ANAPHYLACTIC REACTIONS – GUIDELINES FOR LABORATORY INVESTIGATION

Background

Anaphylaxis is a sudden, severe, potentially fatal, systemic allergic reaction. These reactions are classified as Type I (IgE mediated) hypersensitivity reactions. It can involve many areas of the body with the most significant symptoms affecting the respiratory tract and the cardiovascular system. Symptoms can occur within minutes of contact with the allergen but in rare instances, may occur up to four hours after contact with the allergen. There are other mechanisms that can cause similar symptoms to Type I hypersensitivity and these include direct stimulation of mast cells or indirect mediator release by drugs, reactions mediated by immune complex (IgG), physicochemical interactions between multiple drugs and deficiency of C1 esterase inhibitor.

The annual incidence of anaphylactic reactions is about 30 per 100,000 persons and the most important initiating agents are drugs (e.g. antibiotics and anaesthetic agents), venoms (particularly bee and wasp), foods (e.g. peanuts, egg, fish and shellfish) and other agents (e.g. latex). Anaphylaxis has been reported to many other allergens but these represent the most common inducing agents. Patients with suspected anaphylaxis are most commonly associated with Accident and Emergency and Anaesthetic/Surgery Departments.

- *Symptoms of anaphylaxis*

Clinical features include hypotension, cardiovascular collapse, bronchospasm, rash, erythema, urticaria, angioedema, generalized oedema, pulmonary oedema and gastrointestinal symptoms. The lack of consistent symptoms can make diagnosis difficult.

- *Initial management*

A&E physicians and anaesthetists typically manage patients with suspected anaphylaxis. Treatments include adrenaline, antihistamines, corticosteroids, IV fluids and oxygen.

- *History*

History is vital. Make sure the clinician gets detailed information about the timing of the reaction with respect to the suspected trigger and a detailed history of all exposures over the previous 24 hours (in case there is doubt about the trigger).

Laboratory Investigations

Laboratory investigations aim to identify the type of reaction and the cause of the reaction. They are done in addition to basic biochemical and haematological investigations. However, these do not replace investigation by an allergist in situations where the patient may have had a severe reaction.

This guidance is based on the suggested practice from these documents:

- NICE CG134 2011 Anaphylaxis: assessment and referral after emergency treatment
- National Audit Project NAP6 2018: perioperative anaphylaxis

Mast cell tryptase

- Blood samples 5-7 mL red top (yellow top samples are acceptable)
- Label samples with patient's name, number AND the time of the sample.
- Samples must be sent to Pathology where they will be separated and stored until all samples are ready. Samples will then be sent for tryptase analysis.

Recommended sample collection protocol is:

- First sample as soon as possible after emergency treatment has started

- A second sample, ideally within 1-2 hours (but no later than 4 hours) from the onset of symptoms.
- A third sample taken approximately 24 hours hour after onset of the reaction

However, the practicalities of getting samples from a patient who may be moving from one department to another (e.g. A&E to a ward) over a few hours can be difficult, samples taken between 4 and 24 hours may be useful. Too many samples are better than an inadequate time course!

Complement and C1 esterase inhibitor concentrations

- C3, C4 and C1 esterase inhibitor should be requested on one of the samples for mast cell tryptase. This should be done to investigate hereditary angioedema.

Total and specific IgE *to antigens known to cause anaphylaxis are available. These are best requested at a follow up appointment in an allergy clinic*

Interpretation of serum tryptase results

The serum tryptase concentration reflects both the clinical severity of the reaction and the reaction mechanism. Tryptase has a half-life *in vivo* of 2.5 hours so it is vital to know the sample time with respect to the suspected reaction. The peak tryptase concentration should be considered with the systolic blood pressure and the following table is a guide to the suggested reaction mechanism.

Peak serum tryptase concentration (μg/L)	Systolic BP(mmHg)	Suggested mechanism
>50	0	Type I hypersensitivity (IgE mediated)
20 – 50	20 - 80	Non-immune (a) direct histamine release (b) complement activation
2-20	100-120	Error of essentially bronchospasmic reaction

Tryptase results will be reported from St. George's PRU with a variety of comments. The standard comments are shown here:

Normal tryptase:

Normal serum tryptase concentration – results are not suggestive of an anaphylactic reaction but the results must be interpreted in the context of the time of the reaction, the course of the reaction, and any fluids that may have been used during resuscitation.

No clinical details given. Normal serum tryptase concentration – results are not suggestive of an anaphylactic reaction but the results must be interpreted in the context of the time of any reaction, the course of the reaction, and any fluids that may have been used during resuscitation.

Raised tryptase approx. 20-50 ug/L

Raised serum tryptase concentration – this could be consistent with a Type 1 hypersensitivity "anaphylactic" reaction but this concentration may also be seen in non-immune mechanisms e.g.

direct mast cell degranulation or complement activation. The results must be interpreted in the context of the patient's clinical condition and the time of this sample with respect to the reaction.

Raised tryptase (>50 ug/L)

Raised serum tryptase concentration would be consistent with a Type 1 hypersensitivity "anaphylactic" reaction but the results must be interpreted in the context of the patients clinical condition and the time of this sample with respect to the reaction.

Tryptase ? time and date

The date and time of these samples is not completely clear. This sample appears to have been taken at 14.00 06.06.05.

Further investigation

Patients who have had a severe allergic reaction, either during anaesthesia or during other circumstances will need further investigation. This should identify the causative allergen and, in the case of anaesthetic reactions, identify anaesthetics that the patient does not react to.

Total and specific IgE may be useful to identify for example food allergens or venom allergens and these should be done 4-6 weeks after the reaction.

Investigation of anaphylaxis to anaesthetic agents can be done by the anaesthetists (usually by skin prick testing) with full resuscitation facilities available. Patients can also be referred to:

Allergy and Immunology Department at the Royal Brompton Hospital (Prof. S. Durham)
Allergy Department at Guy's Hospital (Prof. C Corrigan)
Allergy Clinic, St. Helier Hosital (Dr. G. Hayman)

Management

Once the causative allergen has been identified, avoidance is the most useful measure. Self-injecting adrenaline and antihistamines may be prescribed. These drugs "buy time" and should not be used instead of going to hospital immediately after being in contact with the relevant allergen.

References

Protein Reference Unit Handbook of Clinical Immunochemistry Eighth Edition (2004)

NICE CG134 2011: Anaphylaxis: assessment and referral after emergency treatment

National Audit Project NAP6 2018: perioperative anaphylaxis
https://www.nationalauditprojects.org.uk/NAP6Home?newsid=959