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ALPHA-GAL SYNDROME: AN EMERGING TICK-INDUCED ALLERGY TO MAMMALIAN MEAT – CURRENT KNOWLEDGE AND CLINICAL IMPLICATIONS

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ABSTRACT

Background: Alpha-gal syndrome (AGS) is an emerging IgE-mediated allergy to galactose-α-1,3-galactose (α-gal), a carbohydrate epitope present in most non-primate mammals. The condition is typically triggered by tick bites and is characterized by delayed hypersensitivity reactions occurring several hours after ingestion of mammalian meat or exposure to products containing α-gal. Increasing tick populations and environmental changes have contributed to the growing recognition of this condition worldwide.
Aim: This review aims to summarize current knowledge on the epidemiology, immunopathogenesis, clinical manifestations, diagnosis, and management of alpha-gal syndrome, with particular emphasis on its clinical implications and challenges in everyday medical practice.
Materials and methods: A narrative review of the literature was conducted using publications indexed in PubMed. Clinical studies, case series, mechanistic studies, and review articles published between 2009 and 2026 were included. The evidence was analyzed and synthesized across key thematic areas, including epidemiology, pathophysiology, clinical presentation, diagnostic approaches, and management strategies.
Results: AGS represents a unique model of delayed IgE-mediated food allergy. Clinical manifestations range from isolated gastrointestinal symptoms and urticaria to severe anaphylaxis. Diagnosis is primarily based on the detection of serum IgE antibodies to α-gal combined with a compatible clinical history. The cornerstone of management remains avoidance of mammalian-derived foods and prevention of further tick bites. Recent evidence also highlights the potential role of cofactors, biological therapies, and non-dietary exposures in triggering allergic reactions.
Conclusions: Alpha-gal syndrome is an increasingly recognized but still underdiagnosed allergic condition that poses significant diagnostic and clinical challenges. Greater awareness among clinicians and further research into the immunological mechanisms and long-term outcomes of the disease are essential to improve diagnosis and patient management.

KEYWORDS

Alpha-Gal Syndrome, Tick Bite, Red Meat Allergy, IgE, Delayed Anaphylaxis, Galactose-α-1,3-galactose

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1. Introduction

Alpha-gal syndrome (AGS) is a relatively newly recognized form of food allergy characterized by hypersensitivity to galactose-α-1,3-galactose (α-gal), an oligosaccharide present in the tissues of all mammals except humans and Old World monkeys [1]. This key difference in glycoprotein structure explains why humans can develop an immune response to this epitope. Unlike classic IgE-mediated food allergies, in which the reaction occurs within minutes of exposure to the allergen, in AGS, symptoms usually appear only 2-6 hours after consumption of mammalian meat or animal products [2]. This delay is due to the time required for digestion and absorption of α-gal-containing glycolipids, which are then transported in chylomicrons and lipoproteins [3].

A distinctive feature of this disease entity is its association with tick bites, which can lead to the development of specific IgE antibodies against α-gal [4]. All humans naturally produce IgM, IgG, and IgA antibodies against α-gal, but only in some people after tick bites does the immunoglobulin class switch to IgE, which is crucial for the development of AGS [5]. This syndrome is regional in nature, reflecting the occurrence of the relevant tick species – mainly Amblyomma americanum in the United States and other species in Europe [1].

The α-gal syndrome is distinguished not only by its unusual sensitization mechanism, but also by the significant variability of its clinical presentation. In some patients, skin symptoms or anaphylactic reactions predominate, while in others, gastrointestinal complaints are mainly observed. In addition, the presence of

specific IgE antibodies against α-gal is not always associated with clinical symptoms, which further complicates diagnosis [2].

The growing interest in AGS also stems from its potential clinical implications beyond food allergy. The α-gal epitope may be present in certain drugs, vaccines, and medical devices of animal origin, which may be a source of unexpected hypersensitivity reactions in sensitized patients. For this reason, knowledge of the mechanisms of the disease and its clinical manifestations is important for both allergists and physicians of other specialties [4].

In recent years, there has been a significant increase in the number of publications on α-gal syndrome, but many aspects of this disease remain poorly understood, including the immune mechanisms responsible for the development of sensitization, the causes of the delayed nature of the allergic reaction, and the factors determining the variability of the clinical presentation.

2. Methodolgy

2.1. Study Design and Search Strategy

This study was conducted as a narrative literature review aimed at summarizing current knowledge on alpha-gal syndrome (AGS), including its epidemiology, immunopathogenesis, clinical manifestations, diagnosis, and management.

A literature search was performed using the PubMed, Scopus, and Google Scholar databases. Publications published between 2009 and 2026 were considered. The search strategy included the following keywords: alpha-gal syndrome, galactose-α-1,3-galactose, red meat allergy, tick-induced allergy, delayed anaphylaxis, alpha-gal IgE, diagnosis, management, biological products, and medical exposure.

The search aimed to identify relevant studies describing the epidemiology, pathophysiology, clinical presentation, diagnostic approaches, and treatment of alpha-gal syndrome, as well as publications addressing potential exposure to α-gal in medicinal products and medical devices.

