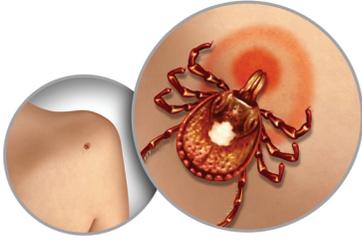


Fiscal Year 2027 Appropriations Requests

Alpha-gal syndrome



Alpha-gal syndrome (AGS) is an emerging tick-bite-associated allergy to alpha-gal (galactose-alpha-1,3-galactose), a sugar molecule found in most mammals and products and ingredients derived from them. Products that contain alpha-gal include foods, drugs, and personal care products. In the U.S., most AGS cases are caused by lone star ticks.

Examples of foods that contain alpha-gal:



Red meat



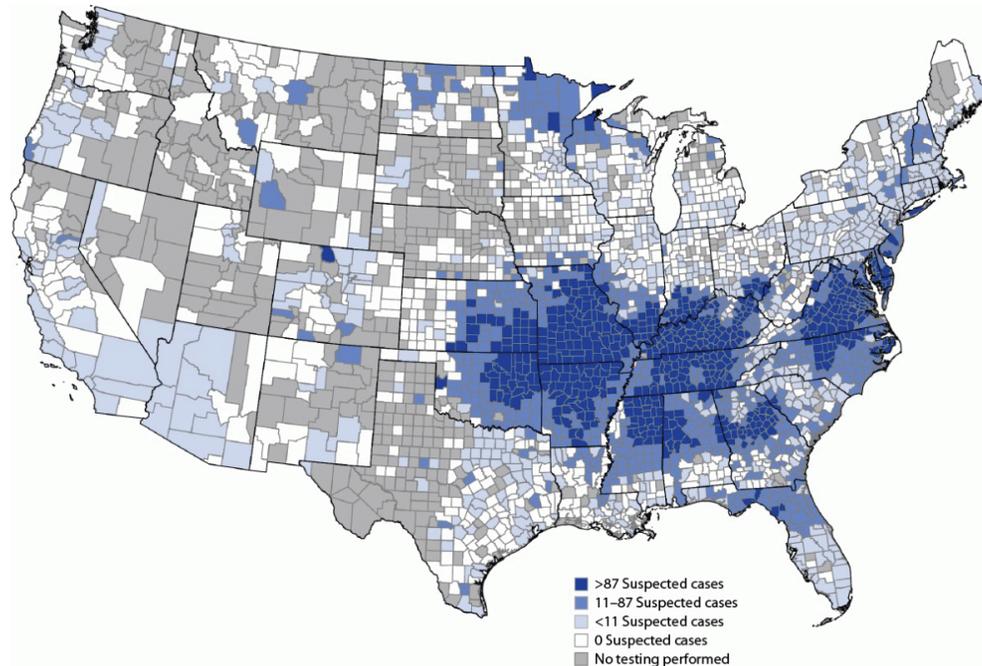
Dairy



Foods made with mammal-derived ingredients

Alpha-gal syndrome is most common in the southern, midwestern, and mid-Atlantic United States, where up to 3% of the population can be affected.¹ However, AGS impacts people in all 50 states. A study of military recruits found that 8% of recruits from Hawaii and 17% of Alaskan recruits tested positive for alpha-gal IgE, showing that AGS is widespread in the U.S.²

Rural areas are most impacted. People living in rural areas are up to 20 times more likely to develop AGS than people in urban areas.^{2,3}



Source: 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.

1. Commins SP. Diagnosis & management of alpha-gal syndrome: lessons from 2,500 patients. *Expert Rev Clin Immunol.* 2020;16(7):667-677.

2. 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

3. Villalta D, Pantarotto L, Da Re M, et al. High prevalence of sIgE to Galactose- α -1,3-galactose in rural pre-Alps area: a cross-sectional study. *Clin Exp Allergy.* 2016;46(2):377-380.

An emerging public health crisis

AGS was discovered in 2009. Today half a million Americans are estimated to be affected by AGS, making it the 10th most common food allergy in the U.S.¹ AGS cases are surging because growing white-tailed deer populations are driving increases in lone star tick populations and allowing the ticks to reach new areas.

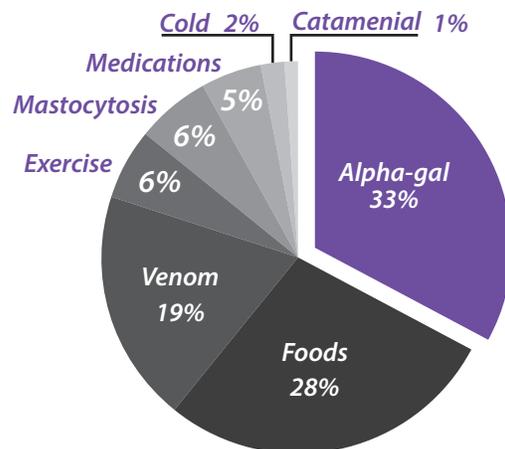


Source: Thompson JM, Carpenter A, Kersh GJ, Wachs T, Commins SP, Salzer JS. Geographic distribution of suspected alpha-gal syndrome cases - United States, January 2017-December 2022. MMWR Morb Mortal Wkly Rep. 2023;72(30):815-820.

