

Alpha-gal Syndrome

(Also known as alpha-gal allergy,
red meat allergy, or tick bite meat allergy)



1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Alpha-gal (galactose- α -1,3-galactose) is a sugar molecule found in most mammals. Alpha-gal is not found in fish, reptiles, birds, or people. Alpha-gal can be found in meat (pork, beef, rabbit, lamb, venison, etc.) and products made from mammals (including gelatin, cow's milk, and milk products). Alpha-gal Syndrome (AGS) (also called alpha-gal allergy, red meat allergy, or tick bite meat allergy) is a potentially life-threatening hypersensitivity reaction to alpha-gal.

B. Clinical Description

Individuals with AGS may experience different reactions and symptoms that can range from mild to severe or even life-threatening. The clinical presentation is broad with no one symptom or cluster of symptoms consistently predominating in patients with AGS. Skin reactions, like urticaria, and anaphylaxis are common; patients may also present with gastrointestinal or respiratory symptoms. AGS symptoms occur after people eat red meat or are exposed to other products containing alpha-gal. Unlike typical food allergies, symptoms are often delayed by two hours or more after exposure and can arise suddenly following years of safe meat consumption. Because these symptoms are delayed, people may wake up with them in the middle of the night after an evening meal. Symptoms may appear sooner if a person is exposed to alpha-gal containing products through intramuscular, intravenous, or subcutaneous administration. AGS symptoms include:

- Rash, hives or itching
- Abdominal pain, nausea, vomiting, or diarrhea
- Cough, shortness of breath, wheezing, or difficulty breathing
- Swelling of the lips, throat, tongue, or eyelids
- Heartburn or indigestion
- Drop in blood pressure
- Dizziness or faintness

Treatment

AGS should be treated and managed under the care of an allergist or another healthcare provider. Management of AGS includes use of antihistamines, epinephrine, and the elimination of mammalian meat and other alpha-gal-containing products from the diet. Anaphylaxis is a potentially life-threatening reaction and may need urgent medical care. Avoidance diets and prevention of additional tick bites allow many patients to slowly reintroduce meat into their diets.

C. Vectors and Reservoirs

Alpha-gal is a molecule carried in the saliva of tick and other potential arthropods typically after feeding on mammalian blood. Growing evidence suggests that AGS in the United States may be triggered by the bite of *Amblyomma americanum* (lone star tick) and *Ixodes scapularis* (blacklegged tick). The bite of some tick species induces immunoglobulin E (IgE) antibodies to alpha-gal,

sensitizing patients to subsequent alpha-gal exposures. One theory as to why tick bites cause AGS is that when ticks feed on mammals, they also uptake alpha-gal sugar molecules from their hosts. These ticks then expose humans to the alpha-gal sugar molecules in their saliva, where the body's immune system classifies the sugar as harmful.

D. Modes of Transmission

Tick bites have been implicated as a main cause of AGS, although more research is needed to understand the role ticks play in starting this reaction, and why certain people develop AGS.

E. Time from Exposure to Symptom Onset

Time to symptom onset may depend on the mode of exposure, with delayed onset (usually 2-6 hours, with longer intervals reported) after consumption of red meat or mammalian-derived products, including gelatin and dairy products. Hypersensitivity reactions in patients exposed to alpha-gal-containing products (e.g., gelatin-containing vaccines, heparin, antivenoms) have been reported to occur within two hours after intravenous, subcutaneous, or intramuscular administration, as well as in patients receiving xenotransplants. Much is not known concerning the level and timing of alpha-gal exposure and the development of AGS. Reactions may not occur after every alpha-gal exposure and symptoms can arise suddenly after years of safe meat consumption.

F. Epidemiology

AGS has been reported worldwide, and in the United States, it is most closely associated with lone star tick (*Amblyomma americanum*) bites. The geographic distribution of AGS in the U.S. overlaps with the geographic range of the lone star tick, although cases outside this geographic range suggests other ticks may play a role. Research has suggested that other tick species, including *Ixodes* spp., may also be associated with AGS development. Additionally, much of the country may be at risk given the expanding geographic range of lone star and other ticks. In New Jersey, *Ixodes scapularis* (blacklegged or deer tick) is found throughout the state. The lone star tick, once found in primarily in the southern half of New Jersey, is moving north and has been found in central New Jersey counties, including Monmouth, Middlesex, and Somerset counties.