2.2. Eligibility Criteria

Publications were included if they met the following criteria:

- Peer-reviewed original articles, review papers, or case reports related to alpha-gal syndrome.
- Studies addressing epidemiological, immunological, clinical, diagnostic, or therapeutic aspects of AGS.
- Publications written in English and available as full-text articles.

The following publications were excluded:

- Articles not directly related to alpha-gal syndrome
- Studies with limited methodological quality
- Publications without available full-text access

2.3. Data Extraction and Synthesis

Relevant information was extracted from the selected publications, including study characteristics, main findings related to disease mechanisms, clinical manifestations, diagnostic approaches, and management strategies.

The evidence was synthesized qualitatively, focusing on key thematic areas such as epidemiology, immunopathogenesis, delayed allergic mechanisms, clinical presentation, diagnostic challenges, and therapeutic management of alpha-gal syndrome.

2.4. Analytic Approach

Due to the heterogeneity of available studies, including clinical studies, case reports, and review articles, a formal meta-analysis was not performed. Instead, a narrative synthesis approach was used to integrate and interpret the available evidence.

Ultimately, 48 publications were included in the qualitative analysis.

3. Results

3.1. Epidemiology and geographic distribution

Alpha-gal syndrome (AGS) is a disease that occurs in many regions of the world, primarily in areas endemic for ticks. However, accurate epidemiological data allowing for a precise estimate of the number of cases on a global scale are limited. The highest prevalence of the disease is observed in the southern United States, Australia, Western Europe, South Africa, and Brazil [1].

In the United States, a large-scale laboratory study covering the years 2017–2022 was conducted, which showed the growing scale of the problem. During this period, more than 357,000 specific IgE antibody tests for alpha-gal were performed, covering nearly 295,000 people, of whom 30.5% tested positive. The number of people with positive results increased from 13,371 in 2017 to 18,885 in 2021. Cases were mainly concentrated in the southern, midwestern, and mid-Atlantic regions of the United States [6].

In Europe, AGS is relatively rare in the general population, but is significantly more common in regions where the Ixodes ricinus tick is endemic and in occupational groups exposed to frequent bites (e.g., forest workers, hunters). The highest number of cases is reported in Western Europe and Scandinavia, where exposure to ticks is common [7, 8]. Population studies from Denmark indicate an increase in the prevalence of serological sensitization to alpha-gal in recent decades, which may be related to environmental changes and increasing exposure to ticks [7].

In Poland, a study was conducted in the population of the north-eastern part of the country (Podlaskie Province), a region with high exposure to ticks. Ixodes ricinus is the dominant species in the analyzed area. A significantly higher prevalence of specific IgE antibodies against α-gal was found among people reporting previous tick bites. However, no correlation was found between the presence of α-gal sIgE and markers of tick-borne infections [9].

The geographical distribution of AGS remains closely linked to the occurrence of specific tick species. In the United States, the most important species is Amblyomma americanum (the so-called lone tick), while in Australia and Europe, Ixodes holocyclus and Ixodes ricinus, respectively, play a key role, with the latter also being the dominant species in Poland [2,9,10].

3.2. Immunopathogenesis

The α-Gal epitope (galactose-α-1,3-galactose) is a sugar structure present on glycoproteins and glycolipids in most mammals. In humans, the gene encoding the α1,3-galactosyltransferase enzyme is inactive, which is why the body does not synthesize α-Gal and recognizes it as a foreign antigen. Under physiological conditions, humans produce natural anti-α-Gal antibodies belonging mainly to the IgM, IgA, and IgG classes. Their presence results from contact with intestinal bacteria exposing structures similar to α-Gal, and these antibodies constitute approximately 0.2–1.0% of all immunoglobulins in serum [11, 12]. However, it is worth noting that some sources report even higher values (up to 1–2% in healthy adults), which may depend on the population and the method of determination [11].

Alpha-gal syndrome develops when the immune response switches to an allergic pathway and specific IgE antibodies against α-Gal are produced. The key factor initiating this process is a tick bite. In the United States, Amblyomma americanum plays the most important role, while in Europe, Ixodes ricinus is the main vector. Tick saliva components, including proteins containing the α-gal epitope, have immunomodulatory properties and promote a Th2 response, leading to a switch to IgE antibodies specific to α-Gal [13,14,15].

The resulting IgE antibodies bind to FcεRI receptors present on the surface of mast cells and basophils. Upon re-exposure to α-Gal, found in mammalian meat and animal products, these cells are activated and release mediators of the allergic reaction [16,17].

Structurally, α-Gal is similar to the B blood group antigen; it differs in the presence of an additional fucose residue. Clinical observations suggest that people with blood group B or AB are less likely to develop AGS, which may be due to partial immune tolerance to similar sugar structures. The mechanism of this partial tolerance is not fully understood and requires further research [11].

It is worth noting that the α-Gal content varies depending on the type of tissue. Porcine kidney has been shown to contain particularly high concentrations of this epitope and is one of the strongest factors causing clinical symptoms in patients with AGS [18].

