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I. ABOUT THE DISEASE

A. Clinical Presentation

Apha-gal Syndrome (AGS) is an allergic reaction that occurs after a tick bite. Symptoms vary from person to person and can range from mild to severe, and sometimes life-threatening reactions, such as anaphylaxis¹.

Patients with AGS may present with a variety of symptoms, such as²:

- Skin reactions (urticaria, rash, hives, and itching)
- Swelling of the lips, throat, tongue or eyelids
- Gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea, heartburn, and indigestion)
- Respiratory symptoms (cough, difficulty breathing, shortness of breath, and wheezing)
- Dizziness, fainting, or drop in blood pressure
- Potentially life-threatening anaphylaxis involving multi-organ systems that require immediate medical attention

Symptoms can appear two to six hours after consuming red meat, dairy products, or exposure to products containing alpha-gal such as gelatin-coated medications². Symptoms may also appear in the middle of the night following an evening meal that contains mammalian products. Symptoms may appear sooner if the person is exposed to alpha-gal containing products intramuscularly, intravenously, or subcutaneously¹. Symptoms can also arise suddenly even though the person has had years of safe consumption of meat and other alpha-gal containing products.

B. Etiologic Agent

AGS is a hypersensitivity reaction to non-primate mammalian meat and products and is primarily triggered by the bite of a tick. Based on where most AGS cases occur, the most likely culprit is the lone star tick (*Amblyomma americanum*)³. During a bite, the tick injects a sugar molecule called galactose-alpha-1, 3-galactose along with its saliva into the bloodstream, sensitizing the human to produce IgE antibodies to alpha-gal. Subsequent human exposure to alpha-gal leads to an allergic reaction³.

Alpha-gal is found in pork, beef, rabbit, lamb, venison and other products of mammalian origin such as gelatin, milk, milk products, gel-coated medications, snake antivenom, heparin, and animal organs used in transplants³. Alpha-gal is not found in fish, reptiles, birds or primates (including people).



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C. Reservoir

Alpha-gal is a sugar molecule carried in the saliva of ticks after feeding on mammalian blood.

Worldwide, AGS is caused by a bite from different tick species. In the United States, the lone star tick (*Amblyomma americanum*) is the most common vector. AGS may also be induced by a bite from a black legged tick (*Ixodes scapularis*).

D. Incubation Period

Onset of symptoms depend on the mode of exposure.

- People exposed to alpha-gal containing products through intravenous, intramuscular, or subcutaneous routes can have reactions within two hours of exposure².
- Consumption (eating or drinking) of red meat or mammalian products may cause reactions to appear two to six hours after exposure².

Little is known about the timing of exposure and onset of AGS. Reactions may arise suddenly even if the person has had years of safe consumption of meat and other alpha-gal containing products.

Delay in symptom manifestation is variable and the severity of reactions is not predicted by specific IgE levels².

E. Mode of Transmission

A bite from a tick is the main cause of AGS. The main suspect in the United States is the lone star tick, but anecdotal evidence suggests that other species could be involved as well⁴. AGS is not transmissible person to person.

F. Period of Communicability

AGS cannot be passed person to person.



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II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

Reduce severe complications of disease by educating healthcare providers and the public about the occurrence of alpha-gal syndrome.

B. Disease Prevention Objectives

Reduce disease risk through public education regarding use of personal protective measures.

C. Disease Prevention and Control Intervention

Avoiding tick bites is the mainstay of alpha-gal syndrome prevention, especially since further introductions of alpha-gal by tick bite can make the condition worse. The following are important personal protective measures that should be followed, especially for people who live, work, or spend their leisure time in an area likely to have ticks:

- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light-colored shirts. Long pants should be tucked into socks when weather permits.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N,N-diethyl-meta-toluamide) and choose a product that will provide sufficient protection for the amount of time spent outdoors. DEET products should not be used on children <2 months of age. The following precautions should be observed when using DEET products⁵:
 - o Avoid using DEET products that combine the repellent with sunscreen. Sunscreens may need to be applied too often, resulting in an over application of DEET.
 - o Apply DEET on exposed skin, using only as much as needed.
 - o Do not use DEET on the hands of young children and avoid applying repellent to areas around the eyes and mouth.
 - o Do not use DEET over cuts, wounds, or irritated skin.
 - o Wash treated skin with soap and water after returning indoors and wash treated clothing.
 - o Avoid spraying DEET products in enclosed areas.
- Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin
 products are not designed to be applied to the skin. Clothing should be treated and allowed
 to dry in a well-ventilated area prior to wearing⁵.
- Check yourself, children, and pets for ticks upon returning from outdoors. Make sure to check the following areas: between the toes, back of the knees, groin, armpits, neck, along the beltline, along the hairline, and behind the ears.



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• Promptly remove attached ticks using fine-point tweezers. Grasp the tick close to the skin and pull straight up using steady pressure. Do not squeeze or twist the tick.

Environmental Measures⁵:

- Prevention of alpha-gal syndrome can also involve actions to keep ticks out of yards.
- Keep grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch or gravel barrier where the lawn meets the woods and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

D. Treatment

There is no recognized treatment for alpha-gal syndrome, however the allergy has been known to wane over time if further lone star tick bites are avoided. Avoidance of allergy triggers is the best management strategy for living with alpha-gal. A non-exhaustive list of things to avoid include⁶:

- Red meat (including but not limited to beef, venison, pork, and goat)
- Dairy products (including milk, cheese, ice cream, etc.)
- Mammalian fats in cooking (lard, tallow)
- Gelatin (Jello, pudding, medicines with gel caps, etc.)
- Stock and bouillon cubes
- Medicines created using mammalian products (Heparin, monoclonal antibodies, artificial hormones, animal organ transplants, antivenom)
- Further bites from lone star ticks⁷
- Stings from other insects (bees, wasps, etc.)⁷

It is best to consult a doctor or pharmacist before starting any new medications to ensure there are no ingredients in them that will cause an alpha-gal reaction. Any severe allergic reactions should be treated at an emergency room.



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III. DISEASE INVESTIGATION

A. Criteria for Case Ascertainment

Clinical Criteria for Reporting⁸

See Case Definition Clinical Criteria

Laboratory/Imaging Criteria for Reporting⁸

Any of the following criteria warrant reporting to public health authorities:

- Serum or plasma immunoglobulin E specific to alpha-gal (slgE) \geq 0.1 IU/mL or \geq 0.1 kU/L.
- 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.

Epidemiologic Linkage Criteria for Reporting⁸

N/A

Vital Records Criteria for Reporting⁸

Report any person whose death certificate lists AGS as a cause of death or a significant condition contributing to death.

Other Criteria for Reporting⁸

Report any person whose healthcare or medical record contains a diagnosis, active problem, or finding of AGS.

B. Case Definition and Case Classification

Clinical Criteria⁸

Acute onset of any one or more of the following allergic and/or gastrointestinal symptoms that occur two to ten 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 (see Appendix 1):

- Abdominal pain
- Nausea
- Diarrhea
- Vomiting
- Heartburn/indigestion



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- 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 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 one to 10 years; <70 mmHg for ages less than one year.

Laboratory/Imaging Criteria⁸

Confirmatory laboratory evidence:

• Serum or plasma immunoglobulin E specific to alpha-gal (slgE) \geq 0.1 IU/mL or \geq 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.

Supportive laboratory evidence: N/A

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

Epidemiologic Linkage⁸

N/A



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Vital Records Criteria⁸

Any person whose death certificate lists AGS as cause of death or significant condition contributing to death.

Other Classification Criteria⁸

N/A

Case Classifications⁸

Confirmed:

• Meets clinical criteria AND confirmatory laboratory evidence.

Probable:

• Meets clinical criteria AND presumptive laboratory evidence.

Suspect:

• Meets confirmatory laboratory evidence with no clinical information available.

A case should only be counted if not previously reported to public health authorities.

