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REVIEW

Alpha-Gal Syndrome: Often Hidden, Under-Recognized, and in Need of Attention—A Rapid Review

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Abstract: Alpha-gal syndrome (AGS), a tick-borne allergy, is increasing as its vectors migrate throughout the US and the world. There were an estimated 450,000 cases in the US. AGS reactions to mammalian foods and medical products include delayed anaphylaxis, urticaria, gastrointestinal and cardiac symptoms often difficult to connect to the source. Despite its seriousness, provider knowledge is limited. This rapid review investigated published works on AGS from 2020 to 24; it also sought to determine the breadth of AGs publications across different fields and specialties. We identified 355 studies of AGS diagnosis and management from 2020 to 2024 via Cochrane Central, Medline via the PubMed interface, and Embase (additional grey literature via Web of Science and Google Scholar). Studies were assessed for quality and risk of bias using JBI critical appraisal tools. Two hundred and nineteen studies met the criteria. One hundred and sixty-eight (77%) were full studies; 51 (23%) were conference presentations. Studies remained largely confined to allergy and immunology literature, despite their implications for other organ systems. Although patients present with symptoms to emergency departments and dermatology clinics there is a paucity of literature in those fields and others; several studies document practitioners' lack of knowledge. Inclusion of content within medical school curricula is needed to establish foundational knowledge on the topic. With the increase in patients presenting with AGS, and with the reach of AGS across multiple fields, physicians and other health care providers need to be able to diagnose and then manage AGS with their patients. This rapid review has documented the problem of silos in disseminating information about AGS widely through the medical field. The remedy for a lack of practitioner knowledge is education.

Keywords: tick-borne, allergy, mammalian products, provider knowledge, immunology, red meat

Introduction

Alpha-gal syndrome (AGS) is a tick-borne disease first described in 2009 on 2 continents by Van Nunen et al[1] and Commins et al.[2] Over the past fifteen years, its geographic reach in the US has widened, and the CDC considers it an "emerging" condition[3] as vectors, particularly the Lone Star Tick (*Amblyomma americanum*), and to a lesser extent *Ixodes Scapularis* and possibly chiggers (*Trombiculidae*) have migrated throughout the US. As the Lone Star tick extended its range into the mid-Atlantic and Northeastern states of the US reports of allergic reactions to red meat appeared and then increased.[4–8] Wilson et al[9] point out that "the prevalence of AGS prior to [its original description] can be debated" (p. 1440); however, Binder et al[8] suggest that the increase in case numbers reflects an increase in sensitization rates.

AGS (galactose-alpha-1,3-galactose) is transmitted to humans when they are bitten by a tick carrying the AGS carbohydrate in its salivary glands. This bite can lead to the development of IgE antibodies, causing an allergic reaction to mammalian meat and other products including vaccines and drugs containing the AGS carbohydrate.[6] Ticks active on other continents carry the same potential for disease (eg, *Ixodes ricinus* in Europe; *Ixodes holocyclus* in Australia).

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AGS was initially identified when the cancer drug Cetuximab, which expresses the alpha-gal carbohydrate, caused fatal reactions in patients undergoing chemotherapy.[10] Linking the IgE antibodies to the reactions required the joint efforts of both clinical and pharmaceutical researchers from the US, Europe, and Australia. Once an assay was available, as Platts-Mills et al[11] indicate, it was possible to see that these cases aligned with both "the distribution of cases of reactions to cetuximab" (p. 1062) and with the distribution of Rocky Mountain Spotted Fever ticks; ticks then became a focus of the detective work (see Wilson et al,[9] Platts-Mills et al,[11] Steinke et al,[12] and Commins et al[13] for an account of the history).

AGS reactions to mammalian foods and medical products include urticaria, anaphylaxis, and gastrointestinal symptoms usually delayed by 2–6 hours and difficult to connect to their source. Because gal-alpha-1,2-gal is a carbohydrate rather than a protein, its presentation can differ from typical allergic reactions. Along with the delay, its varied symptoms complicate identifying it as causative since patients may experience one or more symptoms, sometimes inconsistently. The "red meat allergy" misnomer can further obscure diagnosis since all mammalian meats, dairy, personal and medical products, and cross-reactive allergens may also invoke an allergic response.

