



THE ASSOCIATION OF ANAESTHETISTS  
*of Great Britain & Ireland*

## Management of a Patient with Suspected Anaphylaxis During Anaesthesia **SAFETY DRILL**

(Revised 2009)

### Immediate management **A**

- Use the ABC approach (Airway, Breathing, and Circulation). Teamworking enables several tasks to be accomplished simultaneously.
- Remove all potential causative agents and maintain anaesthesia, if necessary, with an inhalational agent.
- **CALL FOR HELP** and note the time.
- Maintain the airway and administer oxygen 100%. Intubate the trachea if necessary and ventilate the lungs with oxygen.
- Elevate the patient's legs if there is hypotension.
- If appropriate, start cardiopulmonary resuscitation immediately according to Advanced Life Support Guidelines.
- Give adrenaline (epinephrine) i.v.
  - Adult dose: 50 mcg (0.5ml of 1:10 000 solution)
  - Child dose: 1.0 mcg.kg<sup>-1</sup> (0.1ml.kg<sup>-1</sup> 1:100 000 solution)
- Several doses may be required if there is severe hypotension or bronchospasm. If several doses of adrenaline are required, consider starting an intravenous infusion of adrenaline.
- Give saline 0.9% or lactated Ringer's solution at a high rate via an intravenous cannula of an appropriate gauge (large volumes may be required).
  - Adult: 500 - 1 000 ml
  - Child: 20 ml.kg<sup>-1</sup>
- Plan transfer of the patient to an appropriate Critical Care area.

**CONTINUED OVERLEAF**

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## Secondary management (B)

- Give chlorphenamine i.v. (chlorpheniramine)

Adult:	10 mg
Child 6 - 12 years:	5 mg
Child 6 months - 6 years:	2.5 mg
Child <6 months:	250 mc.kg <sup>-1</sup>
- Give hydrocortisone i.v.

Adult:	200 mg
Child 6 - 12 years:	100 mg
Child 6 months - 6 years:	50 mg
Child <6 months:	25 mg
- If the blood pressure does not recover despite an adrenaline infusion, consider the administration of an alternative i.v. vasopressor according to the training and experience of the anaesthetist, e.g. metaraminol
- Treat persistent bronchospasm with an i.v. infusion of salbutamol. If a suitable breathing system connector is available, a metered-dose inhaler may be appropriate. Consider giving i.v. aminophylline or magnesium sulphate.

## Investigation (C)

- Take blood samples (5 - 10 ml blood) for **mast cell tryptase**:
  - Initial sample as soon as feasible after resuscitation has started - do not delay resuscitation to take the sample.
  - Second sample 1 - 2 h after the start of symptoms.
  - Third sample either at 24 h or in convalescence (for example in a follow-up allergy clinic). This is a measure of baseline tryptase levels as some individuals have a higher baseline level.
- Ensure that the samples are labelled with the time and date.
- Liaise with the hospital laboratory about analysis of samples.

## Later investigations to identify the causative agent (D)

The anaesthetist who gave the anaesthetic or the supervising consultant anaesthetist is responsible for ensuring that the reaction is investigated. The patient should be referred to a specialist Allergy or Immunology Centre (see [www.aagbi.org](http://www.aagbi.org) for details). The patient, surgeon and general practitioner should be informed. Reactions should be notified to the AAGBI National Anaphylaxis Database (see [www.aagbi.org](http://www.aagbi.org)).

This guideline is not to be construed as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as knowledge advances. The ultimate judgement with regard to a particular clinical procedure or treatment plan must be made by the clinician in light of the clinical data presented and the diagnostic and treatment options available.

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## Management of a patient with suspected anaphylaxis during anaesthesia

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### INTRODUCTION

The exact prevalence of anaphylaxis during anaesthesia is very difficult to estimate and has been calculated to range from 1 in 3,500 to 1 in 13,000 cases according to research in France.<sup>1,2</sup> A report from Australia estimated the incidence to be between 1 in 10,000 and 1 in 20,000,<sup>3</sup> whereas another report from Norway estimated the incidence to be 1 in 6,000.<sup>4</sup> If anaphylaxis during anaesthesia is recognized promptly and managed optimally, severe adverse reactions may be avoidable. However, in most cases, multiple drugs were administered and correct identification of the causative factor is not always straightforward. The Association of Anaesthetists of Great Britain & Ireland (AAGBI) has produced a management guideline (shown in Figure 1).

### COMMENTARY ON ALGORITHM

Profound understanding of the consensus and guidelines is crucial for timely and effect diagnosis and management of suspected anaphylaxis during anaesthesia. For further detail the guideline is broken into four sections, A to D.

#### Section A - Immediate management

1. Anaphylaxis during anaesthesia may present in a variety of symptoms. In most cases, the clinical features, associated or not, include severe respiratory manifestations, cardiovascular symptoms, and cutaneous signs.

