vector for other serious illnesses:
 - Q fever
 - Ehrlichiosis
 - Heartland virus
 - Bourbon virus
 - Tularaemia (Rabbit Fever)



The Lone Star Tick



Other Ticks?



AGS Incidence in United States

- >90,000 AGS cases identified by CDC between 2017-2021
 - New cases increased ~15,000 each year during study
- Estimated 450,000 people in the U.S. (CDC, July 2023)



AGS Incidence in United States

- HCPs have low awareness of AGS
 - 42% never heard of AGS
 - 35% had low confidence in ability to diagnose/manage AGS





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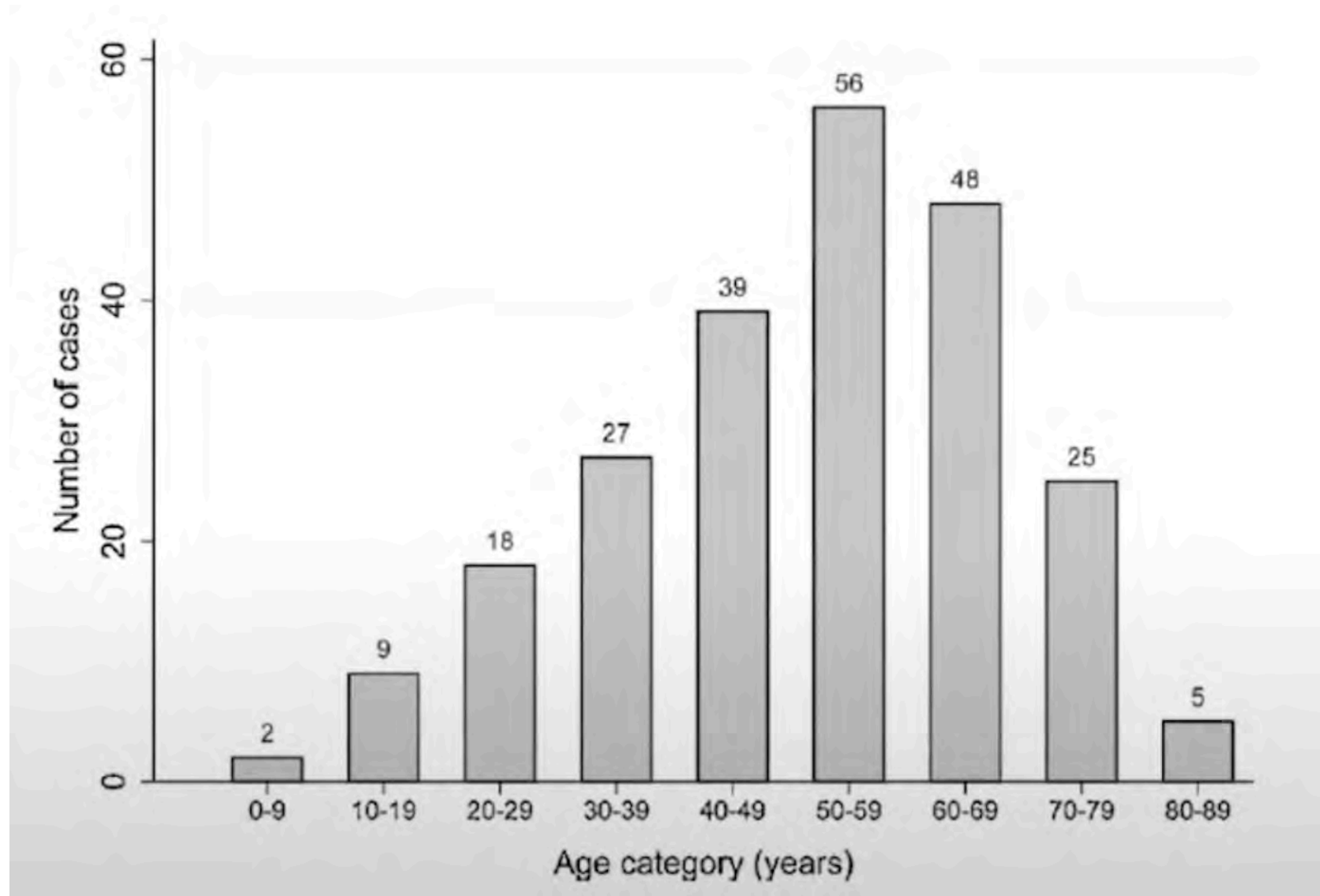
HB 93 Alpha-gal syndrome; added to Board of Health's reportable disease list.

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SUMMARY AS INTRODUCED:

Alpha-gal syndrome; Board of Health; reportable disease list. Directs the Board of Health to add alpha-gal syndrome to the list of diseases required to be reported to the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services.