According to the CDC,[14] there were over 100,000 cases nationally diagnosed by a single reference laboratory in the US from 2010 to the end of 2022; the CDC's estimate of cases totaled 450,000. Cases were identified at a rate of 15,000 per year, and the report indicates that even these numbers are likely an underestimate as AGS is neither nationally reportable nor mandated as reportable in all states.[3] Under-reporting is further exacerbated when AGS is described as rare or when health care providers are unfamiliar with it.

Carpenter et al[15] reported that providers lacked knowledge and confidence in diagnosing it. In their 2022 survey, 42% of the 1500 responding primary care doctors and advanced practice providers had not heard of AGS. Only one-third of those who were aware of AGS knew that it was caused by a tick bite. Under 5% said they were "very confident" in diagnosis and management, and another 17.4% reported that they were "somewhat confident" (pp. 810–811). At the time of their study, then, only about 22% of their respondents had some confidence in diagnosing AGS (p. 811).

Although many respondents in that study were primary care providers, Flaherty et al[16] found in a study of patient attitudes that patients also rated specialists as having "little to no knowledge" (p. 132). The findings in other studies were similar (eg, Hedberg et al[17] and Carson et al[18]). Of the responders to an informal online AGS case challenge in *Medscape Medical News* (a medical news outlet targeted toward health professionals published by WebMD; June 2024)[19] only 48% correctly diagnosed AGS, even though the patient was described as a hiker who also enjoyed "other outdoor activities." As Flaherty et al[20] point out in their interview study, patients seeking diagnoses often relied on "informal networks" in the absence of clinical knowledge.

When health care providers do not recognize symptoms indicating the need for an extensive history or diagnostic testing, AGS patients can remain undiagnosed or misdiagnosed for an average of up to 7 years.[20,21] As Boyce et al[22] argued,"Despite growing numbers of clinicians recognizing AGS as a leading cause of adult-onset anaphylaxis, fewer recognize the nonclassical manifestations of this syndrome, resulting in frequent referrals of patients to nonallergy specialists" (p. 6)—who may themselves be unfamiliar with AGS. That lack of familiarity can be a barrier to diagnosis and can jeopardize patients undergoing cardiac or other surgical procedures. Some anesthesia products contain mammalian components, and bioprosthetic valves; and even existing bio-prostheses can be retroactively vulnerable if patients acquire AGS.[23,24] This danger is not new, as Kuravi et al[25] p. e412 point out: "Alpha-gal has always been an issue in cardiac surgery, despite the paucity of literature on the topic."

Because of the variety of symptoms, patients present in many medical settings[21] from primary care to internal and emergency medicine, dermatology, allergy, and gastroenterology. However, most of the clinical detective work in identifying and describing AGS has in the past been accomplished by allergists and published in allergy/immunology journals. So while the disease crossed several fields, the literature did not, and knowledge generally remained within allergy and immunology. (See the systematic review by Young et al[26] for a comprehensive look at the research up to early 2020).

Aim of the Review

This rapid review sought to describe and appraise the published literature on AGS between 2020–24, focusing on diagnosis and management and assessing the breadth of AGs publications across different fields and specialties. As we conducted the review we found emerging evidence indicating the need to address the implications of AGS for fields in

addition to allergy whose practitioners are likely to encounter patients (internal medicine, emergency medicine, primary care, cardiology, dermatology, gastroenterology, anesthesiology, oncology).

