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Review Article

Safety of Bovine and Porcine Derived Orthopaedic Implants: Growing Concern for Alpha-gal Syndrome

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Background

Alpha-Gal Syndrome (AGS) is a growing concern, particularly in the Northeast United States. AGS is most known for the gastrointestinal and integumentary manifestations after consuming bovine or porcine derived products.

Hypothesis/Purpose

The purpose of this manuscript is to highlight the growing concern of the safety of bovine and porcine derived orthopaedic implants, as they relate to the AGS population. This article reviews the available literature on orthopaedic porcine and bovine implants in the AGS population, and future avenues of research

Study Design

Narrative Review

Methods

Literary search using available PubMed and Embase.

Results

People can develop AGS after being bitten by Lone Star Ticks carrying galactose-α-1,3 galactose, which once introduced to the human immune system, illicits an immune response to subsequent exposures. Being a common carbohydrate found in bovine and porcine derived products, this immune sensitivity makes it dangerous to ingest.

Conclusions

Upon search of the orthopaedic literature, there are no studies researching the immunologic impact of porcine and bovine derived bioprosthesis and patches that would mirror the studies performed in other fields of medicine. There theoretically remains the

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Conflicts of Interest Statement for Dr. Dillon Clancy

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c Dylan Chayes is an orthopedic resident with Inspira Health Network Orthopedic Residency.

Conflicts of Interest Statement for Dr. Dylan Chayes

potential risk of AGS/meat allergy transmission from bovine and porcine derived orthopaedic implants in the field of sports medicine.

Clinical Relevance

There are many orthopaedic biological augments/implants that are derived from bovine and porcine sources. Implants have been investigated in cardiology, demonstrating dangerous effects on the survivability of the implants in the AGS population. Little is known about the effects of orthopaedic porcine and bovine implants on the AGS population.

INTRODUCTION

Alpha-gal syndrome (AGS), described in the literature as an allergic reaction to red meat, is a growing concern worldwide. AGS is a syndrome characterized predominantly by gastrointestinal symptoms and skin manifestations after consuming mammalian derived meat, with severity ranging from mild symptoms to immediate onset anaphylaxis (Román-Carrasco et al. 2021). Generally, this syndrome occurs in patients after being bitten by the Lone Star tick, Amblyomma americanum (Commins et al. 2011). In short, galactose-α-1,3 galactose (alpha-gal) is a carbohydrate found primarily in mammalian tissues, however not present in humans and some species of primates. However, alpha-gal happens to also be carried in the saliva of this tick (and possibly other tick species). The human immune system may become sensitized to alpha-gal with repeated exposure in the setting of tick bites (Román-Carrasco et al. 2021; Young et al. 2021; Zhan, Chen, Xu, et al. 2024). This can cause an IgE mediated response to alpha-gal antigen, which subsequently results in the symptoms described above after meat consumption. A recent systematic review in 2021 reports tick-derived AGS in 20 countries worldwide, however the exact prevalence is unknown (Young et al. 2021).

AGS AND BIOLOGICAL IMPLANTS

As surgeons, everything we expose the human immune system to may trigger an immune reaction, particularly materials and tissues that are designed to remain in the human body. Specifically of interest for this discussion are bovine and porcine derived products, which can elicit IgE immune responses in the human body. Alarmingly, recent cardiology research demonstrates significant evidence of a triggered inflammatory response to implanted bovine and porcine derived aortic valves, and these cardiac patients are at high risk for immune response due to porcine derived, high dose heparin (Veraar et al. 2021; Zvara, Smith, Mazzeffi, et al. 2024). These aortic valves are often subject to early failure by means of breakdown and calcification due to said immune response. Additionally, in 2016, two cases of meat allergies characterized by urticaria and recurrent anaphylactic reactions were reported after implantation of porcine and bovine aortic valves (Hawkins et al. 2016). Prior to implantation, bovine and porcine implants are conventionally treated with glutaraldehyde crosslinking in an effort to mask the alpha-gal antigen. However, due to its chemical instability, the alpha-gal antigen may continue to be a trigger of the immune response that can be detected five years after implantation. This has prompted the exploration of new avenues to chemically treat the implants for greater endurance (Naso et al. 2023).