Reports of AGS in the scientific literature have been increasing over the last decade, but the true burden of cases is unknown. Assessment of commercial laboratory data from 2010-2018 documented that the majority of positive alpha-gal sIgE antibody tests were submitted from the southeast region of the United States, and the number of tests performed increased 81-fold during this period. One commercial laboratory tested 105,674 people between 2010 and 2018, and 32% were positive for alpha-gal sIgE (Binder, 2018). Estimates from 2013 suggest that at least 5,000 cases of AGS had been diagnosed in the United States at that time (Platts-Mills, 2013). Accurate, up-to-date estimates of burden, disease trends and geographic distribution are hampered by the absence of a standardized case definition and reporting.

2 CASE DEFINITION

The NJDOH Zoonotic Disease Program follows the most current case definition as published on the CDC National Notifiable Disease Surveillance System (NNDSS) website.

AGS Case Definition: <https://ndc.services.cdc.gov/conditions/alpha-gal-syndrome-ags/>

Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and should not be used by healthcare providers to determine how to meet an individual patient's health needs.

A. Clinical Criteria (for the purposes of surveillance):

Acute onset of any one or more of the following allergic and/or gastrointestinal symptoms that occur 2–10 hours after ingestion of pork, beef, lamb, any other mammalian meat, or any mammalian-derived product (e.g., gelatin), OR within two hours after intramuscular, intravenous, or subcutaneous administration of alpha-gal-containing vaccination or medication:

- Abdominal pain
- Nausea
- Diarrhea
- Vomiting
- Heartburn/indigestion
- Hives
- Itching
- Anaphylaxis as diagnosed by a provider
- Swelling of one or more of the following: lips, tongue, throat, face, eyelids, or other associated structures
- Shortness of breath
- Cough
- Wheezing
- Acute episode of hypotension*

AND

- the absence of a clear alternative diagnosis.

** Normal values for systolic blood pressure vary by age. Hypotension is classified by systolic blood pressure <90 mmHg for ages 11+ years; < [70 mmHg + 2 x age] for ages 1 -10 years; <70 mmHg for ages less than 1 year.*

B. Laboratory Criteria:

Confirmatory laboratory evidence:

- Serum or plasma immunoglobulin E specific to alpha-gal (sIgE) ≥ 0.1 IU/mL or ≥ 0.1 kU/L

Presumptive laboratory evidence:

- An allergy skin test result that is interpreted by the ordering provider as consistent with alpha-gal allergy based on sensitivity to one or more mammalian meats (e.g., pork, beef, lamb) or other mammalian-derived products.

C. Case classification**CONFIRMED**

A case that meets clinical criteria and confirmatory laboratory evidence

PROBABLE

A case that meets clinical criteria and presumptive laboratory evidence

POSSIBLE

A case that meets confirmatory laboratory evidence with no clinical information available

D. Criteria to Distinguish a New Case from an Existing Case:

A case should only be counted if not previously reported to public health authorities (one case entered in CDRSS).

NOTE: Cases would meet confirmed or probable case definition if not previously reported, even if the initial reaction date or diagnosis was in a prior year. Enter earliest date of diagnosis (if known) or reaction in Illness Onset Date and it will assign the case to the appropriate year.

3 LABORATORY TESTING

Diagnosis generally relies on a history of symptoms following exposure to mammalian products, and an elevated serum IgE specific to alpha-gal. Available diagnostics include allergy skin tests demonstrating sensitization to beef, pork, or lamb antigens and alpha-gal-specific IgE (sIgE) tests that are widely available through commercial laboratories, with a value of ≥ 0.1 k IU/ml or > 0.1 kU/L generally considered positive. Tests for alpha-gal sIgE antibodies are available at several commercial laboratories and may be available at certain academic institutions.

4 PURPOSE OF SURVEILLANCE AND REPORTING

- To better understand the local epidemiology of AGS and compare interstate disease incidence
- To recognize areas in New Jersey where AGS incidence has increased or decreased
- To focus preventive education on tick bite prevention, to reduce overall tickborne disease risk
- To increase healthcare provider awareness of AGS

5 CASE INVESTIGATION

A. Investigation

NJDOH has requested electronic laboratory reporting for positive immunoglobulin E specific to alpha-gal (sIgE) tests effective January 1, 2022. Currently, NJDOH is not asking clinicians to report positive skin prick test results. Local health departments are asked to initiate investigations of laboratory positive cases. AGS would be considered a priority level 5 condition for investigation, with investigations started within 2 weeks and completed within 3 months.