Age Distribution



Reported Symptoms	No. Of Cases	% of Cases
Anaphylaxis	122	51.7
Skin reactions	176	74.6
Urticaria	168	71.2
Angioedema	59	25
Pruritus	34	14.4
Respiratory symptoms	41	17.4
Dyspnea	26	11
Bronchospasm / wheezing	10	4.2
Chest / throat tightness	8	3.4
Gastrointestinal symptoms	71	30.1
Abdominal pain	22	9.3
Diarrhea	20	8.5
Vomiting	16	6.8
Nausea	10	4.2

AGS Diagnosis

- Patient History
- Intradermal Injections
- Positive (>0.01 IU/mL) for IgE to alpha-gal



AGS Diagnosis

The screenshot shows a medical results interface. At the top, there are navigation icons: a refresh icon labeled '1m ago', a checkmark icon labeled 'All Rows', and a back arrow icon. Below these are a key icon, a question mark icon, a close icon, and a 'Time Mark' icon. On the right side, there is a 'Most Recent' section with a date '2023' and a time '7:77' and '15:53'. The main table has a header 'GENERAL SEROLOGY' with an upward arrow. The table contains four rows of data, each with a test name, a date, a numerical value, and an upward arrow icon.

GENERAL SEROLOGY			
Alpha-Gal IgE	06/26/17	27.90	▲
F026 Pork IgE	06/26/17	4.15	▲
F027 Beef IgE	06/26/17	8.44	▲
F088 Lamb IgE	06/26/17	2.16	▲

Delayed Reactions Related to Specific Foods

In the US:

Beef (hamburgers)

Pork (bacon)

Lamb

Minor reports of milk, cheese

- IgE-specific results
- NO IgE-specific to fish, poultry, or non-mammal proteins

In Europe:

Horse

Goat

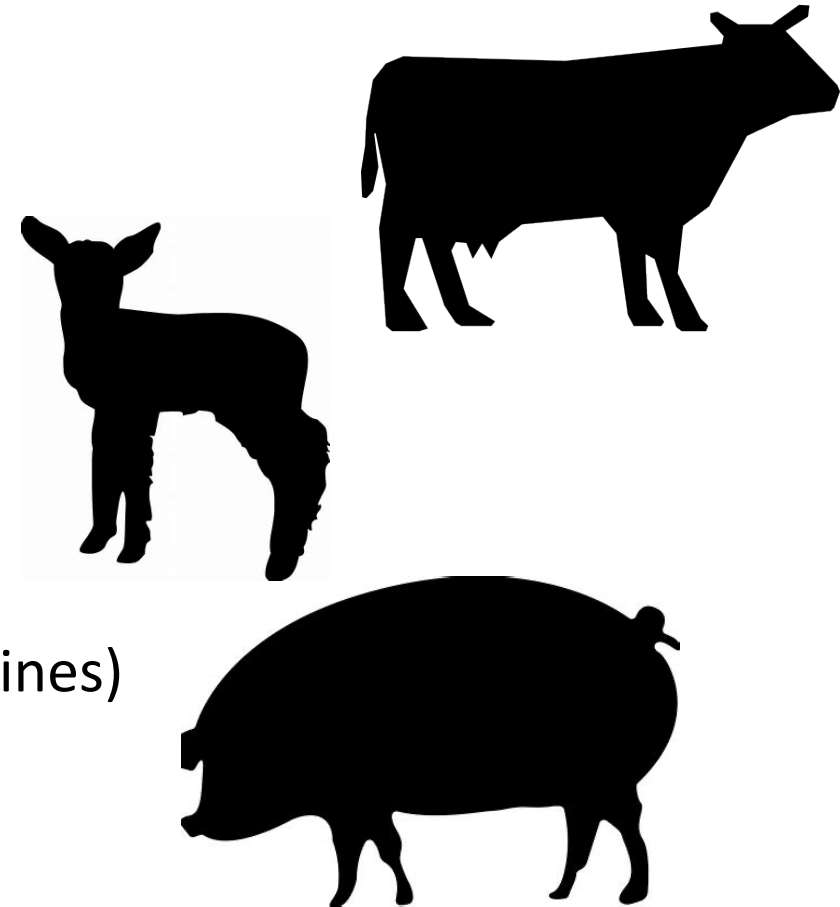
Rabbit

Liver

Heart

Tripe (intestines)

Kidneys



AGS Considerations in the Perioperative Setting

NO Anesthesia / Perioperative
Guidelines or Consensus
Statements
for Managing Patients with AGS

Perioperative Medications

- **Heparin**

- Derived from bovine lung or porcine intestine

Inactive Ingredients

- **Gelatin**

- Derived from collagen (animal bones, cartilage, skin)