Cardiorespiratory	Cutaneous
hypotension	cutaneous flushing
tachycardia or bradycardia	rash
cardiovascular collapse	urticaria
bronchospasm	angioedema
hypoxia	

Multisystem involvement is most common, but not always the case. The absence of cutaneous signs does not exclude the diagnosis of anaphylaxis.<sup>5</sup>

2. The diagnosis of anaphylaxis during anaesthesia is usually problematic because clinical features such as hypotension and bronchospasm more commonly have a different cause. Most common anesthetics may cause vasodilation, hypotension, and cardiopulmonary dysfunction as a result of direct and indirect effects on sympathoadrenergic responses. Bronchospasm and wheeze may be provoked by histamine releasing drugs (such as suxamethonium) and may also develop after endotracheal intubation in smokers or asthmatics. In addition, cutaneous symptoms may be missed as patients are usually hidden by surgical drapes.

3. Up to 90% cases of anaphylaxis during anaesthesia occur within minutes of induction,<sup>6</sup> and are linked mainly to agents administered intravenously.<sup>7</sup> If an adverse event such as hypotension or bronchospasm occurs after drug administration or blood transfusion during anaesthesia, it is appropriate to suspect anaphylaxis unless there exists a significantly more likely cause, such as hypovolaemia, light/deep anaesthesia or extensive regional blockade. Rare but potentially disastrous events should be excluded, for example a misplaced tracheal tube or equipment failure.

4. Recommendations for the treatment of anaphylaxis during anaesthesia, which has a wide variety of presentations, must not be established on a rigid scheme. Treatment should depend on the clinical picture, however, there are general measures used in all cases:

- Immediately *stop administration of the agent* that you suspect to be the causative factor, interrupting the effects of the preformed mediators that were released in response to the antigen, and preventing more mediator release.
- Rapidly control the airway and administer 100% oxygen.* Airway support with 100% oxygen will increase oxygen delivery and compensate for the increased oxygen consumption.

### Summary

If anaphylaxis during anaesthesia is recognized promptly and managed optimally, severe adverse reactions are avoidable.

Follow basic life support with the ABC approach (Airway, Breathing, and Circulation), epinephrine (adrenaline) is the most effective drug in anaphylaxis during anaesthesia and should be given as early as possible.

Serum mast cell tryptase levels may help the retrospective diagnosis of anaphylaxis, though it does not differentiate IgE-mediated reactions from non-IgE-mediated reactions. Follow-up investigation is essential to avoid life-threatening re-exposure of the patient to the offending drug or substance and to tailor a safe alternative.

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- c *Call for help.* In an emergency situation such as this, team-working enables several tasks to be accomplished simultaneously. Do not attempt to resolve every problem unaided. In addition, another person will review the situation and may easily spot something that you have overlooked. Get information from the surgical team as soon as possible which may be helpful to make a decision to cancel, accelerate or stop surgery.
- d *Make detailed notes.* For diagnostic purposes and further investigation after a severe adverse reaction during anaesthesia, it is important to document a detailed description of the reaction (e.g. symptoms, severity, time course) and its treatment. All drugs and/or other substances to which the patient was exposed during anaesthesia, as well as their time onset in relation to the reaction, must be recorded.
- Epinephrine (adrenaline) is the most effective drug in most cases of anaphylaxis and should be given as early as possible. Failure to treat anaphylaxis promptly with epinephrine may result in biphasic or protracted anaphylaxis or in a fatal outcome.<sup>8,9</sup> The  $\alpha$ -agonist activity of epinephrine is able to reverse vasodilatation and oedema. In addition, epinephrine is a valuable  $\alpha$ -agonist which has a positive inotropic action, dilates bronchial smooth muscle, and reduces the release of inflammatory mediators, such as leukotrienes and histamine.<sup>10</sup> In patients taking  $\beta$ -adrenergic blocking agents, it may be necessary to increase the dose of epinephrine rapidly: for example a first bolus of 100mcg, followed when necessary by 1mg or even 5mg, at 1 to 2 minute intervals.<sup>11</sup> Continuous infusion of epinephrine is advantageous in patients who need repeated doses of epinephrine.<sup>12</sup> It is important to note, however, that epinephrine should be titrated carefully to response, especially when administered intravenously, which have been implicated in a few cases of excessive doses of epinephrine.<sup>13</sup>
  - Fluid therapy is important to counteract the large fluid shifts associated with vasodilatation and capillary leakage. Rapidly restore the vascular volume with isotonic crystalloid and consider use of a colloid when the volume of crystalloid exceeds 30ml.kg<sup>-1</sup>.<sup>11</sup> Avoid administering the substances that are suspected to be the cause of the reaction.
  - If appropriate, start cardiopulmonary resuscitation immediately, following the usual resuscitation measures for cardiocirculatory insufficiency.
  - For patients who are refractory to epinephrine, consider other vasoconstrictor drugs such as norepinephrine (starting with 0.1mcg.kg<sup>-1</sup>.min<sup>-1</sup>)<sup>11</sup> or vasopressin – see below.
  - Vasopressin is an important alternative for vasodilatory shock associated with anaphylaxis for anaesthetists who may not have access to epinephrine to treat anaphylaxis. The pressor response to vasopressin may be mainly due to the ability of vasopressin to block the potassium channels in vascular smooth muscle and interfere with multiple signaling pathways.<sup>17,18</sup> In patients with a reasonable arterial blood pressure consider starting at doses of 1–2 units; in patients with cardiac arrest, 40 units are part of Advanced Cardiac Life Support guidelines.<sup>16</sup> It is reported that the effects of vasopressin are similar to those of epinephrine in the management of ventricular fibrillation and pulseless electrical activity, but vasopressin is superior to epinephrine in patients with asystole.<sup>19</sup> Several case reports and experimental models of severe anaphylactic reactions have also suggested vasopressin's efficacy.<sup>20,22</sup>
  - For patients on  $\beta$ -blocker treatment, if epinephrine is not efficient, glucagons could also be effective (1 to 2mg intravenously, repeated every 5 minutes).<sup>10,11</sup>
  - In cases of bronchospasm without arterial hypotension, a  $\beta_2$ -adrenergic agonist (such as salbutamol, 2.5-5mg) can be administered through an inhalation chamber adapted to the ventilatory circuit. If this treatment is resistant, consider the intravenous route: administer a 100 to 200mcg bolus of salbutamol, followed by continuous perfusion of this drug (5 to 25mcg.min<sup>-1</sup>).<sup>11</sup>