Materials and Methods

We conducted a rapid systematic literature review of studies from 2020–2024 of alpha gal diagnosis and management. This rapid review manuscript adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines.[27] A rapid review was deemed the appropriate evidence synthesis methodology for this study as only one reviewer (CT) was available to conduct the initial title and abstract screening and there was no blinding process used. Methodological guidance from the Cochrane Rapid Reviews Methods Group was consulted and utilized when carrying out this study. A study protocol was developed using the Preferred Reporting Items for Systematic Review and Meta -Analysis Protocols (PRISMA-P) and published on the PROSPERO review registry.[28]

Eligibility Criteria

Example key words included: 'alpha AND gal', 'alpha gal syndrome', 'red meat allergy', galactose-alpha-1,3-galactose, galactosylgalactose, tick*"tick borne disease", ixodid*parasit*Trombiculidae, chigger*acari, mite, mites, flea siphonaptera, disease, allergy, and syndrome. Full search strategies including boolean operators, medical subjects headings, and Emtree subject headings are available on the project's Open Science Framework site at: 10.17605/OSF.IO/TWE82.

We included studies using all research designs; peer-reviewed literature dissertations and grey literature are included. Studies published between January 1, 2020, and June 30, 2024, were included if they addressed our required population, disease, and outcomes. Studies containing only a brief mention of alpha-gal, studies limited to alpha-gal only in ticks, or those with a sole focus on biochemical reactions, cells, animal populations, bio-prostheses were excluded.

Information Sources

Studies from 2020–2024 were identified via Cochrane Central, MEDLINE via the PubMed interface and Embase; additional grey literature were retrieved from the Emerging Sources Citation Index via the Web of Science interface and Google Scholar. This time frame was selected as there was a prior systematic review encompassing papers up to 2020.[26] Google Scholar search results were limited to the top 500 results.

Selection Process

Studies were deduplicated using Clarivate EndNote 20 software. The deduplicated articles were then imported into Rayyan.ai software for a first round of abstract screening followed by a second round of full-text screening. Foreign language articles were translated using Google Lens AI transcription software.

Critical Appraisal

Included full-text studies that met the study's inclusion criteria were then assessed for overall quality using JBI critical appraisal worksheets. Specific JBI worksheets were selected based on the study design of the included studies. Both full text screening and the critical appraisal process was conducted independently by at least two team members (CT, AP) with third (EC) adjudicating discrepant responses. Raw data is accessible and archived via the Open Science Framework (see 10.17605/OSF.10/TWE82).

Data Collection Process

A project page on the Open Science Framework was created for the purposes of data management and storage of exported database citation files. Descriptive data from each study was extracted by one research team member (CT) and stored in a shared Google Sheet including the following information: Author, Year, Article Title, Journal, Journal Category, Study Design, JBI, Country.

Results

Our search identified 355 studies published from January 1, 2020, to June 30, 2024. After duplicates were removed, 327 studies remained. We conducted abstract screening and reviewed these studies for full eligibility; 219 studies met the criteria. A total of 51 conference presentations and 168 published full studies were subsequently reviewed.

Study Quality

Studies were assessed using the JBI criteria. Chart reviews and surveys were not scored. Although there were some studies of low quality, the preponderance were of medium to high quality as assessed by the JBI criteria. A few studies were judged to be of low quality, but to describe the research trajectory in the past 4 years as completely as possible, we included all of them. Figure 1 contains the PRISMA flow chart.

