MAST CELL TRYPOTASE

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Serum tryptase is a very useful marker for the detection of mast cell activation. Upon activation, mast cells release a variety of mediators that result in allergic reactions such as systemic anaphylaxis. Tryptase is found in the circulation after a patient suffers an anaphylactic reaction. The half-life of tryptase released into the circulation is considerably longer than that of histamine. Increased levels of tryptase peak at about 1 hour and can be detected from 3 to 6 hours after the anaphylactic reaction. Levels return to normal within 12 - 24 hours after release. An initial increase in tryptase levels followed by a sharp decrease indicates an allergic reaction. If the tryptase remains elevated at high levels, other conditions such as mastocytosis must be considered. Tryptase levels remain stable in stored serum samples for many months.

Indications
- Even when only one specimen can be taken, as in a postmortem case, it is a valuable indicator that anaphylaxis was a likely cause of death.
- We have found that one of the most useful clinical indications for the determination of tryptase levels is intraoperative anaphylaxis. Common drugs causing anaphylaxis during surgery are the muscle relaxants, but latex allergy is also an important cause.
- A recently recognised indication for tryptase determination is the assessment of risk in bee venom-hypersensitive patients. Those who have elevated basal tryptase levels are at greater risk of severe anaphylactic reactions and of more serious adverse reactions during bee venom immunotherapy. In these patients tryptase levels can be used for ongoing monitoring of relative risk.
- Tryptase determination is a valuable marker for the diagnosis and monitoring of systemic mastocytosis.
- Tryptase levels are not raised in patients who have food allergies or atopic dermatitis, but may be useful in acute, severe food-induced anaphylaxis.

Local survey
A retrospective study of 221 patients tested at the Allergy Diagnostic and Clinical Research Unit of the UCT Lung Institute and Groote Schuur Hospital was recently conducted. Mast cell tryptase levels ranging from < 1.0 µg/l to 13.5 µg/l are considered to fall within normal limits. Thirty-nine of the samples submitted to our laboratory had levels > 13.5 µg/l. Seventeen postmortem specimens were tested and values from 3.73 µg/l to 4.275 µg/l were found.

Specific collection
Venous blood is collected, allowed to clot and serum is separated. Ideally serial samples of 2 ml should be taken at 30 minutes to 1 hour, 2 - 3 hours and again at 12 - 24 hours to detect the characteristic rise and fall in tryptase levels during anaphylaxis. On a postmortem specimen a single sample can be taken up to 24 hours later and is informative if significantly elevated.

WHAT IS ANAPHYLAXIS?

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Anaphylaxis is a severe, life-threatening systemic reaction affecting all ages. The clinical syndrome may involve multiple target organs, including skin, respiratory, gastrointestinal and cardiovascular systems. The underlying mechanism is the presence of biologically active mediators released from mast cells or basophils. In a classic IgE-mediated reaction from previously sensitised mast cells or basophils, anaphylactic reaction is the preferred term. Degranulation of mast cells or basophils may occur by non-IgE-mediated mechanisms - these reactions are termed anaphylactoid. Clinically it is not possible to distinguish the two and treatments for both are identical.

Common causes
- Foods: especially nuts, some kinds of fruit, seafood, egg.
- Drugs: especially penicillin, anaesthetic agents, radiocontrast media, aspirin and other NSAIDs.
- Latex: gloves, catheters and other medical/dental products. Sufferers are usually health care workers with a prolonged occupational exposure to latex. Bananas, avocados, kiwi, figs and other fruit/vegetables (e.g. potatoes) may also cause anaphylaxis due to proteins that cross-react with latex.
- Venom: bee/wasp stings.
- Idiopathic/unknown.

Subjective symptoms
- Common – itchy mouth/palate; generalised warmth/flushing; tingling/pruritus of skin (soles/palms, lips); sensation of lump in throat,
Less common – cardiovascular (syncpe, palpitations); abdominal (bloating, nausea, vomiting); upper respiratory (nasal congestion, rhinatorrhoea, sneezing).