- **Glycerin**

- Derived from animal fats/triglycerides

- **Lactic acid and lactose**

- Derived from mammalian blood, tissues, milk

- **Stearate**

- Derived from stearic acid (mammalian saturated fat)



AGS “Safe” Medication Kit



Alpha-gal Content for Select Medications Per Manufacturer (Updated 2019)*

Drug Name	Manufacturer	OK to Use?	Notes
Acetaminophen 325 mg tablet	McNeill, McKesson	No	Contains magnesium stearate and gelatin
Acetaminophen 160 mg/5 mL liquid	Pharmaceutical Associates	No	Contains glycerin
Acetaminophen suppository	G&W, Perrigo	No	-
Acetaminophen-butalbital-caffeine (Fioricet) tablet	American Health	No	-
Acetaminophen-codeine 300mg-30mg tablet	Mallinckrodt	No	-
Acetaminophen-codeine 120mg-12mg elixir	Pharmaceutical Associates	No	Contains glycerin
Alprazolam tablet (all strengths)	Major, Mylan, McKesson	No	-
Alvimopan 12 mg capsule	Cubist	No	Contains gelatin (bovine and porcine)
Aminocaproic acid 500 mg tablet	Hospira	No	Contains magnesium stearate and stearic acid

Aprepitant 40 mg capsule	Merck, Sandoz	No	Contains gelatin (bovine and porcine)
Armour thyroid™	Allergan	Unknown	Animal thyroid extract
Aspirin 81 mg EC tablet	GeriCare	No	-
Aspirin 325 mg EC tablet	McKesson	No	Contains anhydrous lactose (Phone: 855-625-4677)
Bacitracin 50,000 unit injection	X-Gen	No	May contain milk and milk-derivatives (bovine)
Baclofen 10 mg tablet	McKesson & American Health	No	Contains magnesium stearate
Bisacodyl 5 mg tablet	Major, Rugby	No	-
Bupivacaine liposome injection (Exparel)	Pacira	No	Glycerol is of animal origin (could not specify bovine or porcine)
Carbidopa-levodopa 25mg-100mg tablet	McKesson	No	Contains magnesium stearate
Carbidopa-levodopa 25mg-100mg ER tablet	Mylan	No	Contains magnesium stearate
Carisoprodol 350mg tablet	American Health	No	-

Celecoxib 100 mg, 200 mg capsule	Mylan, Major	No	Contains gelatin (bovine and porcine)
Clindamycin injection	Hospira	Unknown	Product divested
Clonazepam tablet	Mckesson	No	-
Clonidine 0.1mg tablet	Mylan	No	-
Cyclobenzaprine tablet-	McKesson, Major, Mylan	No	-
Cyclosporine 25mg, 100mg capsule	Novartis	No	Contains gelatin
Cytomel™	Pfizer	Unknown	Gelatin
Diazepam 5 mg, 10 mg tablet	McKesson, Mylan	No	-
Diphenhydramine tablet	Contract Pharm & Major	No	Need specific lot number; ingredient sources lot-specific (Lactose, Mg stearate, gelatin listed)
Euthyrox™	Provell Pharmaceuticals	Unknown	Magnesium stearate, gelatin
Ezetimibe 10 mg tablet	Sun Pharma, Avkare	No	-
Floseal hemostatic matrix	Baxter	No	Bovine gelatin

Furosemide 20 mg tablet	Sandoz	No	-
Gabapentin capsule (all strengths)	Amneal & McKesson	No	Contains gelatin (bovine and porcine)
Gabapentin capsule (all strengths)	AvKARE	No	Contains gelatin (bovine, porcine) & gluten (not gliaden gluten - type responsible for celiac sprue)
Gabapentin capsule (all strengths)	Mylan & American Health	No	Contains gelatin (bovine and porcine)
Gabapentin capsule (all strengths)	Ascend	No	Gelatin - bovine
Gabapentin capsule (all strengths)	Pfizer	No	Gelatin
Gabapentin (Neurontin) 250 mg/5 mL oral solution	Pfizer	No	-
Gabapentin 250 mg/5 mL oral solution	Greenstone	No	Animal source gelatin
Gelflim 25 mm-50 mm/125 mm-100 mm	Pfizer	No	Contains porcine gelatin
Glucagon injection	Bedford	No	Contains lactose monohydrate (maybe animal-derived)