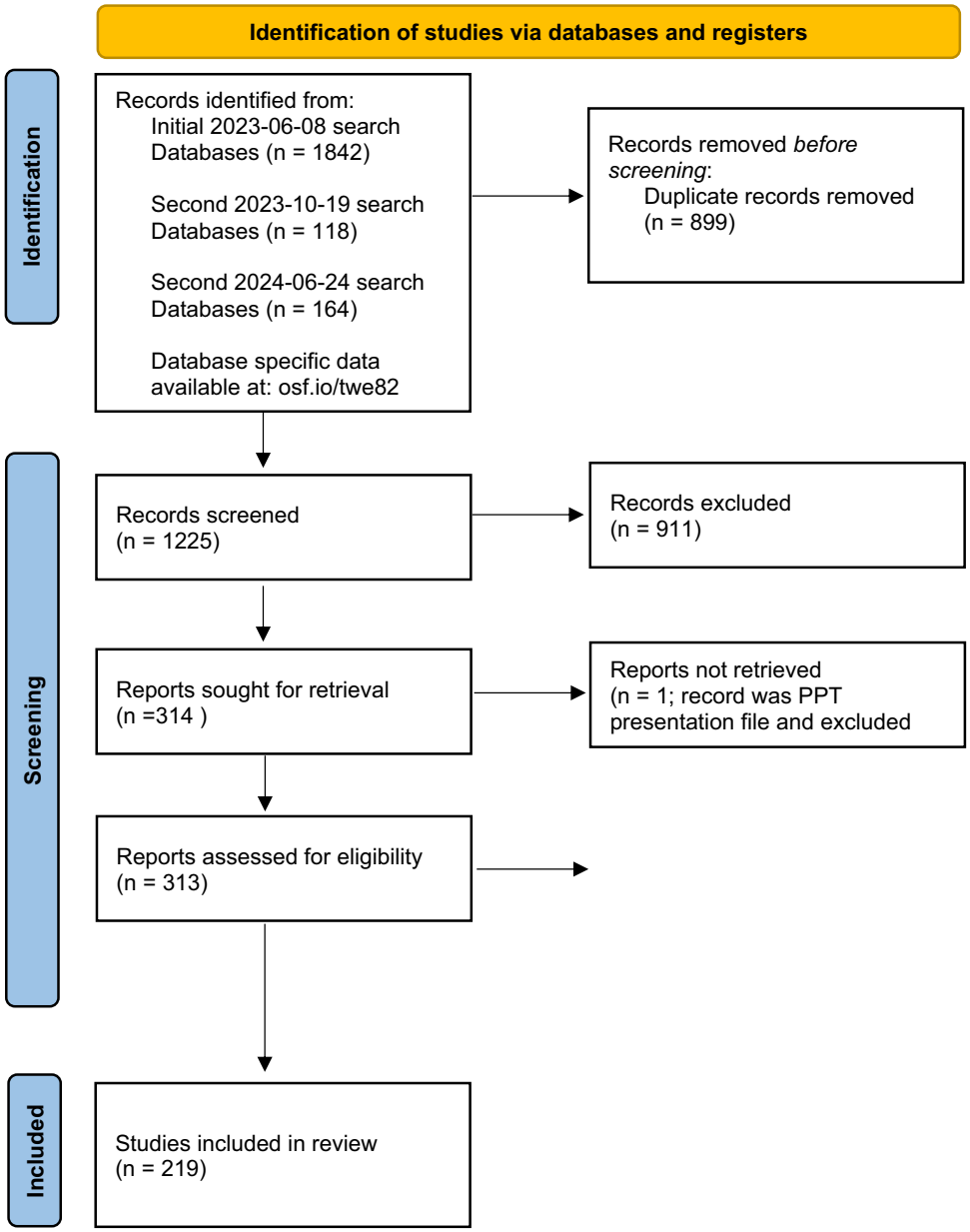

Figure 1 PRISMA flow diagram for identification of studies via databases and registers. PRISMA Figure adapted from Page M J et al . (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ, n71 10.1136/bmj.n71.[29]

Study Types

Of the 219 studies that met the eligibility criteria, 51 were conference presentations, and 168 were published papers. Fifty-two full studies (23%) were case reports or case series, a substantial decrease from Young's 2021 systematic review.[26]

Of the published papers (see Tables 1 and 2), expert opinion pieces comprised 27%; case reports 24%; cohort studies 11%, case series 7%, case control 4%, cross-sectional studies 5%, surveys 1%, and 1 chart review. We found 13 reviews (8%), including one systematic review.[26] Several reviews were extensive, often containing substantial historical and practical information).[9,26,30–33] There were 2 books, 1 qualitative study, and several miscellaneous papers.