C. Reporting Timeframe to Public Health

Report all confirmed or suspected cases to the West Virginia Department of Health within one week.

D. Outbreak Recognition

Alpha-gal Syndrome is not known to be spread through contact with blood or other bodily fluids, so transfusion-based spread and outbreaks in general are unlikely.

E. Healthcare Provider Responsibilities

- 1. Be familiar with AGS clinical presentation, risk factors, diagnosis, testing, and management.
- 2. Diagnostic tests for AGS:
- Allergy skin tests demonstrating sensitization to any kind of mammalian meat or mammalian-derived products (including milk)
- Serum or plasma immunoglobulin E specific to alpha-gal (IgE) tests available through commercial laboratories. Value of ≥0.1k IU/mL or >0.1K U/L is considered positive.
- 3. Be familiar with potential sources of exposure and educate patients about avoidance. <u>Products that contain alpha-gal</u> include but are not limited to:
- Mammalian red meat, organs and tissues
- Milk products, gelatin



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- Products from animal fat, e.g. lard
- Meat broth, bouillon, stock and gravy
- Pharmaceutical products
- Glycerin
- Bovine extract
- 4. Management of AGS: use of antihistamines, epinephrine, and elimination of mammalian meat and other alpha-gal containing products from the diet. Avoidance diets and prevention of additional tick bites allow many patients to slowly reintroduce meat into their diets.
- 5. Educate patients about <u>tick bite prevention</u>.
- Report patients (confirmed or suspected) with AGS to the West Virginia Department of Health within one week of detection by completing the <u>Alpha-gal Syndrome Reporting Form</u> and faxing it to (304) 558-8736.

F. Laboratory Responsibilities

Report positive alpha-gal IgE laboratory results and positive skin test results against mammalian meats or products to the West Virginia Department of Health within one week.

G. Local Health Responsibilities

- 1. Conduct outreach and educate the public about <u>tick bite prevention</u>.
- 2. Be familiar with AGS.
- 3. Educate healthcare professionals about AGS and the reporting process.
- 4. Educate the public about AGS.

H. State Health Responsibilities

- 1. Manage laboratory reports of alpha-gal IgE, positive skin tests, and investigations in the West Virginia Electronic Disease Surveillance System (WVEDSS).
- 2. Complete reporting of alpha-gal syndrome cases to the Centers for Disease Control and Prevention (CDC) through WVEDSS.
- 3. Provide technical expertise and consultation on surveillance, investigation, disease control and prevention of alpha-gal syndrome.
- 4. Notify CDC of suspected clusters.
- 5. Summarize surveillance data on an annual basis and share with partners.

I. Occupational Health

N/A



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IV. DISEASE SURVEILLANCE

A. Public Health Significance

AGS is an emerging tick-borne hypersensitivity reaction to red meat and other mammalian products. This condition is of public health significance because of its potential for severe allergic reaction requiring immediate medical attention. Patients with AGS should be advised to avoid consumption of mammalian meat and products, which can impact their diet and nutrition.

In 2025, AGS became a reportable condition in West Virginia. Healthcare providers are required to report patients with AGS to the West Virginia Department of Health within one week of diagnosis/detection.

Equally important is the widespread distribution of the vector in West Virginia, the lone star tick. Ticks carry many pathogens, so the promotion of tick prevention, such as use of insect repellents, use of long sleeves and long pants, and avoidance of areas populated by ticks are important.

B. Disease Surveillance Objectives

- 1. To detect AGS in West Virginia.
- 2. To determine the epidemiology of AGS in West Virginia and how it compares with other jurisdictions.
- 3. To enhance tick-borne disease prevention including education and outreach.
- 4. To facilitate healthcare provider education and awareness.

C. Surveillance Indicators

- 1. The proportion of cases reported to CDC with complete information (clinical case definition, hospitalization, laboratory testing, etc.).
- 2. The proportion of cases that are confirmed, probable, and suspect.
- 3. The interval between date of symptom onset and date of public health notification.



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