

## AGS background document: Tennessee

### Background

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

People with AGS react to products made from mammals. This includes foods such as beef, pork, lamb, venison, dairy products, and gelatin.<sup>3-5</sup> 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.<sup>3-5</sup> 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.<sup>7</sup> Many people with AGS also react to personal care and household products with mammal-derived ingredients.<sup>3</sup>

Alpha-gal reactions are often severe and can be fatal.<sup>3,4,6</sup> 60-75% of people with AGS experience anaphylactic reactions.<sup>8,9,34</sup>

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

### Tennessee: an alpha-gal syndrome hotspot

Tennessee is an alpha-gal syndrome hotspot. Residents in rural areas are most affected.<sup>12,18</sup> This is coincident with the abundance of lone star ticks. Over 33% of residents in some areas of Tennessee are sensitized to alpha-gal,<sup>18-22</sup> and up to 9% of these individuals may have allergic reactions to alpha-gal.<sup>3,23-25</sup> One Tennessee clinic found that reactions to alpha-gal were the number one cause of anaphylaxis in adults and adolescents, accounting for a third of all cases, *more than all other food allergies combined*.<sup>10</sup>

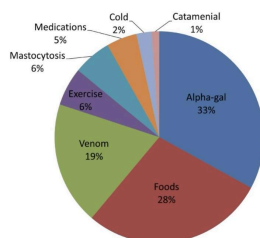


Figure 1. Etiologies of anaphylaxis based on proposed "definitive cause." Alpha-gal, galactose- $\alpha$ -1,3-galactose.

A recent study found that more than 2% of the population in high-prevalence areas may have alpha-gal syndrome.<sup>24</sup> Other estimates suggest that up to 3% of people in the hardest hit areas may be affected.<sup>3,23,25</sup> 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 high-prevalence areas.<sup>26,27</sup> 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.<sup>22,28</sup>

### **A call to action**

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

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 \(AGS\)](#)<sup>29</sup> and creating an [Alpha-gal Syndrome Case Report Form](#).<sup>30</sup> In September, 2023 Arkansas became the first state to make AGS a mandatory, reportable health condition,<sup>32</sup> 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- $\alpha$ -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  $\alpha$ -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  $\alpha$ -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  $\alpha$ -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.
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-galactose specific 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.  $\alpha$ -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- $\alpha$ -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  $\alpha$ -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- $\alpha$ -1,3 ( $\alpha$ -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](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](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>
34. Binder AM, Cherry-Brown D, Biggerstaff BJ, et al. Clinical and laboratory features of patients diagnosed with alpha-gal syndrome - 2010-2019. *Allergy*. Published online September 30, 2022. doi:10.1111/all.15539