

ALPHA-GAL SYNDROME

Background | Management | Key points



What is it?

Alpha-gal syndrome (AGS) is an IgE mediated allergy to alpha-gal, a carbohydrate found in most mammals (excluding humans, apes and some monkeys). It develops after exposure to tick bites

Incidence?

Currently unknown, AGS has only recently been confirmed to exist in the UK. The ticks capable of transmitting AGS are found UK wide. Incidence is rising due to increased testing, awareness and climate change.

Symptoms?

Classically anaphylactoid reactions 2-6 hours after eating **mammalian** meat, or any mammalian derived products, such as **dairy**. Symptoms vary widely between patients and can worsen with repeated exposure to tick bites. Patients may also react to food products containing **carrageenan**, a red seaweed that is used as an alternative to gelatine in a wide range of products. Birds, reptiles and fish **do not** contain alpha-gal.

How to test?

Refer to Immunology. Blood tests include: Tryptase, total IgE level, Sp IgE to alpha-gal thyroglobulin bovine. IgE levels vary depending on exposure to tick bites. Consider measuring IgE levels prior to admission. Higher levels could worsen reaction if exposed to mammalian products, and can increase the risk of desensitisation strategies.

Why is this relevant to cardiac surgery?

Multiple medical products contain alpha-gal. Some products are exposed to mammalian derived excipients during the production process. Some drugs contain alpha-gal as a capsule or tablet but not as an IV preparation.

Every drug that might be used during a patient's perioperative period needs to be checked by the pharmacy department and high risk products should be excluded from treatment with alternatives sought. Below is a table with the medicines and products that we identified for a patient we treated in Wales however this is not an exhaustive list. Each hospital should conduct their own pharmacy review as different manufacturers may be used.

Drug or product	Concerning excipient
Pericardial patches and bio-prosthetic heart valves	Bovine or porcine origin - all contain alpha-gal
Type B blood products	Cross reactivity between Group B antigen and alpha-gal
Heparin, including LMWH	Derived from porcine intestinal mast cells - each batch contains different amounts of alpha-gal
Ramipril capsules (Aurobindo). All strengths	Capsule shell contains gelatine
Spironolactone 25mg tablets (Accord)	Contains lactose likely from mammalian source
Furosemide tablets (Accord). All strengths	Contains lactose likely from mammalian source
Amiodarone tablets (Accord). All strengths	Contains lactose likely from mammalian source
Metoprolol 50mg tablets (Bristol laboratories)	Contains lactose likely from mammalian source
Bisoprolol tablets (Sandoz Ltd). All strengths	Contains lactose from bovine source, and prepared using calf rennet
Floreal (Baxter)	Bovine-derived gelatin matrix
Bone wax (Ethicon)	Isopropyl palmitate - potentially mammalian source
Gelaspan (Braun)	Contains succinylated gelatin from mammalian source



Take home messages

- Alpha-gal syndrome is a rare condition that is increasing in incidence. More work is being done to establish true incidence and develop a guideline.
- If a patient presents with symptoms suggestive of AGS they should have their procedure delayed if possible until all relevant investigations have been done.
- We advise they are urgently referred to Immunology who can establish likelihood of allergy and conduct the relevant blood tests.
- In patients with confirmed AGS a careful MDT approach is needed to ensure high risk products are not given to the patient during their peri-operative period. A heparin desensitisation strategy has been used successfully in an increasing number of cases, but an individualised approach is advised and in close collaboration with each patient.

What about anticoagulation for cardiopulmonary bypass?

There are relatively safe alternatives that can be used (argatroban or bivalirudin) however use is rare and can be unfamiliar.

There are case reports of heparin desensitisation being utilised which can allow patients to be heparinised safely for cardiopulmonary bypass. In Cardiff we successfully used a strategy detailed in a case report published in 2022 (McRae et al). The same batch of heparin was used throughout the peri-operative period to ensure alpha-gal levels remained consistent. There has been reports of patients with AGS suffering lethal anaphylactic reactions when given heparin if they have not been adequately desensitised prior to cardiopulmonary bypass.

Post operative anticoagulation:

The patient was continued on a heparin infusion post-operatively until warfarin was at an adequate therapeutic level. For future community bridging fondaparinux was chosen due to its synthetic nature as the lowest risk option despite not being licensed for this use. Alternatives such as argatroban were excluded due to the complexities of admission, and low molecular weight heparin was ruled out due to its porcine origin.

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References:

- 1) McRae AS, Tidwell WP, Patel S et al (November 2022). Heparin desensitisation prior to cardiopulmonary bypass in a patient with alpha-gal allergy. *Anaesthesia Reports* 2022, 10, e 12203. DOI: 10.1002/
- 2) Hawkins et al. (2021) Safety of Intravenous Heparin for Cardiac Surgery in Patients With Alpha-Gal Syndrome. *Annals of Thoracic Surgery* 2021, The Society of Thoracic Surgeons. <https://doi.org/10.1016/j.athoracsur.2020.07.050>
- 3) Carrageenan, A Guide for People with Alpha-Gal Syndrome. <https://alphagalinformation.org/carrageenan>