To collect surveillance data on AGS, much of the information can be gathered by the patient's healthcare provider, but a patient interview is also needed to characterize all symptoms and exposures. To assist with the investigation, the AGS Investigation Worksheet can be used to obtain essential information from the healthcare provider and when interviewing the patient: <https://www.nj.gov/health/cd/topics/alphagal.shtml>.

Refer to Key CDRSS Fields Specific for AGS section for additional investigation details.

B. Key CDRSS Fields Specific for AGSCDRSS Screen	
	Required Information
Disease Information	<ul style="list-style-type: none"> • <u>Illness Onset Date</u>: Enter date of 1st AGS diagnosis (if known) or earliest reaction date. If exact date is unknown, enter month and year and "1" for day, e.g., May 2017 should be entered as 5/1/2017.
Laboratory and Diagnostic Test Information	<ul style="list-style-type: none"> • If a clinician reports skin prick testing consistent with AGS, select "Skin prick testing for alpha-gal component reactivity" under Test Name

B. Key CDRSS Fields Specific for AGSCDRSS Screen	Required Information
Clinical Status	<ul style="list-style-type: none"> • <u>Illness Onset Date</u>: If not entered in Disease Information Section, enter date of 1st AGS diagnosis (if known) or earliest reaction date. If exact date is unknown, enter month and year and “1” for day, e.g., May 2017 should be entered as 5/1/2017. • Enter if patient was hospitalized for the current AGS reaction and if patient died (include cause of death if known and check “died during investigation” if related to AGS).
Medical Facility and Provider Information	<ul style="list-style-type: none"> • If patient was seen in an Emergency Department or was hospitalized (admitted) for the current AGS reaction, update patient status, admission, and discharge dates.
Signs and Symptoms	<ul style="list-style-type: none"> • Signs and symptoms should be asked about ANY AGS reaction the patient had, not only the current reaction. • The clinical presentation for AGS is broad and much is unknown. Please ask about all default signs and symptoms and add any additional reported symptoms.
Risk Factors	<ul style="list-style-type: none"> • Tick exposures 12 months prior to earliest AGS diagnosis or reaction.
Additional Requirements	<ul style="list-style-type: none"> ○ Dates of earliest and current AGS reaction and earliest diagnosis (if exact dates of prior onset or diagnosis are not known, enter year and month (if known)) ○ Consumed products associated with any AGS reaction (not just current reaction) ○ Pharmaceutical/medical products (IM, IV, SC) associated with any AGS reaction (not just current reaction) ○ Physician diagnosed anaphylaxis associated with AGS ○ If patient was ever hospitalized for AGS (any reaction, not just current reaction)

B. Key CDRSS Fields Specific for AGSCDRSS Screen	Required Information
Case Comments	<ul style="list-style-type: none"> AGS investigation information should be obtained by both the healthcare provider and the patient. If the healthcare provider and patient were unresponsive, list the dates attempts were made to obtain information and the outcomes. For example, 1/12/22 faxed AGS worksheet to provider; 1/31/22 left voice mail for patient, 2/5/21, spoke with patient; 2/15/22, re-faxed worksheet to provider. Provider non-responsive.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (NJAC 8:57-1.10) / Protection of Contacts of a Case

There are no isolation or quarantine restrictions.

B. Managing Special Situations

Removing a Tick

Ticks should be removed as soon as they are found on the skin. Fine-tipped tweezers should be used to firmly grasp the tick very close to the skin. Using a steady motion, the tick's body should be pulled away from the skin. Efforts should be made to not twist or jerk the tick – this can cause the mouthparts to break off and remain in the skin. If this happens, the mouthparts should be removed with tweezers. If mouthparts can't be removed, leave them alone and let the skin heal. After the tick is removed, the bite area should be cleaned with rubbing alcohol, an iodine scrub, or soap and water.

Dispose of a live tick by submersing it in alcohol, placing it in a sealed bag/container, wrapping it tightly in tape, or flushing it down the toilet. Never crush a tick with fingers. Petroleum jelly, a hot match, nail polish, or other products should not be used to remove a tick.

Tick Testing and Identification

Tick testing of individual ticks is not useful because AGS is not caused by an infectious agent.