3.3. Mechanism of delayed reaction

A key factor explaining the delayed nature of the reaction in α-gal syndrome is the fact that the allergen is not a classic protein, but rather the oligosaccharide α-gal, which occurs in mammalian meat in both protein-bound (glycoproteins) and lipid-bound (glycolipids) forms [3,19].

Experimental studies indicate that lipid-bound α-gal can be absorbed in the small intestine along with fats and transported in the form of chylomicrons to the systemic circulation, while the protein-bound form is digested and is not transported in the same form [3,14].

The transport of lipids via chylomicrons through the lymphatic system to the systemic circulation is a slow process, which explains the 3-6 hour delay in the onset of symptoms after consumption of mammalian meat [1,14]. Only after reaching an adequate concentration of circulating molecules containing α-gal are mast cells and basophils coated with specific IgE antibodies against α-gal activated, leading to symptoms of an allergic reaction [1].

3.4. Clinical presentation

The spectrum of clinical symptoms of α-gal syndrome is broad and ranges from asymptomatic sensitization to severe anaphylactic reactions. A characteristic feature is the delayed onset of symptoms, usually 3–6 hours after consuming mammalian meat [20].

In some patients, gastrointestinal symptoms such as cramping abdominal pain, nausea, vomiting, and diarrhea predominate, sometimes without concomitant skin symptoms [4,20,22]. This gastrointestinal phenotype can lead to diagnostic difficulties and is sometimes misinterpreted as functional gastrointestinal disorders [22].

Skin symptoms, including urticaria, pruritus, and angioedema, are often observed [20,21]. Respiratory symptoms, such as cough and dyspnea, may also occur [20].

In more severe cases, an anaphylactic reaction occurs, accompanied by hypotension, tachycardia, dizziness, or loss of consciousness [20].

Rarer manifestations have also been described, including joint discomfort and nonspecific systemic symptoms, but their clinical significance remains unclear. In addition, in recent years, attention has been drawn to the potential link between α-gal sensitization and cardiovascular diseases, including the presence of unstable atherosclerotic plaques and an increased risk of coronary events, suggesting possible implications beyond classic allergic reactions [23].

It should be emphasized that the presence of specific IgE antibodies against α-gal is not always associated with clinical symptoms – population studies have shown a significant percentage of people with asymptomatic sensitization [24,25].

3.5. Diagnosis

The α-gal syndrome remains a rarely recognized condition, which often leads to delayed diagnosis. Diagnosis is based on three key elements:

1. A detailed clinical history with attention to unexplained, nonspecific gastrointestinal symptoms. (abdominal pain, nausea, vomiting, diarrhea) – skin symptoms may not always be present.
2. Confirmation of the presence of specific IgE antibodies against α-gal in serum.
3. Assessment of improvement after elimination of mammalian products from the diet [4,27].

According to AGA guidelines, the following clinical features are present in most patients with AGS:

1. Onset of disease in adulthood after years of tolerance to mammalian meat.
2. Reactions including pruritus, urticaria, angioedema, or anaphylaxis.
3. Possibility of gastrointestinal symptoms only, without accompanying skin, cardiovascular, or respiratory symptoms.
4. Delayed symptoms 2–6 hours after consumption of mammalian meat or meat products.
5. History of severe local reactions to tick bites, often described as an “index” bite that differs from previous bites.
6. Characteristic waking up at night with gastrointestinal symptoms [4,27].

Laboratory tests

The basic test is to determine the concentration of specific IgE antibodies against α-gal in serum. Interpretation of results according to AGA guidelines:

- ≥0.1 kU/L – result suggestive of AGS diagnosis
- <0.1 kU/L – result against allergy

- ≥2 kU/L or >2% of total IgE – increases the likelihood of clinically significant allergy in populations with a high percentage of sensitization
- ≥5.5 kU/L – high positive predictive value (>95%) [4,27]

Elevated α-gal sIgE levels alone are not sufficient for diagnosis, as some sensitized individuals remain asymptomatic. Confirmation of the diagnosis requires demonstration of symptom improvement after an elimination diet [4,27].

Additional tests

Provocation testing is rarely performed due to the delayed (2–6 hours) and unpredictable nature of the reaction and the inconsistency of symptoms between exposures. [4,27] In diagnostically difficult cases, the basophil activation test (BAT) may help distinguish patients with symptomatic AGS from those with asymptomatic sensitization. [26]

Skin tests with commercial meat extracts have limited diagnostic value and are not routinely recommended [4,27].

3.6. Management

The basis for treatment in α-gal syndrome is a strict elimination diet that excludes mammalian products and prevention of further tick bites, which can lead to an increase in specific IgE antibodies and worsening of symptoms [27].

Elimination diet

Patients should avoid mammalian meat, including beef, pork, lamb, venison, rabbit, goat, buffalo, bison, and horse meat, as well as offal (kidneys, liver, heart, intestines, lungs). Products containing beef or pork gelatin (e.g., jelly beans, marshmallows), as well as lard and tallow, should also be eliminated. It is necessary to educate patients on how to read product labels [27].