Haloperidol 5 mg/mL injection	Fresenius Kabi	No	Lactic Acid may be animal-derived
Heparin	All (porcine)	No	Porcine derived
Hydrocodone-acetaminophen tablet	Mallinckrodt	No	Magnesium stearate; typically gluten-free, but due to sourcing there may be cross-contamination. Final testing is done for this.
Hydromorphone injection	Hospira	No	Lactic Acid may be animal-derived
Hydromorphone 2mg, 4mg tablet	Westward, Rhodes	No	-
Hydromorphone ER tablet	Paddock	No	-
Ibuprofen tablet (all strengths)	LNK; Major & McKesson	No	Contains lactose (bovine)
Ibuprofen 100 mg/5 mL suspension	Precision Dose	No	Contains glycerin
Imitrex 100 mg tablet	GSK	No	Magnesium stearate - animal-derived
Influenza vaccine (Flulaval)	GSK	No	Sodium deoxycholate may be of animal origin - ovine or bovine

Instat Microfibrillar Collagen Hemostat	Ethicon	No	Contains bovine collagen
Isosorbide Dinitrate 5 mg tablet	Sandoz	No	-
Lacosamide 10 mg/mL oral solution	UCB	No	Contains glycerin
Lacosamide tablet (all strengths)	UCB	No	-
Levetiracetam tablet	American Health	No	Contains magnesium stearate
Levothroid™	Pfizer	Unknown	Magensium stearate
Levothyroxine (authorized generic)	Bryant Ranch Prepack	Unknown	Magensium stearate
Levoxyl™	Pfizer	Unknown	Magensium stearate
Lidocaine (Lidoderm) patch	Qualitest	No	Contains gelatin which is bovine-derived
Liothyronine sodium (authorized generic)	Greenstone	Unknown	Gelatin
Lisinopril tablet (all strengths)	Major	No	Contains magnesium stearate
Lorazepam tablet	McKesson	No	-

Magnesium hydroxide solution	Pharmaceutical Assoc	No	Contains glycerin
Magnesium oxide	-	Unknown	-
Methadone 5 mg, 10 mg tablet	Westward, Roxane	No	-
Methadone 5 mg/5 mL oral solution		No	Contains glycerin
Methocarbamol 500 mg tablet	McKesson	Unknown	-
Methylergonovine 0.2 mg tablet	Lupin	No	-
Metoclopramide 1 gm/mL oral solution	Vistapharm	No	Glycerin - may be animal-derived
Metoclopramide 5 mg orally disintegrating tablet	Lupin	No	Magnesium stearate - animal-derived
Metoclopramide 10 mg tablet	Impax, Mylan	No	Magnesium stearate - animal-derived
Metoprolol tartrate tablets (all strengths)	Major	No	-
Montelukast 10 mg tablet	Various	No	-
Mycophenolate 500 mg tablet	Mylan	No	-
Mycophenolate 180mg EC tablet (Myfortic)	Mylan	No	-

Morphine ER tablet (MS Contin)	Mallinckrodt	No	-
Morphine 15 mg, 30 mg IR tablet	Westward, Roxane	No	-
Morphine oral solution		No	Contains glycerin
Nature-Throid™	RLC Labs	Unknown	Animal thyroid extract, magnesium stearate, lactose monohydrate
Naproxen 500mg tablet	McKesson	No	-
Nitroglycerin 0.4 mg tablet	Pfizer	No	-
Nystatin oral suspension		Unknown	*couldn't find in the pharmacy
Oxybutynin tablet	American health	No	Contains magnesium stearate
Oxycodone 5 mg tablet	Hospira, mallinkroft	No	Contains animal-derived stearic acid
Oxycodone oral solution	Vista	No	contains glycerin
Oxycontin tablet	Purdue	No	contains magnesium stearate
Oxycodone-acetaminophen 5mg-325mg tablet	Mallinckrodt	No	-
Pantoprazole 20 mg, 40 mg DR tablet	Mylan	Unknown	Contains no gluten
Phenazopyridine 100 mg, 200 mg tablet	ECI & Gemini	No	Contains magnesium stearate

Pregabalin capsule (all strengths)	Pfizer	No	Gelatin of animal origin; lot-specific ingredient sourcing
Promethazine 25 mg/mL injection	West-Ward	Unknown	Company not able to confirm or deny the presence of alpha-galactose in the raw materials
Prothrombin complex concentrate (Kcentra)	CSL Behring	No	Heparin porcine
Rifampin capsule	Eon Labs, Mylan	No	Gelatin - Porcine, bovine derived
Sennokot S tablet	Major	No	Contains bovine
Sotalol 80 mg tablet	Teva	No	-
Spirolactone 25 mg tablet	Amneal	No	-
Sumatriptan 25 mg, 50 mg, 100 mg tablet	Mylan, Sun Pharma	No	Magnesium stearate - animal-derived
Surgifoam powder	Ethicon	No	Contains porcine gelatin
Surgifoam Absorbable Gelatin Sponge	Ethicon	No	Contains porcine gelatin
Synthroid™	AbbVie	Unknown	Magnesium stearate, lactose monohydrate
Tamsulosin capsule 0.4 mg capsule	Boehringer Ingelheim	No	Bovine and porcine derivatives