Tick identification may be of value when discussing tick bite exposures with a healthcare provider. County mosquito control agencies or agricultural extension offices may offer tick identification services. The TickEncounter Resource Center also has tick identification resources online:

http://www.tickencounter.org/tick_identification

C. Preventive Measures

Preventing ticks in the yard: Involves keeping wildlife (especially deer and rodents) out of the yard and outdoor areas, making it less attractive to ticks.

- Clear tall grasses and brush around homes and at the edge of lawns.
- Place a 3-ft wide barrier of wood chips or gravel between lawns and wooded areas and around patios and play equipment. This will restrict tick migration into recreational areas.
- Mow the lawn frequently and keep leaves raked.
- Stack wood neatly and in a dry area (discourages rodents that ticks feed on).
- Keep playground equipment, decks, and patios away from yard edges and trees and place them in a sunny location, if possible.
- Remove old furniture, mattresses, or trash from the yard that may give ticks a place to hide.

- When using acaricides (tick pesticides) around the home, always follow the label instructions and never use near streams or other bodies of water.

Preventing ticks on pets: Pets can bring infected ticks into the home or yard. Check pets for ticks daily, especially after they spend time outdoors. If a tick is found on the pet, remove it right away. Pet owners should discuss tick preventives with their veterinarian.

Preventing tick bites on people: The best preventive measure is to avoid tick-infested areas.

Tick Species by Seasonality and Habitat in New Jersey

Tick	Life Stage	Seasonality	Habitat
Lone star tick (<i>A. americanum</i>)	Nymph	March – September ¹	Generally: Forests, woodlands, fields, and areas along edges. Nymphs/Adults: Tall grass in shade or at the tips of low-lying plants. Geographic range: Primarily central/southern NJ
	Adult	March – July ¹	
Blacklegged tick (<i>I. scapularis</i>)	Nymph	March – September ¹	Nymphs: Moist leaf litter in wooded areas or forest edges Adults: Mostly edge of woods Geographic range: Throughout NJ
	Adult	September – June ¹ (Depending on temperature)	

¹ Jordan, R. A., & Egzi, A. (2019). The growing importance of lone star ticks in a Lyme disease endemic county: passive tick surveillance in Monmouth County, NJ, 2006–2016. *PLoS One*, 14(2), e0211778.

Note: Some months for seasonality are approximated when ranges between seasons are described from the literature rather than between months.

In areas where contact with ticks may occur, individuals should be advised to do the following:

- Wear long-sleeved shirts and long, light-colored pants tucked into socks or boots.
- Stay on trails when walking or hiking and avoid high grass.
- Use repellent that contains 20 percent or more DEET, picaridin or IR3535 on exposed skin for protection that lasts several hours. Always follow product instructions. Parents should apply this product to their children, avoiding hands, eyes, and mouth.
- Use products that contain permethrin on clothing. Treat clothing and gear, such as boots, pants, socks, and tents with products containing 0.5% permethrin. It remains protective through several washings.
- Bathe or shower as soon as possible after coming indoors (preferably within 2 hours) to wash off and more easily find ticks that are crawling on the body.
- Conduct a full-body tick check using a hand-held or full-length mirror to view all parts of the body upon returning from tick-infested areas. Parents should check their children for ticks under the arms, in and around the ears, inside the belly button, behind the knees, between the legs, around the waist and especially in their hair.

- Examine gear and pets. Ticks can ride into the home on clothing and pets, then attach to a person later, so carefully examine pets, coats, and day packs.
- Tumble dry clothes in a dryer on high heat for 10 minutes to kill ticks on dry clothing after coming indoors.

Resources

NJDOH:

- [Fight the Bite NJ](#)
- [Alpha-Gal Syndrome](#)

CDC:

- [Alpha-Gal Syndrome](#)
- [Products that may contain alpha-gal](#)

OTHER:

- [American Academy of Allergy, Asthma & Immunology \(AAAAI\) Alpha-gal and Red Meat Allergy](#)
- Binder AM, Commins SP, Altrich ML, et al. [Diagnostic testing for galactose-alpha-1,3-galactose, United States, 2010 to 2018](#). Annals of Allergy, Asthma & Immunology 2021;S1081120620312746.
- Platts-Mills TA, Commins SP. [Emerging antigens involved in allergic responses. Current Opinion in Immunology](#) 2013;25(6):769–74.