It has been reported that particularly strong reactions may occur after consumption of pork kidney, which is associated with the high α-gal content in this organ [18,28].

Tolerance to dairy products varies. Some patients tolerate milk and dairy products well, while others may experience symptoms, especially with higher concentrations of α-gal sIgE. The decision to eliminate dairy products should be made on an individual basis [28].

Unlike celiac disease, where even trace amounts of gluten can cause intestinal damage, the AGS diet allows for greater flexibility and individualization, especially in terms of dairy tolerance, but the two conditions should not be confused, despite partial similarity in gastrointestinal symptoms [29].

Avoiding tick bites

Avoiding further exposure to ticks is a key element of treatment. Studies have shown that in a significant percentage of patients (approximately 89%), there is a gradual decrease in α-gal sIgE levels when bites are successfully avoided [30]. It is recommended to wear clothing that covers the skin, use EPA-registered repellents (e.g., DEET), impregnating clothes with permethrin, avoiding tall grass and bushes, walking in the middle of paths, and, after returning from green areas, bathing quickly and thoroughly checking the skin and removing ticks with tweezers [27].

Management of anaphylactic reaction

Patients diagnosed with AGS should be provided with an epinephrine auto-injector. In the case of mild symptoms, oral antihistamines may be considered, while in the case of systemic symptoms, standard anaphylaxis management should be implemented. This is standard practice [31].

Other treatment methods

Patients with alpha-gal syndrome should not take glucocorticosteroids on a permanent basis or undergo desensitization (allergen immunotherapy), as the basis of treatment is the elimination of products containing alpha-gal and avoidance of tick bites, and immunotherapy and chronic steroid treatment are not currently recommended [4,31].

Prevention and prognosis

According to the guidelines of the American Gastroenterological Association, tolerance to mammalian products may change over time. In patients who show a decrease in specific IgE levels, it is possible to consider gradually reintroducing selected products under the supervision of a specialist [4].

Clinical improvement occurs in most patients who follow an elimination diet; studies have shown a high percentage of partial improvement and a significant percentage of symptom remission [4].

3.7. Medical products and biological agents containing α-gal

The best-documented example is cetuximab, which can cause severe anaphylaxis, but potential exposure may also involve preparations containing gelatin, porcine heparin, bioprostheses, or certain excipients [32].

The most important groups of medical products potentially associated with the risk of reactions are presented in Table 1.

Table 1. Medical products and biological agents containing α-gal

Category	Examples	Comments	Source
Biological drugs	Cetuximab, Infliksymab	Severe anaphylactic reactions have been documented in patients with IgE antibodies against α-gal; avoidance is recommended in patients with confirmed AGS.	32,33
Intravenous gelatin preparations	Gelofusine	Hypersensitivity reactions associated with the presence of mammalian gelatin have been reported; caution is advised and alternatives should be considered.	34,35
Heparin	Heparin	Reports of perioperative reactions, particularly with unfractionated heparin; data limited and inconclusive; individual risk assessment recommended.	36,37
Thyroid hormones,	Armour tyroid	Pork-derived preparations may contain α-gal; synthetic levothyroxine preparations are preferred.	38
Pancreatic enzymes	Pancreatin	Pork-derived preparations; presence of α-gal and activity demonstrated in immunological tests; clinical significance not fully determined.	38
Gelatin capsules	Medicines and supplements in gelatin capsules of mammalian origin	Potential source of exposure to mammalian gelatin; limited clinical data; gelatin-free formulations should be preferred whenever possible.	39,40,41
Vaccines	Zostavax, MMR, yellow fever	Vaccines containing gelatin as an excipient; cases of anaphylaxis have been reported in patients with AGS; consider administration under allergy supervision.	42,43,44
Bioprosthetic implants	Bioprosthetic heart valves / mammalian implants	Possible immune response associated with the presence of α-gal; cases of accelerated degeneration have been reported; limited data.	45,46,47,48

4. Discussion

4.1. Clinical implications

Alpha-gal syndrome represents a significant diagnostic and clinical challenge due to its unusual sensitization mechanism and delayed onset of allergic reactions. Symptoms occurring several hours after the consumption of mammalian meat are often not initially recognized as food allergy, which may lead to delayed diagnosis or misdiagnosis. In patients presenting predominantly with gastrointestinal symptoms, the condition may be mistaken for functional gastrointestinal disorders or other gastroenterological diseases.

A detailed clinical history, including previous tick bites and the characteristic delay between food ingestion and symptom onset, is therefore essential. Detection of serum IgE antibodies to α-gal remains the key diagnostic tool; however, results should always be interpreted in the context of clinical presentation, as sensitization does not necessarily correlate with symptomatic disease.

Patient education plays a crucial role in management, particularly regarding avoidance of mammalian-derived foods and prevention of further tick bites, which may sustain or exacerbate sensitization. Clinicians should also be aware of the potential presence of α-gal in certain medications, vaccines, and animal-derived medical products, which may trigger hypersensitivity reactions in sensitized individuals.