Tirosint™	IBSA Pharma	Unknown	Gelatin
Tirostat™	Par Pharmaceutical	Unknown	Animal thyroid extract
Thrombin		No	-
Thyrolar™	Allergan	Unknown	Magnesium stearate and gelatin
Verapamil ER 100 mg capsule	Mylan	No	-
Visipaque	GE Healthcare	Unknown	No information available from manufacturer
Zofran 4 mg orally disintegrating tablet	Novartis	No	Contains gelatin; company does not perform tests to determine if ingredients are animal-sourced

Inactive Compounds	Common Perioperative drugs and materials containing inactive Compounds
Gelatin *	Acetaminophen tablet, celecoxib tablet, pregabalin tablet, gabapentin tablet, lidocaine patch, surgifoam
Glycerin	Acetaminophen and codeine elixir, acetaminophen liquid, ibuprofen suspension, morphine solution
Lactic Acid	Hydromorphone injection by Hospira
Magnesium Stearate	Acetaminophen tablet, oxycontin tablet, diphenhydramine tablet, Lisinopril tablet
Steric Acid	Oxycodone tablet by Hospira, Mallinckrodt

Perioperative AGS Triggers

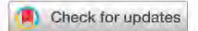
- Biologic mesh (porcine)
 - Hernia repairs
 - Synthetic mesh available
- Thrombin glues (bovine)
 - Newer formulations utilize human fibrinogen and thrombin
- Biosynthetic implants, grafts, valves (bovine, porcine)
 - Ex: Heart valves, corneal implants

Perioperative AGS Triggers

- Surgical Gut / Catgut / Plain Gut sutures (collagen)
 - Utilized in many open abdominal surgeries, fast absorbing for fatty/subcutaneous tissues
- Hydrocolloid dressings (gelatin)
 - Allevyn, Aquacell, Duoderm, Tegaderm Hydrocolloid, etc.
- Topical hemostatic matrix agents (Gelatin)
 - Surgifoam, Gelfoam, FloSeal, SurgiFlo, etc.

Perioperative AGS Case Study

Safety of Intravenous Heparin for Cardiac Surgery in Patients With Alpha-Gal Syndrome



Robert B. Hawkins, MD, MSc, Jeffrey M. Wilson, MD, PhD,
J. Hunter Mehaffey, MD, MSC, Thomas A. E. Platts-Mills, MD, PhD, and
Gorav Ailawadi, MD

Division of Thoracic and Cardiovascular Surgery, Department of Surgery, University of Virginia, Charlottesville, Virginia; and Division of Allergy and Clinical Immunology, University of Virginia, Charlottesville, Virginia

Background. Alpha-gal syndrome is a tick-acquired disease caused by immunoglobulin E (IgE) to the oligosaccharide galactose-alpha-1,3-galactose (alpha-gal), causing allergic reactions to meat and products sourced from nonprimate mammals. As heparin is porcine-derived, we hypothesized that patients with alpha-gal syndrome who received high-dose heparin for cardiac surgery would have increased risk of anaphylaxis.

Methods. All cardiac surgery patients at an academic medical center from 2007 to 2019 were cross-referenced with research and clinical databases for the alpha-gal IgE blood test. Clinical data were obtained through the institutional Society of Thoracic Surgeons Adult Cardiac Database and chart review. Patients were stratified by development of an allergic reaction for univariate statistical analysis.

Results. Of the 8819 patients, 17 (0.19%) had a positive alpha-gal test before cardiac surgery. Of these 17 patients, 4 (24%) had a severe allergic reaction. The median alpha-

gal titer was significantly higher in patients with a reaction (75 [interquartile range, 61-96] IU/mL vs 8 [interquartile range, 3-18] IU/mL; $P = .006$). There were no differences in median heparin loading dose, total dose, or maximum activated clotting time (all $P > .05$). In a subgroup of 8 patients with recent alpha-gal IgE level, 4 (50%) developed an allergic reaction.

Conclusions. Although alpha-gal is rare in patients undergoing cardiac surgery, there is up to a 50% risk of serious allergic reaction to heparin for cardiopulmonary bypass. Higher preoperative alpha-gal titers may confer a higher risk of severe allergic reaction. For patients with a clinical suspicion of alpha-gal syndrome, we recommend prescreening with IgE levels and premedicating before receiving high doses of intravenous heparin.