Letters, editorials, and commentaries were also included. There were 1 editorial, 2 commentaries, and 14 letters. Five letters were categorized as expert opinion and 9 contained presentations of research; those were not considered to be peer-reviewed but were categorized and assessed by study type. The study types are summarized in Table 1.

As the research data has emerged over the past 4 years and the research on the AGS-vector and symptoms has been increasingly settled, case reports and case series play a somewhat less pronounced role. They remain an important study type for unusual presentations or first occurrences in parts of the US and in countries where AGS is uncommon or not previously found.

Country of Origin

The preponderance of studies in our collection were conducted in US research institutions in toto or in collaboration with another country (136). Six were from the UK and 42 from Europe (Spain, Germany, Italy, Turkey, Poland, Cyprus; Spain had the largest number of studies at 13). In addition, there were 6 from Australia and several from South America. This international research mirrors the reach of alpha-gal, which is now spread world-wide.

Studies as by Field

To see the extent to which provider knowledge was field-dependent, we listed the numbers of publication venues by medical field. Table 2 indicates the distribution of alpha-gal literature across the fields of allergy/immunology, infectious

Table 1 Studies by Type and Publication Mode

Type	Mode	
	Conference Abstract (n = 51)	Papers (n = 168)
Case control	1	6
Case report	21	41
Case series	5	11
Chart review	4	2
Cohort	11	18
Cross-sectional	2	7
Quasi-experimental	1	4
Survey	4	3
Informational	2	
Clinical Communications		
Qualitative		1
Expert opinion		37
Reviews		13
Commentary		2
Letters		14
Books		2
Trade /news reports		3
Miscellaneous (editorials, errata, masters, website)		4

Table 2 Studies by Publication Field

	Combined Studies (n = 219)	Conference Abstract (n = 51)	Papers (n = 168)
Allergy/immunology	92	37	55
General	36		36
Gastroenterology	17	9	9
Infectious disease	11		11
Dermatology	11		9
Cardiology.	7	2	7
Case reports	5		6
Pediatrics	5		5
Anesthesiology	5		5
Ophthalmology	5		5
Emergency medicine	4		4
Molecular diagnostics	2		2
Oncology	2		2
Pharmacology	2		1
Nephrology	1		–
Respiratory	1		–
Toxicology	1	1	1
Internal medicine	1	1	1
Occupational health	1	1	1
Endocrinology	1		1
Animal [wildlife; ethics]	2		2
Acupuncture	1		1
Complementary	1		1
Misc	1		1
Law	1		1
Technology	1		1

disease gastroenterology, dermatology, cardiology, emergency medicine, primary care, anesthesiology. Of the 219 studies, allergy and immunology journals comprised 42% (92). General journals were the next largest number at 36 (16%), with gastroenterology at 17 (8%) and infectious disease and dermatology at 11 each (5% each). Other fields trailed behind (see Table 2). The raw data is accessible and archived via the Open Science Framework (see 10.17605/OSF.10/TWE82).

Studies on Diagnosis and Management

Most of the full studies in our collection directly or indirectly address diagnosis or management of AGS; however, of the 168 papers from 26 fields, only 50 (from 14 fields)—fewer than 30%—addressed both (see Table 3). Thirty-five others described, mentioned or listed symptoms, sometimes in cursory fashion. As might be expected, most papers addressing both were published in allergy and immunology journals (13) with general and gastroenterology journals following at 9 and 7, respectively.

Four reviews in particular provide extensive information, both historical and current, on both diagnosis and management.[11,26,31,34] Both Commins's and Van Nunen & Ratchford's studies contain copious practical information for clinicians; the Platts-Mills et al report outlines specific research recommendations. Other detailed diagnostic information is found in Vaz-Rodriguez et al,[35] Diaz,[36] McInnis et al,[37] Houchens et al,[38] McGill et al[39] among others. Hawkins et al[40] provide explicit advice on testing prior to surgery; Wilson et al[9] describe the need to consider AGS as the differential diagnosis when patients live in an area where ticks are endemic.