The growing number of reports highlights the need for increased awareness of alpha-gal syndrome not only among allergists, but also among primary care physicians, gastroenterologists, dermatologists, and emergency medicine specialists.

4.2. Limitations of current evidence

Despite the increasing number of publications on alpha-gal syndrome, the available evidence still has several important limitations. Many studies are based on small patient cohorts, case reports, or retrospective analyses, which makes it difficult to accurately determine the true prevalence of the disease and its risk factors.

Diagnostic challenges also remain. Currently, there are no universally accepted diagnostic criteria for AGS, and interpretation of α-gal-specific IgE levels may be complicated by the presence of asymptomatic sensitization in the general population.

Furthermore, the pathophysiological mechanisms underlying the disease are not yet fully understood, particularly the processes leading to IgE class switching after tick bites and the mechanisms responsible for the delayed onset of allergic reactions.

In addition, data regarding the safety of medications and medical products containing α-gal in patients with AGS remain limited and are often based on individual case reports.

Further large-scale studies are therefore needed to better characterize the natural history of the disease, identify predictors of severe reactions, and improve diagnostic and therapeutic strategies.

4.3. Future research directions

1. Mechanistic studies on the immunological properties of tick saliva and its role in inducing α-gal sensitization.

2. Identification of biomarkers that predict disease severity and the risk of anaphylactic reactions.

3. Development of standardized diagnostic criteria and optimal thresholds for interpreting α-gal sIgE concentrations.

4. Conducting long-term cohort studies to better understand the natural course of the disease and factors conducive to remission.

5. Evaluation of potential therapeutic strategies, including immunomodulatory therapies, which could in the future be an alternative to dietary management alone.

6. Evaluation of the safety of medicinal products and medical devices containing α-gal in patients with AGS.

5. Conclusions

The α-gal syndrome is a unique form of food allergy characterized by a delayed IgE-mediated reaction after consumption of mammalian products. This disease is distinguished by an atypical sensitization mechanism associated with tick bites and significant variability in the clinical picture. The delayed nature of symptoms and the possibility of gastrointestinal complaints dominating make the diagnosis of AGS difficult and often delayed.

Proper diagnosis requires consideration of the characteristic clinical history and determination of specific IgE antibodies against α-gal, while taking into account the possibility of asymptomatic sensitization. The basis of treatment remains an elimination diet and prevention of further tick bites.

It is also clinically important to be aware of the potential presence of α-gal in animal-derived medicines and medical devices, which may be a source of unexpected hypersensitivity reactions. Further research is needed to better understand the mechanisms of disease pathogenesis, develop more precise diagnostic criteria, and evaluate new therapeutic strategies.

Disclosure:

