AGS background document: Virginia

Background

Alpha-gal syndrome (AGS), is an IgE-mediated allergy to the sugar galactose-α-1,3-galactose (alpha-gal), which is found in all mammals except some primates.[1] Its onset is associated with tick bites.[2] In the U.S., lone star ticks are responsible for the majority of cases.[3]

People with AGS react to products made from mammals. This includes foods such as beef, pork, lamb, venison, dairy products, and gelatin.[3-5] It also includes drugs and medical products, such as monoclonal antibodies, heparin, bioprosthetic heart valves, some vaccines, antivenom, medication in gelatin capsules, and many other medical products.[3-5] Over 75% of people with AGS report reacting to a medication, and about 50% report that they have experienced anaphylactic reactions to a health product.[7] Many people with AGS also react to personal care and household products with mammal-derived ingredients.[3]

Alpha-gal reactions are often severe and can be fatal.[3,4,6] Over 60% of people with AGS experience anaphylactic reactions.[8,9] In areas of high prevalence, reactions to alpha-gal can be the number one cause of anaphylaxis in adults and adolescents, accounting for a third of all cases, more than all other food allergies combined.[10]

Due to growing lone star tick populations, the number of cases of AGS is increasing at an alarming rate.[11,12] In July, 2023, the CDC reported that between 2010 and 2022, more than 110,000 suspected cases of AGS were identified.[12] The CDC estimates that up to 450,000 Americans may be affected, making AGS the 10th most common food allergy.[12,13] Yet alarmingly, 78% of physicians know little to nothing about AGS, and only 5% feel very confident in diagnosing and managing it.[14]

Virginia: an alpha-gal syndrome hotspot

Virginia is an alpha-gal syndrome hotspot. Residents in rural areas and in the lower-elevation Piedmont and Coastal Plain regions are most affected.[12,18] This is coincident with the abundance of lone star ticks, which account for the vast majority of all human tick encounters within the state.[15-17] Over 20% of residents in some areas of Virginia are sensitized to alpha-gal,[18-22] and up to 9% of these individuals may have allergic reactions to alpha-gal.[3,23-25] A recent study found that more than 2% of an unselected cohort from central Virginia had AGS.[24] Other estimates suggest that up to 3% of people in the hardest hit areas may be affected.[3,23,25] In addition, small studies suggest that AGS may be a frequent cause of both IBS-like symptoms and rheumatological issues, accounting for up to 25% of such cases in central Virginia.[26,27] Concerningly, research

conducted at UVA and elsewhere found that people who are sensitized to alpha-gal, even if they do not develop allergic reactions, may be at increased risk of cardiovascular disease.[22,28]

A call to action

In a July 2023 report, the CDC recognized AGS as a growing clinical and public health concern.[12] Due to the current lack of surveillance, they state, the true prevalence of AGS is largely unknown.[12] The CDC identified a "critical need" for state and local health authorities to initiate surveillance and encourages them to do so.[12,31]

The CDC recently laid the groundwork for states to make AGS reporting mandatory, publishing a National Notifiable Diseases Surveillance System case definition for alpha-gal syndrome (AGS)[29] and creating an Alpha-gal Syndrome Case Report Form .[30] In September, 2023 Arkansas became the first state to make AGS a mandatory, reportable health condition,[32] and other states in high prevalence regions are expected to follow suit.

References:

1. Commins SP, Satinover SM, Hosen J, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. 2009;123(2):426-433.
2. Commins SP, James HR, Kelly LA, et al. The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose-α-1,3-galactose. *J Allergy Clin Immunol*. 2011;127(5):1286-1293.e6.
3. Commins SP. Diagnosis & management of alpha-gal syndrome: lessons from 2,500 patients. *Expert Rev Clin Immunol*. 2020;16(7):667-677.
4. Platts-Mills TAE, Li RC, Keshavarz B, Smith AR, Wilson JM. Diagnosis and Management of Patients with the α-Gal Syndrome. *J Allergy Clin Immunol Pract*. 2020;8(1):15-23.e1.
5. Center for Disease Control and Prevention: Alpha-gal Syndrome; retrieved June 5, 2023. https://www.cdc.gov/ticks/alpha-gal/index.html
6. Steinke JW, Platts-Mills TAE, Commins SP. The alpha-gal story: lessons learned from connecting the dots. *J Allergy Clin Immunol*. 2015;135(3):589-596; quiz 597.
7. Alpha-gal in health products triggers anaphylaxis in half of alpha-gal syndrome patients. Richard Gawel. *Healio*. Published online June 27, 2023.
8. Wilson JM, Schuyler AJ, Workman L, et al. Investigation into the α-Gal Syndrome: Characteristics of 261 Children and Adults Reporting Red Meat Allergy. *J Allergy Clin Immunol Pract*. 2019;7(7):2348-2358.e4.
9. Fischer J, Yazdi AS, Biedermann T. Clinical spectrum of α-Gal syndrome: from immediate-type to delayed immediate-type reactions to mammalian innards and meat. *Allergo J*. 2016;25:55-62.