### SECTION C - Investigation

- Serum tryptase is a mast cell protease that is increased in cases of anaphylaxis, signaling an immune-mediated mechanism. Tryptase concentrations can be measured in serum (or plasma) 30 minutes after onset of symptoms and reach a peak between 15 minutes and one hour.<sup>23</sup> The half-life of tryptase is about 120 minutes and the levels gradually decrease over time.
- Mast cell tryptase can also be released by pharmacologic drugs that cause direct non-immunologic mast cell activation.<sup>24</sup> Therefore, an increase of serum tryptase does not differentiate IgE-mediated reactions from non-IgE-mediated reactions. There have been a few reports of anaphylaxis with positive tests for IgE antibodies and an absence of serum tryptase.<sup>25</sup> In other words, a negative test for serum tryptase does not exclude an anaphylactic reaction.
- To enable comparison with baseline levels, a control sample value should be measured either on a pre-operative sample or a minimum of 24 h after the reaction.
- If the sample tubes cannot be transported to the local laboratory within 2 hours, they must be stored in a refrigerator at +4°C (for not longer than 12 hours). After centrifugation, the serum should be stored at -20°C in several aliquots.

### SECTION B - Secondary management

- Antihistamines and corticosteroids have a place as secondary treatment for anaphylaxis and help to prevent oedema, cutaneous symptoms and relapse of the anaphylactic reaction as seen in biphasic or protracted anaphylaxis.<sup>14</sup> Hydrocortisone is the preferred steroid because it has a fast onset. If intubated, the endotracheal tube should be left in place after successful treatment of a severe anaphylactic reaction, because airway swelling and inflammation may continue for up to 24h.<sup>15</sup>

- In order to make a valid interpretation of serum tryptase values, the timing of blood sampling in relation to the reaction should be recorded.

#### SECTION D - Later investigations to identify the causative agent

- Follow-up investigation is necessary in order to identify the drug or substance responsible and the mechanism behind the reaction. This is essential to help a patient avoid potentially life-threatening re-exposure to the offending substance and tailor a safe alternative. If necessary, the anaesthetist should consider referral to an immunologist or allergy specialist for further investigation.
- The anaesthetist is responsible for:
  - Initiating the investigation, in collaboration with a consulting allergy specialist.
  - Informing the patient about the reaction and giving written and verbal recommendations for subsequent anaesthesia.
  - Reporting the event to the pharmaco-vigilance centre if a drug is suspected to be the cause.
- Given the present state of knowledge, skin tests (prick and intradermal reaction) remain the gold standard for the detection of IgE-dependent allergies.<sup>11</sup>
- Currently, radioallergosorbent test (RAST) and fluoroimmunoassay (Pharmacia CAP System) are available in some centres to measure specific IgE antibodies in the blood. However, IgE measurement is only commercially available for a few drugs used during anaesthesia.
- Other cellular assays based either on the release of sulphidoleukotrienes or on flow cytometry are not sufficiently validated to enter daily clinical practice.

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