Author Contributions

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REFERENCES

1. Wilson, J. M., Erickson, L., Levin, M., Ailsworth, S. M., Commins, S. P., & Platts-Mills, T. A. E. (2024). Tick bites, IgE to galactose-alpha-1,3-galactose and urticarial or anaphylactic reactions to mammalian meat: The alpha-gal syndrome. *Allergy, 79*(6), 1440–1454. https://doi.org/10.1111/all.16003
2. Van Nunen, S. A., O'Connor, K. S., Clarke, L. R., Boyle, R. X., & Fernando, S. L. (2009). An association between tick bite reactions and red meat allergy in humans. *The Medical Journal of Australia, 190*(9), 510–511. https://doi.org/10.5694/j.1326-5377.2009.tb02533.x
3. Wilson, J. M., & Platts-Mills, T. A. (2018). The oligosaccharide galactose-α-1,3-galactose and the α-gal syndrome: Insights from an epitope that is causal in immunoglobulin E-mediated immediate and delayed anaphylaxis. *EMJ Allergy Immunology, 3*(1), 89–98.
4. McGill, S. K., Hashash, J. G., & Platts-Mills, T. A. (2023). AGA clinical practice update on alpha-gal syndrome for the GI clinician: Commentary. *Clinical Gastroenterology and Hepatology, 21*(4), 891–896. https://doi.org/10.1016/j.cgh.2022.12.035
5. Platts-Mills, T. A. E., Gangwar, R. S., Workman, L., & Wilson, J. M. (2025). The immunology of alpha-gal syndrome: History, tick bites, IgE, and delayed anaphylaxis to mammalian meat. *Immunological Reviews, 332*(1), e70035. https://doi.org/10.1111/imr.70035
6. Thompson, J. M., Carpenter, A., Kersh, G. J., Wachs, T., Commins, S. P., & Salzer, J. S. (2023). Geographic distribution of suspected alpha-gal syndrome cases—United States, January 2017–December 2022. *MMWR. Morbidity and Mortality Weekly Report, 72*(30), 815–820. https://doi.org/10.15585/mmwr.mm7230a2
7. Kiewiet, M. B. G., Apostolovic, D., Starkhammar, M., Grundström, J., Hamsten, C., & van Hage, M. (2020). Clinical and serological characterization of the α-gal syndrome-Importance of atopy for symptom severity in a European cohort. *The Journal of Allergy and Clinical Immunology: In Practice, 8*(6), 2027–2034.e2. https://doi.org/10.1016/j.jaip.2020.02.016
8. Leth-Møller, K. B., van Hage, M., Apostolovic, D., Sørensen, J. A., Vestergaard, C., Madsen, F., Kjær, L. J., Hansen, T., Jonsson, A., Thomsen, S. F., & Linneberg, A. (2025). Increasing prevalence of galactose-α-1,3-galactose sensitization in the Danish general adult population. *Allergy, 80*(1), 297–308. https://doi.org/10.1111/all.16360
9. Rutkowski, K., Sowa, P., Mroczko, B., Pancewicz, S., Rutkowski, R., Czupryna, P., Groblewska, M., Łukaszewicz-Zając, M., & Moniuszko-Malinowska, A. (2022). Sensitisation and allergic reactions to alpha-1,3-galactose in Podlasie, Poland, an area endemic for tick-borne infections. *Infectious Diseases, 54*(8), 572–579. https://doi.org/10.1080/23744235.2022.2057583
10. Hamsten, C., et al. (2013). Red meat allergy in Sweden: Association with tick sensitization. *Journal of Allergy and Clinical Immunology.*
11. Perusko, M., Grundström, J., Eldh, M., Hamsten, C., Apostolovic, D., & van Hage, M. (2024). The α-Gal epitope - the cause of a global allergic disease. *Frontiers in Immunology, 15*, 1335911. https://doi.org/10.3389/fimmu.2024.1335911
12. Galili, U. (2013). Anti-Gal: An abundant human natural antibody of multiple pathogeneses and clinical benefits. *Immunology, 140*(1), 1–11. https://doi.org/10.1111/imm.12110
13. Apostolovic, D., Grundström, J., Kiewiet, M. B. G., Perusko, M., Hamsten, C., Starkhammar, M., Paulie, S., & van Hage, M. (2023). Th2-skewed T cells correlate with B cell response to α-Gal and tick antigens in α-Gal syndrome. *The Journal of Clinical Investigation, 133*(6), e158357. https://doi.org/10.1172/JCI158357
14. Román-Carrasco, P., Hemmer, W., Cabezas-Cruz, A., Hodžić, A., de la Fuente, J., & Swoboda, I. (2021). The α-Gal syndrome and potential mechanisms. *Frontiers in Allergy, 2*, 783279. https://doi.org/10.3389/falgy.2021.783279
15. Sharma, S. R., Choudhary, S. K., Vorobiov, J., Commins, S. P., & Karim, S. (2024). Tick bite-induced alpha-gal syndrome and immunologic responses in an alpha-gal deficient murine model. *Frontiers in Immunology, 14*, 1336883. https://doi.org/10.3389/fimmu.2023.1336883
16. Carson, A. S., Gardner, A., & Iweala, O. I. (2022). Where's the beef? Understanding allergic responses to red meat in alpha-gal syndrome. *Journal of Immunology, 208*(2), 267–277. https://doi.org/10.4049/jimmunol.2100712
17. Kepley, C. L., Wang, Y., Yelton, A., Siebert, E. R., & Iweala, O. I. (2025). Ticked off: Allergic effector cells in the pathogenesis of alpha-gal syndrome. *Current Allergy and Asthma Reports, 25*(1), 57. https://doi.org/10.1007/s11882-025-01237-2
18. Morisset, M., Richard, C., Astier, C., Jacquenet, S., Croizier, A., Beaudouin, E., Cordebar, V., Morel-Codreanu, F., Petit, N., Moneret-Vautrin, D. A., & Kanny, G. (2012). Anaphylaxis to pork kidney is related to IgE antibodies specific for galactose-alpha-1,3-galactose. *Allergy, 67*(5), 699–704. https://doi.org/10.1111/j.1398-9995.2012.02799.x
19. Chakrapani, N., Fischer, J., Swiontek, K., Codreanu-Morel, F., Hannachi, F., Morisset, M., Mugemana, C., Bulaev, D., Blank, S., Bindslev-Jensen, C., Biedermann, T., Ollert, M., & Hilger, C. (2022). α-Gal present on both glycolipids and glycoproteins contributes to immune response in meat-allergic patients. *The Journal of Allergy and Clinical Immunology, 150*(2), 396–405.e11. https://doi.org/10.1016/j.jaci.2022.02.030