Between 2012 and 2019 a few studies had suggested a link with alpha-gal and blood groups (eg, Cabezas-Cruz et al[41] and Wilson et al[42]). Seven in our current collection[35,43–48] continued to investigate a "strong association" of AGS and

Table 3 Diagnosis & Management by Field

Field (N = 14)	Number
Allergy/immunology	13
General	9
Gastroenterology	7
Anesthesiology	4
Dermatology	4
Pediatrics	3
Emergency medicine	2
Ophthalmology	2
Cardiology	1
Infectious disease	1
Nursing	1
Oncology	1
Molecular diagnostics	1
Misc	1

blood group; see Vanegas et al on the "growing evidence" of a link (p. 174)[44] and Rutkowski et al[46] on blood type as a "risk factor" (p. 897). de la Fuente et al[45] argue that ABO blood group is one of the "co-factors in the clinical history that play an important role in diagnosis of the [sic] AGS" (p. 4), and Gilstad et al[48] recommend avoiding blood group antigen B when managing non-group B patients with AGS.

Barriers to Diagnosis

Eight studies investigated the frequent underdiagnosis[49] or misdiagnosis of alpha-gal as gastrointestinal difficulties, idiopathic urticaria, idiopathic anaphylaxis, and neuro-psychiatric behavior.[37,49–56] McInnis[37] (p. 1082) discussed the importance of considering both "the full range of symptoms" and the implications of patients' use of medical and job-related products; 3 studies discuss the diagnosis of "idiopathic" disease.[44,45,50] Vanegas[45] reported the diagnostic challenges in settings without immediate access to testing.

Although a review of the studies in our collection indicates that the research on symptoms and diagnosis appears largely settled, the major barrier to diagnosis is the lack of provider knowledge. We found 4 studies indicating a low number of providers who can correctly and confidently diagnose AGS.[15,17,18,57]

Discussion

Alpha-gal patients present in clinical settings from primary care to dermatology, cardiology, emergency medicine, gastroenterology, and surgery. However, publications remain predominantly in allergy and immunology, and the often-limited practitioner knowledge in other fields can result in misdiagnosis. Fewer than 30% of the published papers addressed both diagnosis and management (see Table 3).

AGS diagnosis has historically been challenging, given its protean presentations confounding diagnosis and leading to frequent delays of about seven years.[11,20,21] When symptoms are understood to indicate possible AGS, diagnosis can now be accomplished with a good history and inexpensive serologic testing. However, it is important to note the conflicting research on whether IgE level indicates the strength of possible reactions.[34] This is because the presence of circulating alpha-gal specific IgE does not necessarily mean there will be clinical symptoms of alpha-gal syndrome, similar to conventional IgE-mediated food allergies.[54] The antibody profile may predict clinical symptoms with symptomatic individuals having higher levels of alpha-gal specific IgG1 and IgG3 and lower levels of IgG4..[54,55] Of note, food-specific IgG4 is considered a marker of tolerance to food antigens.[58]

One intriguing connection is that of AGS to blood group, since people with B or AB groups are hypothesized to be less vulnerable to AGS. Cabezas-Cruz et al[41] had asked in 2017 whether the link was "overlooked", and Wilson et al had noted in

2019[42] (p. 2348) that "blood group B trended toward being under-represented." In our collection, we found studies continuing to show a "strong association" of AGS and blood group (see the de la Fuente et al review of 8 studies, p. 4)[45] and "growing evidence" of a link.[42] Others discussed non-B blood groups as cofactors in or conferring risk for AGS.[34,43,44] While these studies are not definitive, Gilstad's warning about transfusion reactions, especially in non-B patients, indicates the serious implications of alpha-gal for blood groups.[48]

Barriers to Diagnosis

Misdiagnosis is common and health care professionals' reliance on idiopathic diagnoses can be a default. Edlow[50] noted (p. 1) that emergency "clinician awareness of alpha-gal syndrome is low." He points out that patients leaving the emergency department are likely to leave without a clear understanding of the presenting issue; "as many as 10% of patients diagnosed with idiopathic anaphylaxis have alpha-gal syndrome."[50] Two other studies (McInnis[37] and Zurbano-Azqueta et al[52]) pointed out how reliance on the ill-defined category of "idiopathic" disease can divert practitioners from considering a more accurate diagnosis. This is also the case with the misnomer of "red meat allergy" as patients may encounter the allergen not through red meat but through dairy or other food or medical products.