(Ann Thorac Surg 2021;111:1991-7)
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Perioperative AGS Case Study





Ticks and Tick-borne Diseases

Volume 13, Issue 1, January 2022, 101869



A retrospective evaluation of heparin product reactions in patients with alpha-gal allergies

[Ugochi Nwamara](#)^a, [Marcus C. Kaplan](#)^b, [Niel Mason](#)^b, [Amanda I. Ingemi](#)^b  

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Perioperative AGS Case Study

[Case Reports](#) > [Anaesth Rep.](#) 2022 Dec 16;10(2):e12203. doi: 10.1002/anr3.12203.

eCollection 2022 Jul-Dec.

Heparin desensitisation prior to cardiopulmonary bypass in a patient with alpha-gal allergy

[A S McRae](#)¹, [W P Tidwell](#)¹, [S Patel](#)², [F W Lombard](#)³

Affiliations + expand

PMID: 36561536 PMID: [PMC9758002](#) DOI: [10.1002/anr3.12203](#)

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Abstract

This case report describes the implementation of a heparin desensitisation strategy for a patient with confirmed galactose-alpha-1,3-galactose (alpha-gal) allergy, prior to cardiac surgery. We describe the pre-, intra- and postoperative management. We believe this report can enhance the limited data currently in existence on alternative strategies for heparin utilisation in cardiopulmonary bypass in a previously intolerant patient population.

Keywords: cardiopulmonary bypass; desensitisation; heparin.

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[PubMed Disclaimer](#)

Perioperative AGS Case Study

[J Allergy Clin Immunol Pract.](#) Author manuscript; available in PMC 2015 Sep 1.

PMCID: PMC4163007

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NIHMSID: NIHMS598554

[J Allergy Clin Immunol Pract.](#) 2014 Sep-Oct; 2(5): 637–638.

PMID: [25213067](#)

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Porcine or Bovine Valve Replacement in Three Patients with IgE Antibodies to the Mammalian Oligosaccharide Galactose-alpha-1,3-Galactose

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Anesthesia Management Pearls

- Perioperative management of AGS begins at pre-operative visit and continues through discharge
- Mainstay of management
 - Prevention and avoidance of triggering agents
 - Consider pretreatment options
 - Early recognition of signs and symptoms of AGS reaction



Pre-Operative Screening

- Allergies?
 - Consumes red meat (pork, beef, lamb)?
 - Tolerates other animal products (milk, cheese)?
 - Onset of intolerance (childhood vs. adulthood)?
 - Spend time outdoors? Recent tick bites?
- Formal testing/diagnosis of AGS?
- Previous anesthesia records?
- Current medication list?

Consider Pre-Treatment Options

- Steroids
 - 40 mg IV methylprednisolone
OR
 - 200mg IV hydrocortisone
OR
 - 7.5mg IV dexamethasone
- H1 Blockers
 - 50mg IV diphenhydramine
OR
 - 10mg IV cetirizine
- H2 Blockers?
 - 20mg IV famotidine



Multidisciplinary Discussion/Plan

- Allergist consult?
 - Intradermal/IgE testing for alpha-gal
 - Heparin desensitization?
- Pharmacy
 - Identification of alpha-gal safe medications
- Surgeon
 - Alternatives for alpha-gal safe products and materials
- Circulator
 - Ensuring alpha-gal safe products, materials, medications on the field

Bivalirudin (Angiomax, Angiox)

- Reversible **direct** thrombin inhibitor
 - Inhibits the cleavage of prothrombin to thrombin by directly binding to Factor Xa
 - Considered off-label for CPB anticoagulation
 - Usually reserved for patients with heparin-induced thrombocytopenia (HIT)
 - Short half-life (25 min), renally excreted
 - Expensive! (~\$750/vial)
 - No specific reversal agent


Bivalirudin (Angiomax, Angiox)

Suggested bivalirudin dosing for CPB:

- 1mg/kg initial IV bolus achieves ACT ~350 sec
 - Goal CPB ACT 400-500 sec
 - Additional boluses, infusion 1-5 mg/kg/hr
- ACT rechecked Q20 min on CPB and Q20 min after terminating CPB
 - ACT values declined by ½ every two hours spontaneously by renal excretion

Anaphylaxis Review: Signs and Symptoms Under GETA

- Bronchospasm, angioedema
 - High Inspiratory Pressure
 - Decreased Vt
- Sudden, severe hypotension
- Tachycardia/arrhythmia



Cognitive Aids for Perioperative Crises - V4.4 2022
Stanford Anesthesia Cognitive Aid Program