20. Commins, S. P., Satinover, S. M., Hosen, J., Mozena, J., Borish, L., Lewis, B. D., Woodfolk, J. A., & Platts-Mills, T. A. (2009). Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. *The Journal of Allergy and Clinical Immunology, 123*(2), 426–433. https://doi.org/10.1016/j.jaci.2008.10.052
21. Reddy, S., Yi, L., Shields, B., Platts-Mills, T., Wilson, J., & Flowers, R. H. (2023). Alpha-gal syndrome: A review for the dermatologist. *Journal of the American Academy of Dermatology, 89*(4), 750–757. https://doi.org/10.1016/j.jaad.2023.04.054
22. Rao, S., Rathore, S. S., Goyal, R. M., Narakornpichit, A., Karkra, R., Al-Khazraji, A., & Grover, M. (2026). Understanding alpha-gal syndrome: A systematic review and meta-analysis of clinical manifestations and outcomes. *Neurogastroenterology and Motility, 38*(1), e70245. https://doi.org/10.1111/nmo.70245
23. Vernon, S. T., Kott, K. A., Hansen, T., Finemore, M., Baumgart, K. W., Bhindi, R., Yang, J., Hansen, P. S., Nicholls, S. J., Celermajer, D. S., Ward, M. R., van Nunen, S. A., Grieve, S. M., & Figtree, G. A. (2022). 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. *Arteriosclerosis, Thrombosis, and Vascular Biology, 42*(3), 352–361. https://doi.org/10.1161/ATVBAHA.121.316878
24. Fischer, J., Lupberger, E., Hebsaker, J., Blumenstock, G., Aichinger, E., Yazdi, A. S., Reick, D., Oehme, R., & Biedermann, T. (2017). Prevalence of type I sensitization to alpha-gal in forest service employees and hunters. *Allergy, 72*(10), 1540–1547. https://doi.org/10.1111/all.13156
25. McGill, S. K., Commins, S. P., Peery, A. F., Galanko, J., Keku, T. O., Shaheen, N. J., Anderson, C., & Sandler, R. S. (2023). Alpha-Gal sensitization in a US screening population is not associated with a decreased meat intake or gastrointestinal symptoms. *The American Journal of Gastroenterology, 118*(7), 1276–1281. https://doi.org/10.14309/ajg.0000000000002219
26. Mehlich, J., Fischer, J., Hilger, C., Swiontek, K., Morisset, M., Codreanu-Morel, F., Schiener, M., Blank, S., Ollert, M., Darsow, U., Biedermann, T., & Eberlein, B. (2019). The basophil activation test differentiates between patients with alpha-gal syndrome and asymptomatic alpha-gal sensitization. *The Journal of Allergy and Clinical Immunology, 143*(1), 182–189. https://doi.org/10.1016/j.jaci.2018.06.049
27. Naseem, Z., Muhammad, A., Chatterjee, A., & Rubio-Tapia, A. (2025). Alpha-gal syndrome: Recognizing and managing a tick-bite-related meat allergy. *Cleveland Clinic Journal of Medicine, 92*(5), 311–319. https://doi.org/10.3949/ccjm.92a.24072
28. Patel, C., & Iweala, O. I. (2020). 'Doc, will I ever eat steak again?': Diagnosis and management of alpha-gal syndrome. *Current Opinion in Pediatrics, 32*(6), 816–824. https://doi.org/10.1097/MOP.0000000000000955
29. Awosika, A., & Balaji, P. (2026). Misdiagnosis of alpha-gal syndrome as non-celiac gluten sensitivity or lactose intolerance: A diagnostic blind spot for clinicians. *World Journal of Gastroenterology, 32*(3), 116350. https://doi.org/10.3748/wjg.v32.i3.116350
30. Kim, M. S., Straesser, M. D., Keshavarz, B., Workman, L., McGowan, E. C., Platts-Mills, T. A. E., & Wilson, J. M. (2020). IgE to galactose-α-1,3-galactose wanes over time in patients who avoid tick bites. *The Journal of Allergy and Clinical Immunology: In Practice, 8*(1), 364–367.e2. https://doi.org/10.1016/j.jaip.2019.08.045
31. Iglesia, E. G. A., Kwan, M., Virkud, Y. V., & Iweala, O. I. (2024). Management of food allergies and food-related anaphylaxis. *JAMA, 331*(6), 510–521. https://doi.org/10.1001/jama.2023.26857
32. Emerson, A. G., Mundy, L., Murphy, B. A., & Stone, C. A. (2026). Cetuximab hypersensitivity in the setting of asymptomatic alpha-gal sensitization. *Head & Neck, 48*(3), E33–E36. https://doi.org/10.1002/hed.70030
33. Chinuki, Y., & Morita, E. (2019). Alpha-Gal-containing biologics and anaphylaxis. *Allergology International, 68*(3), 296–300. https://doi.org/10.1016/j.alit.2019.04.001
34. Mullins, R. J., James, H., Platts-Mills, T. A., & Commins, S. (2012). Relationship between red meat allergy and sensitization to gelatin and galactose-α-1,3-galactose. *The Journal of Allergy and Clinical Immunology, 129*(5), 1334–1342.e1. https://doi.org/10.1016/j.jaci.2012.02.038
35. Uyttebroek, A., Sabato, V., Bridts, C. H., De Clerck, L. S., & Ebo, D. G. (2014). Anaphylaxis to succinylated gelatin in a patient with a meat allergy: Galactose-α(1, 3)-galactose (α-gal) as antigenic determinant. *Journal of Clinical Anesthesia, 26*(7), 574–576. https://doi.org/10.1016/j.jclinane.2014.04.014
36. Hawkins, R. B., Wilson, J. M., Mehaffey, J. H., Platts-Mills, T. A. E., & Ailawadi, G. (2021). Safety of intravenous heparin for cardiac surgery in patients with alpha-gal syndrome. *The Annals of Thoracic Surgery, 111*(6), 1991–1997. https://doi.org/10.1016/j.athoracsur.2020.07.050
37. Zvara, J., Smith, A. L., Mazzeffi, M. A., Kleiman, A. M., Tanaka, K., Smith, A. R., Wilson, J. M., & McNeil, J. S. (2024). Alpha-gal syndrome and cardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia, 38*(11), 2805–2811. https://doi.org/10.1053/j.jvca.2024.07.035
38. Swiontek, K., Morisset, M., Codreanu-Morel, F., Fischer, J., Mehlich, J., Darsow, U., Petitpain, N., Biedermann, T., Ollert, M., Eberlein, B., & Hilger, C. (2019). Drugs of porcine origin-A risk for patients with α-gal syndrome? *The Journal of Allergy and Clinical Immunology: In Practice, 7*(5), 1687–1690.e3. https://doi.org/10.1016/j.jaip.2018.12.005