10. Pattanaik D, Lieberman P, Lieberman J, Pongdee T, Keene AT. The changing face of anaphylaxis in adults and adolescents. *Ann Allergy Asthma Immunol*. 2018;121(5):594-597.
11. Monzón JD, Atkinson EG, Henn BM, Benach JL. Population and Evolutionary Genomics of Amblyomma americanum, an Expanding Arthropod Disease Vector. *Genome Biol Evol*. 2016;8(5):1351-1360.
12. Thompson JM, Carpenter A, Kersh GJ, Wachs T, Commins SP, Salzer JS. Geographic distribution of suspected alpha-gal syndrome cases - United States, January 2017-December 2022. MMWR Morb Mortal Wkly Rep. 2023;72(30):815-820.
13. Mysterious meat allergy passed by ticks may affect hundreds of thousands in US, CDC estimates. CNN. Updated 2:05 PM EDT, Sat July 29, 2023
14. Carpenter A, Drexler NA, McCormick DW, et al. Health care provider knowledge regarding alpha-gal syndrome - United States, march-may 2022. *MMWR Morb Mortal Wkly Rep*. 2023;72(30):809-814.
15. Gaines DN, Operario DJ, Stroup S, et al. Ehrlichia and spotted fever group Rickettsiae surveillance in Amblyomma americanum in Virginia through use of a novel six-plex real-time PCR assay. *Vector Borne Zoonotic Dis*. 2014;14(5):307-316.
16. Nadolny RM, Wright CL, Sonenshine DE, Hynes WL, Gaff HD. Ticks and spotted fever group rickettsiae of southeastern Virginia. *Ticks Tick Borne Dis*. 2014;5(1). doi:10.1016/j.ttbdis.2013.09.001
17. Ehrlichiosis Factsheet. Virginia Department of Health. Accessed Jan 7, 2023. https://www.vdh.virginia.gov/epidemiology/epidemiology-fact-sheets/ehrlichiosis/
18. Ailsworth SM, Susi A, Workman LJ, et al. Alpha-gal IgE Prevalence Patterns in the United States: An Investigation of 3000 Military Recruits. *J Allergy Clin Immunol Pract*. Published online October 31, 2023. doi:10.1016/j.jaip.2023.10.046
19. Commins S, Kelly L, Ronmark E, HR J, Pochan S, Peters E, et al. Galactose-alpha-1,3-galactosespecific IgE is associated with anaphylaxis but not asthma. Am J Respir Crit Care Med. 2012;185(7):723-30.
20. Richards NE, Richards Jr RD. Alpha-Gal Allergy as a Cause of Intestinal Symptoms in a Gastroenterology Community Practice. Southern Medical Journal. 2021;114(3):169-73.
21. Wilson JM, Keshavarz B, James HR, Retterer MK, Schuyler AJ, Knoedler A, et al. α-Gal specific-IgE prevalence and levels in Ecuador and Kenya: Relation to diet, parasites, and IgG4. Journal of Allergy and Clinical Immunology. 2021;147(4):1393-401. E7.
22. Wilson JM, Nguyen AT, Schuyler AJ, Commins SP, Taylor AM, Platts-Mills TA, et al. IgE to the mammalian oligosaccharide galactose-α-1, 3-galactose is associated with increased atheroma volume and plaques with unstable characteristics—Brief Report. Arteriosclerosis, thrombosis, and vascular biology. 2018;38(7):1665-9.
23. Fischer J, Lupberger E, Hebsaker J, et al. Prevalence of type I sensitization to alpha-gal in forest service employees and hunters. *Allergy*. 2017;72(10):1540-1547.

24. Richards N, Keshavarz B, Workman L, Patel J, Platts-Mills T, Wilson J. Prevalence of α-Gal IgE and Mammalian Meat Allergy in a COVID-19 Vaccine Employee Cohort. *J Allergy Clin Immunol*. 2022;149(2):AB207.
25. Bianchi J, Walters A, Fitch ZW, Turek JW. Alpha-gal syndrome: Implications for cardiovascular disease. *Global Cardiology Science and Practice*. 2020;2019(3).
26. Richards NE, Richards RD Jr. Alpha-Gal Allergy as a Cause of Intestinal Symptoms in a Gastroenterology Community Practice. *South Med J*. 2021;114(3):169-173.
27. Kimpel D, Wilson J, Lewis J. SAT0456 SERO-REACTIVITY TO GALACTOSE-ALPHA-1,3-GALACTOSE AND CLINICAL PRESENTATIONS OF PATIENTS SEEN IN A RHEUMATOLOGY OUTPATIENT PRACTICE. *Ann Rheum Dis*. 2019;78(Suppl 2):1317-1318.
28. Vernon ST, Kott KA, Hansen T, et al. Immunoglobulin E sensitization to mammalian oligosaccharide galactose-a-1,3 (α-Gal) is associated with noncalcified plaque, obstructive coronary artery disease, and ST-segment-elevated myocardial infarction. *Arterioscler Thromb Vasc Biol*. Published online January 20, 2022:ATVBAHA121316878.
29. CDC National Notifiable Diseases Surveillance System (NNDSS) Alpha-gal syndrome 2022 case definition. https://ndc.services.cdc.gov/case-definitions/alpha-gal-syndrome-ags/
30. CDC alpha-gal syndrome case report form. https://www.cdc.gov/ticks/alpha-gal/pdfs/328065-A_NCEZID_FRM_Alpha_gal_CRF_508_2.pdf
31. Alpha-gal syndrome for public health officials. Accessed online Jan 7, 2023. https://www.cdc.gov/ticks/alpha-gal/for-public-health-officials.html
32. Arkansas Department of Health (ADH) Mandatory Reportable Diseases List and Instructions. Accessed online Jan 7, 2023. https://www.healthy.arkansas.gov/images/uploads/pdf/List_and_Instructions_Reportable_Diseases.pdf
33. Emerging Tick Bite-Associated Meat Allergy Potentially Affects Thousands: Many healthcare providers not familiar with allergic condition. CDC press release. July 27, 2023. Accessed online Jan 7, 2023. https://www.cdc.gov/media/releases/2023/p0727-emerging-tick-bites.html