A leading cause of anaphylaxis

Up to 75% of people with alpha-gal syndrome have life-threatening anaphylactic reactions, an even higher percentage than for peanut allergy.² In high-prevalence areas, alpha-gal reactions can be the number one cause of anaphylaxis in adults, causing more adult and adolescent anaphylaxis than all other food allergies combined.³ A number of fatalities have occurred.

“...this report demonstrates that AGS is both a severe allergy, with nearly 75% of patients meeting criteria for anaphylaxis, and also distinct from other food allergies in its symptom profile.”



Etiologies of anaphylaxis based on proposed "definitive cause." Alpha-gal, galactose-a-1,3-galactose

Source: Pattanaik D et al³

1. 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.

2. Binder AM, Cherry-Brown D, Biggerstaff BJ, et al. Clinical and laboratory features of patients diagnosed with alpha-gal syndrome - 2010-2019. Allergy.

3. 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.

Priority #1: Fund Alpha-gal Syndrome Provider Education and Surveillance

\$4.5M Total Requested

Fiscal Year 2027 Labor, Health and Human Services, Education and Related Agencies Appropriations bill
Title II – Department of Health and Human Services
Centers for Disease Control and Prevention
Account: Emerging and Zoonotic Disease

Funding Requested:

Within the total for EZID, the Committee recommends the following amounts:

Alpha-gal Syndrome.....\$4,500,000 (\$4.5 Million)

Report Language Requested:

Alpha-gal Syndrome — The Committee appreciates the work of the Division of Vector-Borne Diseases to prevent the transmission of and promote health provider awareness of Alpha-gal Syndrome (AGS). AGS is an emerging tick-borne condition and allergy characterized by a potentially life-threatening hypersensitivity to galactose-alpha-1,3- galactose (alpha-gal). Its prevalence is closely associated with the range of the lone star tick. AGS is a growing clinical and public health concern for persons in the United States. Exploding lone star tick populations may be driving an alarming increase in cases. Health care provider knowledge is limited and can lead to delayed diagnosis and inappropriate treatment.

The Committee encourages CDC to accelerate measures to improve AGS surveillance, patient care, and public awareness with an emphasis on healthcare provider education, in keeping with the three public health priorities identified in the CDC 2023 report. CDC is encouraged to focus on high or growing prevalence States. CDC may also benefit from a focused increase in its collaboration and partnership with local governments, health, education, community, non-profit, and faith-based sectors in those same high-incidence communities.



Justification

“ If testing trends continue, and the geographic range of the lone star tick continues to expand, the number of AGS cases in the United States is predicted to increase during the coming years, presenting a critical need for synergistic public health activities including 1) community education targeting tick bite prevention to reduce the risk for acquiring AGS, 2) HCP education to improve timely diagnosis and management, and 3) improved surveillance to aid public health decision-making.¹ ”

“ Increased HCP education and awareness of AGS are needed to hasten and improve the accuracy of AGS diagnoses, patient care, and the understanding of the epidemiology of this emerging condition.² ”

Alpha-gal syndrome (AGS) is a growing clinical and public health concern for persons in the United States.¹ Exploding lone star tick populations are driving an alarming increase in cases. In high prevalence states, AGS represents the bulk of the tick-borne disease burden. Far more people in these areas are affected by AGS than than all other tick-borne diseases combined.³

Healthcare provider knowledge is limited. CDC survey data indicates that only one in five healthcare providers are somewhat or very confident they can diagnose or manage patients with AGS. As a result, AGS is significantly underdiagnosed and misdiagnosed. On average, it takes more than seven years for a patient with AGS to be diagnosed.⁴

During this long time interval, people affected by AGS often experience debilitating symptoms. On average, more than half require emergency department-based treatment, 7% require multiple hospitalizations, and many are subjected to unnecessary, invasive procedures and surgeries, at a high cost to our healthcare system and to the affected individuals.⁴

Increasing awareness of AGS among healthcare providers is a critical first step towards improved diagnosis, better patient care, and reduced economic burden on both patients and healthcare systems.

In keeping with the three public health priorities identified in the CDC 2023 report, additional CDC funding is required to:

- Educate healthcare providers in the diagnosis and management of AGS
- Improve AGS surveillance
- Raise public awareness
- Build local capacity through partnerships with local governments, health, education, community, non-profit, and faith-based sectors, with an emphasis on high-incidence communities



1. 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.