In addition to continued patient suffering if AGS is unrecognized, misdiagnoses increase the likelihood of increasingly severe reactions including during medical and surgical procedures. This lack of provider knowledge directly affects how patients manage AGS; since management requires avoidance not only of mammalian foods but also of potential cross-reactions (eg, with anti-snake venom[59] and insect venom[60,61] and more commonly, with many medical products among them those used in cardiac procedures.

A majority of studies (42%) were published in allergy and immunology. Eighteen were in gastroenterology journals, but according to Ijeoma's study, even gastroenterologists diagnosed AGS only 4% of time.[62] Gastroenterologists' knowledge is important as gastrointestinal difficulties are a frequent channel for diagnosis, and as Richards and Richards[63] point out, in their endemic area nearly a third of patients presenting with unexplained gastrointestinal symptoms tested positive to IgE for alpha-gal and that it is under-recognized.

Ophthalmology is considered less frequently than most other fields as a route to diagnosis, but AGS has implications even there. Ruland and Kirzhner's account[23] of an ophthalmology patient whose graft degenerated is instructive, and as they point out, is a warrant for allergy testing prior to using any mammalian product. That only 4 studies were published in emergency medicine is especially concerning, as patients with anaphylaxis and angioedema are likely to use the ED as their first point of contact.

We also found 5 studies published in journals in anesthesiology and 7 in cardiology. Two threats to cardiology and cardiovascular surgery have been reported. First are Heparin and xenografts; we found few papers detailing these problems. The second problem is the probable link between AGS and CAD. Vernon[64] notes a "clinically important effect of a-gal sensitization on the development of CAD and acute MI" (p. 358). Pitsios[65] assessed the link as "alarming." This possible connection is critical for two reasons. First, AGS appears to be related to a buildup of unstable atherosclerotic plaque. While noting that a "causal relationship… remains to be established", Wilson et al[9] hypothesized that subclinical inflammation is at work. The assumption of an AGS/CAD connection is likely; the AGS/CAD connection is potentially modifiable, though this is uncertain; see also these studies.[66–68]

There is still controversy as to the extent to which AGS sensitization can cause coronary artery disease, how much remission might decrease it; and whether continuing exposure to gal even without symptoms promotes progression of disease. Whether or not the risk is modifiable, there are major implications for public health. Given these implications, it is surprising that we found only 34 studies in our collection with some mention of both alpha-gal and alpha-gal-promoted CAD (17 reviews; 10 research reports, 2 abstracts, 2 letters to editors, 1 workshop report, 1 commentary, and 1 master's thesis). Further, of those 34 studies, only 3 were in journals focusing on cardiology. Nineteen were published in journals focused on allergy or immunology; 4 in general journals; 2 in gastroenterology; 2 in pediatrics; 2 in dermatology; and 1 each in molecular diagnostics and microbiology. Many studies contained only brief mentions of the implications of AGS for atherosclerosis. The lack of cardiovascular research on a problem of such connection to the field is a striking example of the siloing of information that creates a substantial barrier to both diagnosis and management. The 2024 study by Keet et al[67] on the link of allergy to CVD may prompt further attention with stronger study designs.

Finally, there continue to be few studies on patient self-diagnosis (eg, Flaherty et al[16]). Desensitization and remission remain enticing but largely unexplored topics.[69–71] Current studies continue to explore the effect of blood type on AGS as patients with B blood type have a lower association with AGS, possibly due to immunological tolerance induced by the structural similarity between the B antigen and the α-Gal epitope. There is at present no cure, but management, which consists of avoiding further tick bites, foods, and medical products with mammalian origins, is effective. There is evidence that management will decrease sensitivity over time with some patients experiencing remission.