AGS IN ORTHOPAEDIC SURGERY

Xenografts account for 16.6% of orthopaedic sports medicine implants (Lauck, Reynolds, van der List, et al. 2024). There are many available bovine and porcine derived implants commonly used in orthopaedics today, including the BEAR, Regeneten, Permacol, and Biobrace. The publicly available information for each implant varies, along with how many have been implanted, but range significantly from roughly one thousand implants to over 100,00 implants used (Chand et al. 2014; “Smith+Nephew Launces Revolutionary REGENETEN Bioinductive Implant in Japan, Providing an Advanced Healing Option for Patients with Rotator Cuff Tears” 2023; “Real-User Feedback: Dr. Sigman’s 26- Month Clinical Experience with BioBrace” 2023). The authors feel that research into bovine and porcine orthopaedic implants is lacking. There has been some research into the use of porcine derived bone xenograft with mixed results. Current literature cannot support the use of these xenografts for bony defects (Bracey et al. 2019). Even less available are studies concerning bovine and porcine derived implants in the field of orthopaedic sports medicine. Galili et al (Galili and Stone 2021) demonstrates moderate success with porcine derived ACL bioprosthesis, which did not happen to illicit AGS. However, this clinical trial included just 10 subjects. On the other hand, Yeazell et. Al (Yeazell et al. 2022) recently demonstrated an increase in reoperation rate and postoperative stiffness in patients treated with bovine derived collagen patches used to augment partial rotator cuff repairs compared to patients treated with routine repair without a bioinductive collagen patch.

Upon search of the orthopaedic literature, there are no studies researching the immunologic impact of these bioprosthesis and patches that would mirror those studies on

the safety of bovine and porcine derived aortic valves. There theoretically remains the potential risk of AGS/meat allergy transmission from bovine and porcine derived orthopaedic implants in the field of sports medicine. Additionally, there are currently no published studies on the impact of bovine/porcine derived bioprotheses and collagen augments on patients affected by tick-borne AGS. The use of these implants in affected patients likely can result in skin and visceral manifestations, and hypothetically may be lethal given the possibility of anaphylaxis.

The authors feel it is imperative to institute standardized questions about meat allergies, tick exposures, and porcine and bovine sensitivities if considering to use these implants as an orthopaedic surgeon. This is particularly important for the east coast of the United States, where AGS allergies are increasing (Wilson and Platts-Mills 2019). The authors suggest implementation of AGS related questions into the already well-developed screening processes that patients receive at their respective facilities throughout the country. Allergy screenings are performed at multiple checkpoints: operating surgeon, surgical coordinators, pre-surgical medical clearance, anesthesiologists/CRNA, and pre-operative nursing staff. Whenever possible, these allergies can be added to the electronic medical record alongside the other food and drug allergies the patient may have. Some suggested questions that may be added to a screening:

1. Do you have a history of tick bites or tick-borne illness?
2. Do you have an allergy to meat and/or pork/beef derived foods?
3. Have you been diagnosed with Alpha-gal syndrome?
4. Do you have a history of any surgery involving medical implants?

Answering yes to any of these questions would be an indication to ask follow up questions and counseling regarding the potential added risks that accompany AGS patients using bovine/porcine implants.

CONCLUSION

A changing climate is putting new geographical areas at risk to this tick-borne disease. Also, as more and more people have been affected by this syndrome, there is a heightened national and global awareness of AGS. With research in other medical fields suggesting complications with use of bovine and porcine derived implants, it is imperative that further research be done into the safety and efficacy of these implants, particularly in connective tissue augments and bioprostheses, in the field of orthopaedic sports medicine.

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