2. 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.

3. State health department statistics and CDC surveillance data

4. Flaherty MG, Kaplan SJ, Jerath MR. Diagnosis of Life-Threatening Alpha-Gal Food Allergy Appears to Be Patient Driven. J Prim Care Community Health. 2017;8(4):345-348.

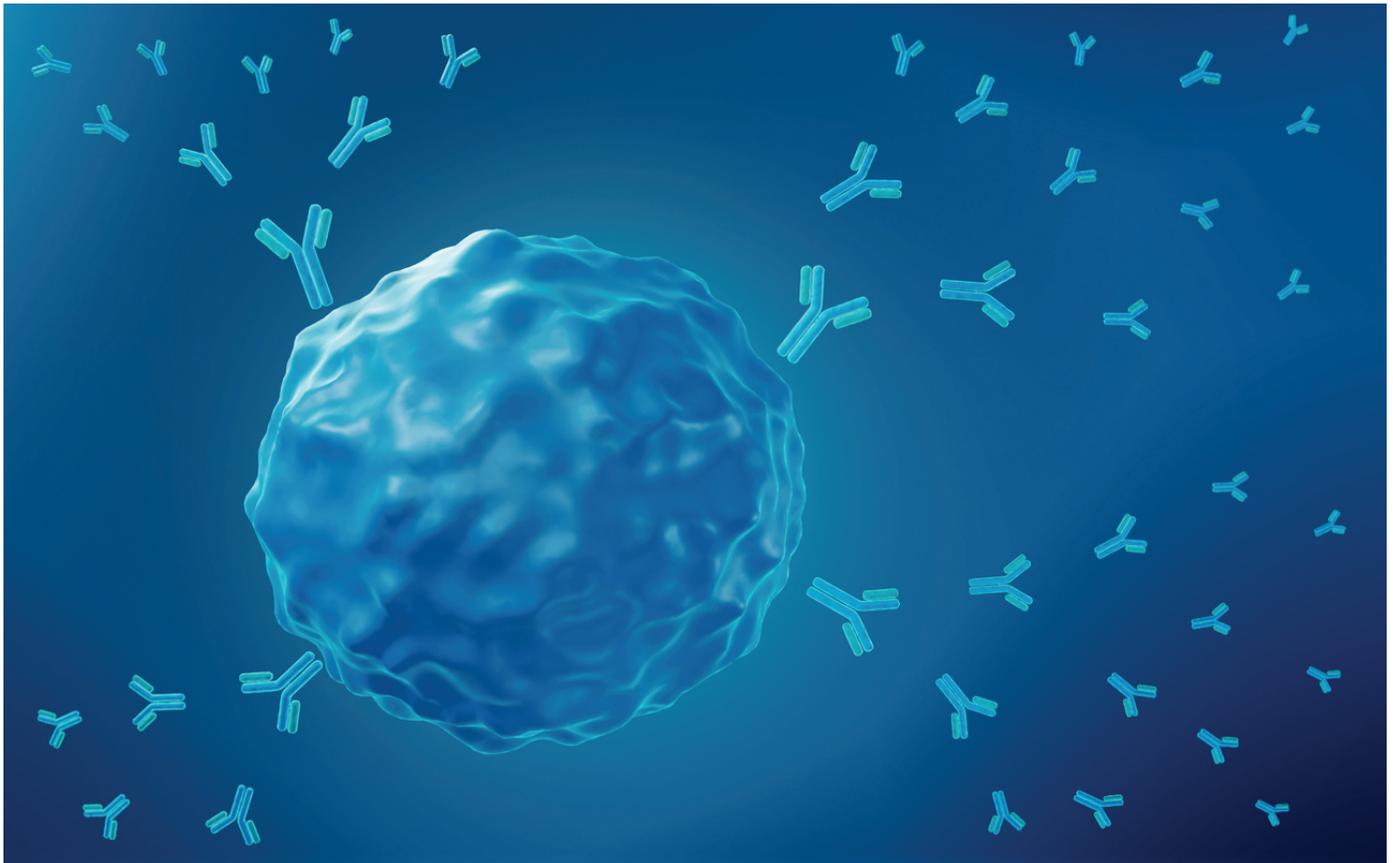
Priority #2: Fund NIH NIAID Alpha-gal Syndrome Research

Language Modification

Fiscal Year 2027 Labor, Health and Human Services, Education and Related Agencies Appropriations bill
Title II – Department of Health and Human Services
National Institutes of Health (NIH)
Lyme Disease and Related Tick-Borne Illnesses

Report Language Requested:

Alpha-gal Syndrome — The Committee is concerned about the rise in incidence of alpha-gal syndrome which is an emerging, growing, tick bite-associated allergic condition characterized by a potentially life-threatening hypersensitivity to galactose-alpha-1,3-galactose (alpha-gal). The Committee encourages NIH to accelerate their efforts to deepen our understanding of the immunological mechanisms and natural history of alpha-gal syndrome and develop new protocols, therapies, and other tools for the management of AGS.