EMERGENCY MANUAL


FREE DOWNLOAD

ACLS	Bradycardia	2
	SVT - Unstable and Stable	3
	VFIB / VTACH	4
	Anaphylaxis	5
OTHER EVENTS	Bronchospasm	6
	Delayed Emergence	7
	Difficult Airway / Cric	8
	Embolism - Pulmonary	9
	Fire - Airway	10
	Fire - Non-Airway	11
	Hemorrhage	12
	High Airway Pressure	13
	High Spinal	14
	Hypertension	15
	Hypotension	16
	Hypoxemia	17
	Local Anesthetic Toxicity	18
	Malignant Hyperthermia	19
	Myocardial Ischemia	20
	Oxygen Failure	21
Pneumothorax	22	
Power Failure	23	
Right Heart Failure	24	
Transfusion Reaction	25	
Trauma	26	
SOURCES	Crisis Resource Management	27
	Emergency Manual Use	28

Anaphylaxis Review: Signs and Symptoms Under GETA

Under the drapes:

- Decreased breath sounds
- Flushing
- Urticaria
- Angioedema



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Anaphylaxis Algorithm and Cognitive Aid

Anaphylaxis

Severe hypotension Cardiac arrest Bronchospasm Wheezing High inspiratory pressure	Angioedema Airway swelling Tachycardia Arrhythmia Flushing	Rash Itching Hives (or no skin findings)
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TREATMENT	Task	Actions
Crisis Resources		<ul style="list-style-type: none"> Inform team Identify leader
		<ul style="list-style-type: none"> Call for code cart Consider pausing procedure
Airway	<ul style="list-style-type: none"> 100% O₂ 10 - 15 L/min 	<ul style="list-style-type: none"> Secure airway. If angioedema: consider early intubation
IV Access		<ul style="list-style-type: none"> Ensure functional large bore IV or IO access
Primary Meds		<ul style="list-style-type: none"> Give epinephrine to prevent mast cell degranulation: <ul style="list-style-type: none"> Epinephrine 10 - 100 mcg IV (if no IV: 500 mcg IM); Increase IV dose every 2 min until clinical improvement. May require > 1mg. Start early epinephrine infusion See Infusion List #29 If hypotensive: turn off volatile anesthetics and vasodilating drips and consider amnestic agent (e.g. midazolam)
Fluid		<ul style="list-style-type: none"> Give rapid IV fluid bolus. May require many liters Consider head down position; elevate legs
Stop Allergens		<ul style="list-style-type: none"> Remove allergens: e.g. antibiotics, muscle relaxants, chlorhexidine, dyes, blood products, latex, contrast, colloids, protamine, sugammadex
ACLS		<ul style="list-style-type: none"> Check pulse. If no pulse or SBP < 50 mmHg: <ul style="list-style-type: none"> CPR rate 100 - 120 compressions/min Depth ≥ 5 cm; allow chest recoil; consider backboard Keep EtCO₂ > 10 mmHg and diastolic BP > 20 mmHg Rotate compressors with rhythm check every 2 min Check pulse ONLY if signs of ROSC (sustained increased EtCO₂, spontaneous arterial waveform, rhythm change) If mask ventilation: ratio 30 compressions to 2 breaths If airway secure: 10 breaths/min; tidal volume 6 - 7 mL/kg Place defibrillator pads in case rhythm changes Consider ECMO or cardiopulmonary bypass

Page 2 Anaphylaxis

RULE OUT	Task	Actions
	<ul style="list-style-type: none"> Anesthetic overdose See Local Anesthetic Toxicity #18 	<ul style="list-style-type: none"> Hypotension See Hypotension #16
	<ul style="list-style-type: none"> Aspiration Distributive or obstructive shock Embolism e.g. air, clot, fat See Embolism #9 Hemorrhage See Hemorrhage #12 	<ul style="list-style-type: none"> Myocardial infarction See Myocardial Ischemia #20 Pneumothorax See Pneumothorax #22 Sepsis

TREATMENT	Task	Actions
Additional Access		<ul style="list-style-type: none"> Consider additional IV access Consider arterial line placement
	Secondary Meds	<ul style="list-style-type: none"> If hypotension: Continue epinephrine infusion. May add vasopressin and/or norepinephrine See Infusion List #29 If bronchospasm, give bronchodilator: <ul style="list-style-type: none"> If unable to ventilate, treat intravenously: <ul style="list-style-type: none"> epinephrine 5 - 10 mcg IV (or 200 mcg subq) or ketamine 10 - 50 mg IV (or 40mg IM) or magnesium sulfate 1 - 2 g IV If able to ventilate: <ul style="list-style-type: none"> albuterol 4 - 8 puffs MDI or 2.5 mg nebulized and sevoflurane titrated to 1 MAC If persistent bronchospasm, consider: <ul style="list-style-type: none"> H₁ antagonist: diphenhydramine 25 - 50 mg IV H₂ antagonist: famotidine 20 mg IV Corticosteroid: hydrocortisone 100 mg IV or methylprednisolone 125 mg IV
ECHO		<ul style="list-style-type: none"> Consider TEE / TTE to assess volume status and function
Labs		<ul style="list-style-type: none"> Send peak serum tryptase 1 - 2 hr after reaction onset
Dispo		<ul style="list-style-type: none"> Monitor for at least 6 hr. If severe, biphasic response is more likely so monitor in ICU for 12 - 24 hours If intubated: consider keeping intubated
Allergy Follow-up		<ul style="list-style-type: none"> Consider adding allergens to patient's allergy list Refer the patient for follow-up allergy testing