Our rapid review has analyzed 219 AGS studies published from 2020 to 2024. Studies prior to 2020 (Commins,[34] Platts-Mills et al,[11] and Diaz,[36]) were invaluable in tracing the trajectory of AGS research. The 2020–2024 studies, both at the conference and journal level, continue to ratify previously published papers on characteristic symptoms (including onset delay), diagnosis, and management; diagnosis and management protocols in our collection remained largely unchanged from prior research. However, the mammalian meat allergy has been underrecognized and underdiagnosed.

Limitations

This study has several limitations. Although we used several thorough search strategies in several customary databases, it is possible that not all pertinent literature was found. We used Google Translate and Google Lens where translated copies of studies were not available, both of which may have inaccuracies. Current data reported in the studies on prevalence and incidence is subject to inaccuracy and revision.

Conclusion

The large increase in AGS cases to an estimated 450,000 by 2022[14] has been paralleled by growth in both the total number of studies and in the number of those in journals. A smaller proportion of studies are now case reports as compared with Young's findings in 2021,[26] indicating a maturing research field. However, AGS remains mis- and under-diagnosed. The most urgent finding is that the literature continues to be disseminated primarily through the field of allergy/immunology. Although situating publications in general journals is helpful, it only partially addresses the issue of dissemination if connections are not explicit across fields. The continuing siloing of knowledge into a single specialty helps to constrain provider knowledge, encouraging the use of default "idiopathic" diagnoses, and affecting how and when patients are diagnosed and how soon their disease can be effectively managed. The proportion of alpha-gal studies in specialties outside of allergy and immunology almost certainly contributes to the lack of provider awareness. There is also a need for clear clinical guidelines for diagnostic testing across clinical disciplines. The lack of both awareness and guidelines is regrettable as, with the exception of countries that have constrained access to testing, diagnosis is for the most part simple and achievable. Both Scott Commins, MD, Medical Associate Chief of Allergy & Immunology UNC, and Thomas Platts-Mills, Chief of Allergy and Immunology at UVA, and their colleagues elsewhere have provided an admirable and large segment of the research on AGS but it may not be reaching health care workers outside the field. This work should be extended to areas of the country and world now experiencing heavy AGS exposure.

Remedying the lack of awareness has been a recommendation not only in the scholarship but also in the Alpha-gal Syndrome Subcommittee of the now-inactive HHS Tick-borne Disease Working Group whose authorization expired in 2022. The AGS subcommittee, which was earlier inactivated, cited a "knowledge gap" and the need for "education and awareness" of providers, including first-responders and government agencies (that group was remarkable in its inclusion of patient perspectives and information). While the CDC has informational pages, it does not appear to have an interprofessional group to integrate knowledge across specialties and is not a replacement for the HHS working group. Reinstating the funding for that group would offer an opportunity for researchers to integrate and disseminate their knowledge across fields. The siloing of information could also be remedied by editorial policies promoting collaboration across fields. Our findings in cardiology are a case in point, and the surprising lack of studies in even primary care and internal and emergency medicine, where patients are likely to turn first with their symptoms, indicates the need for both collaboration and dissemination. The disease crosses many fields, and the literature must follow.

It is also critical that those who train clinicians incorporate the knowledge and skills that they need into curricula at every level. Inclusion of content within medical school curricula is needed to establish foundational knowledge on the topic, but it must be reinforced among faculty, and training mandated at the undergraduate, graduate, and CME levels.

With the increase in patients presenting with AGS, and with the reach of AGS across multiple fields, physicians and other health care providers need to be able to diagnose and then manage AGS with their patients.

This rapid review has documented the problem of silos in disseminating information about AGS widely through the medical field. The remedy for a lack of practitioner knowledge is education.

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