Justification

“ Arguably, the most important public health consequence of tick bites, might well be the increased burden of atherosclerosis in alpha-gal sensitized individuals, first described by Wilson et al. and confirmed in a large cohort by Vernon et al.¹ ”

“ We are beginning to recognize that alpha-gal food allergy is the tip of the iceberg for this immune response.² ”

There is an urgent need to deepen our understanding of how tick-borne disease mechanisms drive chronic illness. This includes not just mechanisms related to tick-borne disease caused by pathogens, but also mechanisms related to immunological responses to tick bites themselves.

Alpha-gal syndrome (AGS) is a paradigm-shifting tick-borne disease caused by an immune response to tick bites. This immune response causes a life-threatening allergy to alpha-gal, a sugar found in mammals.

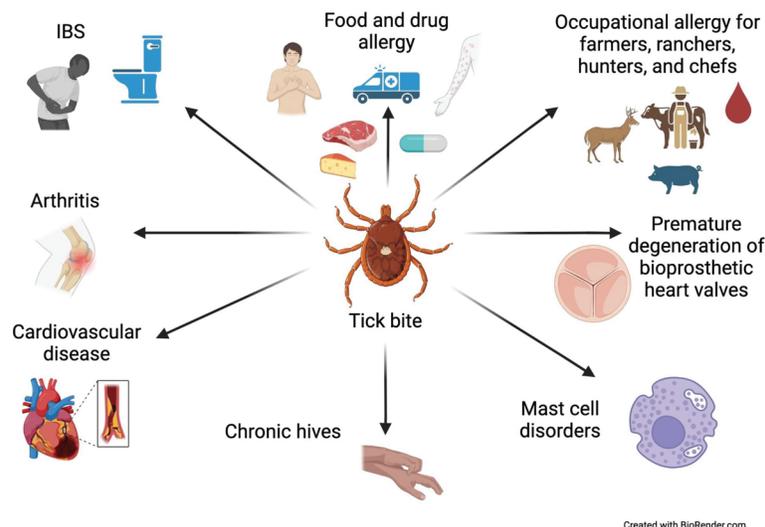
Unfortunately, classic allergic symptoms like hives and anaphylaxis are the tip of the iceberg. AGS is also a major driver of chronic disease. In high-prevalence areas, AGS may be responsible for up to 25% of IBS.³ Just having the allergic antibody to alpha-gal, which is true for 50% of the population in some areas of the U.S., is an independent risk factor for atherosclerosis and cardiovascular disease.^{4,5,6}

The alpha-gal immune response has also been implicated in arthritis, mast cell disorders, chronic urticaria, and autoimmune disease. AGS researchers are also exploring its possible connection to Alzheimer's disease and post-infectious syndromes.

Understanding alpha-gal syndrome's cellular and molecular mechanisms and natural history is a prerequisite to understanding how ticks drive allergy and other chronic disease so that effective therapies can be developed.

Funds are needed to:

- Deepen our understanding of the immunological mechanisms and natural history of alpha-gal syndrome
- Develop new protocols, therapies, and other tools for the management of AGS.
- Clarify the role of AGS and related immunological responses to tick bites in driving chronic disease.



Alpha-gal syndrome: more than a food allergy

1. van Nunen S. Quantifying the allergenic potency of mammalian meat sources, an important step in providing a framework for improved management of mammalian meat allergy after tick bite (alpha-gal syndrome/AGS). *Allergy*. Published online November 4, 2024. doi:10.1111/all.16381

2. Commins SP. Invited Commentary: Alpha-Gal Allergy: Tip of the Iceberg to a Pivotal Immune Response. *Curr Allergy Asthma Rep*. 2016;16(9):61.

3. 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.

4. Wilson JM, Nguyen AT, Schuyler AJ. Investigation of increased prevalence of IgE specific for galactose alpha-1, 3-galactose in patients with coronary artery disease. Published online 2019.

5. Vernon ST, Kott KA, Hansen T, et al. Immunoglobulin E Sensitization to Mammalian Oligosaccharide Galactose- α -1,3 (α -Gal) Is Associated With Noncalcified Plaque, Obstructive Coronary Artery Disease, and ST-Segment-Elevated Myocardial Infarction. *Arterioscler Thromb Vasc Biol*. 2022;42(3):352-361.

6. Figtree GA, Vernon ST, Harmer JA, et al. Clinical Pathway for Coronary Atherosclerosis in Patients Without Conventional Modifiable Risk Factors: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2023;82(13):1343-1359.



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