39. Muglia, C., Kar, I., Gong, M., Hermes-DeSantis, E. R., & Monteleone, C. (2015). Anaphylaxis to medications containing meat byproducts in an alpha-gal sensitized individual. *The Journal of Allergy and Clinical Immunology: In Practice, 3*(5), 796–797. https://doi.org/10.1016/j.jaip.2015.04.004
40. Dunkman, W. J., Rycek, W., & Manning, M. W. (2019). What does a red meat allergy have to do with anesthesia? Perioperative management of alpha-gal syndrome. *Anesthesia and Analgesia, 129*(5), 1242–1248. https://doi.org/10.1213/ANE.0000000000003460
41. Vidal, C., Méndez-Brea, P., López-Freire, S., & González-Vidal, T. (2016). Vaginal capsules: An unsuspected probable source of exposure to α-Gal. *Journal of Investigational Allergology & Clinical Immunology, 26*(6), 388–389. https://doi.org/10.18176/jiaci.0105
42. Stone, C. A., Jr, Hemler, J. A., Commins, S. P., Schuyler, A. J., Phillips, E. J., Peebles, R. S., Jr, & Fahrenholz, J. M. (2017). Anaphylaxis after zoster vaccine: Implicating alpha-gal allergy as a possible mechanism. *The Journal of Allergy and Clinical Immunology, 139*(5), 1710–1713.e2. https://doi.org/10.1016/j.jaci.2016.10.037
43. Retterer, M. K. C., Workman, L. J., Bacon, J. R., & Platts-Mills, T. A. E. (2018). Specific IgE to gelatin as a cause of anaphylaxis to zoster vaccine. *The Journal of Allergy and Clinical Immunology, 141*(5), 1956–1957. https://doi.org/10.1016/j.jaci.2017.08.047
44. Stone, C. A., Jr, Commins, S. P., Choudhary, S., Vethody, C., Heavrin, J. L., Wingerter, J., Hemler, J. A., Babe, K., Phillips, E. J., & Norton, A. E. (2019). Anaphylaxis after vaccination in a pediatric patient: Further implicating alpha-gal allergy. *The Journal of Allergy and Clinical Immunology: In Practice, 7*(1), 322–324.e2. https://doi.org/10.1016/j.jaip.2018.06.005
45. Mozzicato, S. M., Tripathi, A., Posthumus, J. B., Platts-Mills, T. A. E., & Commins, S. P. (2014). Porcine or bovine valve replacement in 3 patients with IgE antibodies to the mammalian oligosaccharide galactose-alpha-1,3-galactose. *The Journal of Allergy and Clinical Immunology: In Practice, 2*(5), 637–638. https://doi.org/10.1016/j.jaip.2014.04.016
46. Mangold, A., Szerafin, T., Hoetzenecker, K., Hacker, S., Lichtenauer, M., Niederpold, T., Nickl, S., Dworschak, M., Blumer, R., Auer, J., & Ankersmit, H. J. (2009). Alpha-Gal specific IgG immune response after implantation of bioprostheses. *The Thoracic and Cardiovascular Surgeon, 57*(4), 191–195. https://doi.org/10.1055/s-0029-1185395
47. Hawkins, R. B., Frischtak, H. L., Kron, I. L., & Ghanta, R. K. (2016). Premature bioprosthetic aortic valve degeneration associated with allergy to galactose-alpha-1,3-galactose. *Journal of Cardiac Surgery, 31*(7), 446–448. https://doi.org/10.1111/jocs.12764
48. McGregor, C., Byrne, G., Rahmani, B., Chisari, E., Kyriakopoulou, K., & Burriesci, G. (2016). Physical equivalency of wild type and galactose α 1,3 galactose free porcine pericardium; A new source material for bioprosthetic heart valves. *Acta Biomaterialia, 41*, 204–209. https://doi.org/10.1016/j.actbio.2016.06.007