Clinical manifestations
- Upper airway obstruction (laryngeal oedema) – with increasing severity:
  - swollen lips, tongue, uvula
  - hoarseness
  - inspiratory stridor
  - total closure
- Lower airway obstruction (bronchospasm) – with increasing severity:
  - cough
  - wheeze
  - tachypnoea
  - dyspnoea
  - hypoxia
  - cyanosis … respiratory arrest
- Vascular collapse (shock) – with increasing severity:
  - increased capillary permeability
  - generalised vasodilation
  - urticarial wheals
  - hypotension
  - shock

In one large series of fatal reactions, 70% of deaths were from respiratory causes and 24% from cardiovascular causes. Death may occur within minutes of the onset of symptoms.

The more rapidly anaphylaxis develops, the more likely the reaction is to be severe and potentially life threatening. Prompt recognition of signs and symptoms is critical. If there is any doubt, it is generally better to administer adrenaline.

Generally, the later symptoms begin after exposure to causative agents, the less severe the ensuing reaction.

Adrenaline
Prompt injection of adrenaline is the cornerstone of systemic anaphylaxis treatment. Adrenaline stimulates α-adrenoceptors and increases peripheral vascular resistance, thus improving blood pressure and coronary perfusion, reversing peripheral vasodilatation, and decreasing angioedema.

Stimulation of β₁-adrenoceptors has both positive inotropic and chronotropic cardiac effects. Stimulation of β₂-receptors causes bronchodilation and increases intracellular cyclic adenosine monophosphate production in mast cells and basophils, reducing release of inflammatory mediators.

Table I lists the adrenaline dosage for anaphylaxis. Adrenaline should be given via deep intramuscular injection (IMI).

Table I. Anaphylaxis: adrenaline dosage

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose of adrenaline (1/1 000, 1mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 1 year</td>
<td>0.05 ml</td>
</tr>
<tr>
<td>1 year</td>
<td>0.1 ml</td>
</tr>
<tr>
<td>2 years</td>
<td>0.2 ml</td>
</tr>
<tr>
<td>3 - 4 years</td>
<td>0.3 ml</td>
</tr>
<tr>
<td>5 years</td>
<td>0.4 ml</td>
</tr>
<tr>
<td>6 - 10 years</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Adult</td>
<td>0.5 - 1.0 ml*</td>
</tr>
</tbody>
</table>

* The lower dose should be given to children over 10 years of slight build and to the elderly.

Why deep IMI?
Studies by Simons et al.¹ have shown that peak plasma concentrations of adrenaline were significantly higher (p < 0.01) after adrenaline was injected intramuscularly into the thigh, than after intramuscular or subcutaneous injection into the upper arm.

Despite coaching on inhalation techniques, plasma adrenaline concentrations are not significantly increased after inhalation of adrenaline, and these inhalants are no longer available.

In South Africa prefilled auto-injectable syringes are expensive. They do not allow for repeated injections of adrenaline or dose titration according to body weight, and the needles are too short for deep IMI administration.

An emergency kit, consisting of a small rigid plastic box containing 2 x 1 ml syringes, 2 needles and 2 amps of adrenaline, promethazine tablets, and a label with individual patient details, emergency contact numbers and personalised adrenaline dose (in ml) is a cost-effective alternative.

Patients are instructed to inject straight through their clothing into the upper thigh and spend 20 minutes with a nursing sister to receive instructions on administration.

Treatment
All the As:
- Ask about allergies
- Advanced directives: protocol, equipment, skills/training
- Accurate assessment: serious/non-life-threatening
- Airway protection: position, oxygen, ET tube, cricothyroidotomy
- Administer fluids
- Antihistamine: promethazine 25 - 50 mg deep IMI or slow IV [children: titrate according to body weight]
- Adrenergic agents
- Anticholinergic agents
- Adrenocorticosteroids: anaphylaxis has a biphasic or delayed reaction in a small percentage of patients, so monitor for possible late-phase reaction.

Summary
Anaphylaxis is a severe life-threatening reaction that can affect all age groups. The severity of previous reactions does not predict the severity of subsequent reactions. Deep intramuscular adrenaline is the first-line treatment for anaphylaxis. Early use of adrenaline in anaphylaxis is associated with improved outcomes. Adrenaline cannot help you if you do not have it with you.

Further reading available on request.