Anaphylaxis Algorithm and Cognitive Aid

- Alert OR team/inform surgeon, call for code cart/anesthesia backup
- Secure airway. early intubation, **100% FiO₂ 10-15L**
- Large bore IV access
- **Epinephrine (10-100 mcg IV OR 500 mcg IM)**, increase dose Q2min
 - Start early epi infusion
 - If hypotensive, d/c volatile and vasodilating agents, consider midazolam
- Rapid IV fluid bolus
- Remove allergens
- ACLS protocol

Anaphylaxis Algorithm and Cognitive Aid

Secondary meds:

- If hypotensive, continue epi gtt, may add vasopressin and/or norepinephrine
- If bronchospasm, give bronchodilator
 - Albuterol 4-8 puffs or 2.5 mg nebulizer
 - Sevoflurane 1 MAC

Anaphylaxis Algorithm and Cognitive Aid

- If unable to ventilate d/t bronchospasm, treat IV
 - Epi 5-10 mcg IV or 200 mcg IM
 - Ketamine 10-50 mg IV or 40mg IM
 - Mag sulfate 1-2 g IV
- If persistent bronchospasm, consider
 - H1 blocker diphenhydramine 25-50 mg IV
 - H2 blocker famotidine 20 mg IV
 - Corticosteroid hydrocortisone 100 mg IV or methylprednisolone 125 mg IV

Anaphylaxis Algorithm and Cognitive Aid

- Monitor for >6 hours
 - If severe reaction, biphasic response is more likely so monitor in ICU for 12-24 hours
- If intubated, consider keeping intubated



That's all Folks!



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References

BH O'Neil, R Allen, DR Spigel, TE Stinchcombe, DT Moore, JD Berlin. High incidence of cetuximab-related infusion reactions in Tennessee and North Carolina and the association with atopic history. *Journal of Clinical Oncology*. Volume 25 issue 24.

D'Ercole FJ, Dhandha VH, Levi ML, Todd AB, Kumar PA. Perioperative challenges in patients with alpha-gal allergy. *J Clin Anesth Pain Manag* 2019;3(1):70-78.

Dewachter P, Kopac P, Laguna JJ, et al. Anaesthetic management of patients with preexisting allergic conditions: a narrative review. *Br J Anaesth* 2019;123(1):65-81.

Dunkman WJ, Rycek W, Manning MW. What does a red meat allergy have to do with anesthesia?: perioperative management of alpha-gal syndrome. *Anesth Analg* 2019;129(5):1242-1248. doi: 10.1213/ANE.0000000000003460.

Kuravi KV, Sorrells LT, Nellis JR, et al. Allergic response to medical products in patients with alpha-gal syndrome. *J Thorac Cardiovasc Surg* 2022;164(6):411-424. doi: 10.1016/j.jtcvs.2021.03.100.

Hawkins RB, Wilson JM, Mehaffey JH, PlattsOMills TAE, Ailawadi G. Safety of intravenous heparin for cardiac surgery in patients with alpha-gal syndrome. *Ann Thorac Surg* 2021;111(6):1991-1997. doi: 10.1016/j.athoracsur.2020.07.050.

Lied GA, Lund KB, Storaas T. Intraoperative anaphylaxis to gelatin-based hemostatic agents: a case report. *J Asthma Allergy* 2019;12:163-167. doi: 10.2147/JAA.S202784.

Young I, Prematunge C, Pussegoda C, Corrin T, Waddell T. Tick exposures and alpha-gal syndrome: A systematic review of the evidence. *Ticks and Tick-borne Diseases*. (2021). Vol 21, issue 3.

<https://inpharmd.com/inquiries/7b59a192d887a7bce18eb339b9cbc82289c04016bae4cfb8656cbb41a53ce033>

<https://www.cdc.gov/media/releases/2023/p0727-emerging-tick-bites.html>

<https://www.med.unc.edu/anesthesiology/enhancedrecovery/wp-content/uploads/sites/492/2019/12/JCAPM-3-016-4.pdf>

https://web.stanford.edu/dept/anesthesia/em/SEM_interactive.pdf