



# Perioperative anaphylaxis management guideline

## Background paper

### 1. Purpose

Anaphylaxis is a life-threatening emergency that requires prompt recognition and institution of life-saving therapy. It is one of the mandatory emergency response activities that anaesthetists are required to complete as part of their continuing professional development (CPD).

Perioperative anaphylaxis remains the most common cause of death directly attributable to anaesthesia and is classified under Category 1 deaths by the Australian and New Zealand College of Anaesthetists (ANZCA) Safety of Anaesthesia report for the 2015-2017 triennium<sup>1</sup>. Of the thirty-five such deaths identified in this report, eighteen were reviewed in detail and of these eight were judged to be due to anaphylaxis.

This background paper includes a review of the evidence for the management of anaphylaxis during anaesthesia. A modified version of the National Health and Medical Research Council (NHMRC) levels of evidence and the NHMRC grades of recommendation<sup>2</sup> have been applied and are presented at the end of the document (Appendix 1). The levels of evidence and grades of recommendations shown throughout this document are taken from published reviews and other guidelines on the management of anaphylaxis.

The difference between the Australian and New Zealand Anaesthetic Allergy Group (ANZAAG) and ANZCA guideline and other published anaphylaxis management guidelines is in its presentation format rendering it applicable to crisis management in the perioperative setting. (See cards presented as Appendices 1–6 of the ANZAAG-ANZCA guideline).

### 2. Background

As part of the development process for the original guideline, a literature review was undertaken by ANZAAG. This concluded that there were no randomised controlled trials of sufficient quality on the management of anaphylaxis. Consequently, the original guideline was a consensus statement. The intent was to optimise management of perioperative anaphylaxis and to provide a cognitive aid for use during crisis management.

ANZCA endorsed the document in February 2013.

The 2015/2016 review was a collaboration between ANZAAG and ANZCA that resulted in the document being co-badged by both parties.

The second edition of the guideline was modified to address observations made during simulation, feedback from anaesthetists having managed episodes of intraoperative anaphylaxis, and from the many anaphylaxis workshops that had been conducted since the initial guideline was introduced throughout Australasia. The intervening three years witnessed some limited improvement in the evidence base for anaphylaxis management in the literature.

The key changes to the 2016 guideline were:

- The development of two paediatric cards for the Immediate and Refractory Management of anaphylaxis in children.
- Introduction of cardiac arrest recommendations at the top of the Immediate Management cards.
- Increased emphasis on rapid, large volume fluid resuscitation.
- Emphasis on the cessation/removal of possible triggers in both the Immediate Management and Refractory Management cards.
- Changes to the Diagnostic Card to make it a differential checklist rather than a textbook differential diagnosis list.
- Changing the drug name *adrenaline* to *adrenaline (epinephrine)* to be consistent with the Australian [Therapeutic Goods Administration](#) approach to International Harmonisation of drug and ingredient names. For ease of reading the dual nomenclature is restricted to headings in most instances.

The 2020/2021 review was performed as part of a routine 5 yearly review of ANZCA guidelines. It is timely as there have been a number of significant publications in the years since the 2016 guideline was published. These include the following:

- NAP6 (6<sup>th</sup> National Audit Project: Perioperative Anaphylaxis) was published in May 2018 and reported the findings of a year-long UK-wide audit of perioperative anaphylaxis focussing on Grade 3, 4 and 5 reactions<sup>3</sup>.
- In July 2019 the British Journal of Anaesthesia published a special Perioperative Anaphylaxis issue with international consensus guidelines and reviews<sup>4</sup>. This was the work of a multidisciplinary group of clinicians and academics from around the world called the International Suspected Perioperative Allergy (ISPAR) Group.
- Updated resuscitation guidelines have also been released by a number of bodies including the Resuscitation Council of the UK<sup>5</sup>, European Resuscitation Council<sup>6</sup>, American Heart Association<sup>7</sup>, Association of Anaesthetists of Great Britain and Ireland (AAGBI)<sup>8</sup>, Brazilian Society of Anaesthesiology and Brazilian Association of Allergy and Immunology<sup>9,10</sup>, Japanese Society of Anesthesiologists<sup>11</sup>, Australian and New Zealand Committee on Resuscitation (ANZCOR)<sup>12</sup> and Australasian Society of Clinical Immunology and Allergy (ASCI)<sup>13</sup>. The AAGBI, Japanese and Brazilian guidelines are specific for perioperative hypersensitivity reactions.

The key changes to the 2021 guideline are:

- Cardiac compressions should be initiated at a systolic blood pressure of less than 50mmHg in the anaesthetised patient.
- A graded approach to volume replacement with an initial crystalloid fluid bolus of 500mL in a moderate (Grade 2) and 1000mL in a life threatening (Grade 3) reaction to be repeated as required and titrated to clinical response. In the case of a cardiac arrest (Grade 4) reaction the recommendation remains for an initial bolus of 2000mL.
- A more graded approach to IV adrenaline bolus dosing with lower starting doses for each grade of reaction and guidance on how to escalate doses if there is no response.
- Manual left uterine displacement (LUD) should be applied during the management of hypotension or cardiac arrest due to anaphylaxis in the pregnant patient to minimise aortocaval compression (in preference to left lateral tilt).

- Oesophageal intubation has been added to the differential diagnosis list for refractory bronchospasm and has been included on the immediate management card<sup>14</sup>.

### 3. Nomenclature

A revised nomenclature for allergy has been incorporated into the accompanying guideline, which is based on the position statement of the European Academy of Allergy and Clinical Immunology (EAACI) nomenclature task force<sup>15</sup>.

**Hypersensitivity** is an umbrella term to cover reproducible symptoms or signs, initiated by exposure to a substance at a dose tolerated by normal subjects and that is outside the primary pharmacological actions. It can be due to immune mechanisms (allergic hypersensitivity) or non-immune mechanisms (non-allergic hypersensitivity).

**Anaphylaxis** is a severe, life-threatening, generalised or systemic hypersensitivity reaction. It can be due to immune mechanisms (allergic anaphylaxis) or non-immune mechanisms (non-allergic anaphylaxis).

### 4. Pathophysiology and clinical features of perioperative anaphylaxis

An understanding of the mechanisms and pathophysiology is essential to guide early diagnosis and effective management of perioperative anaphylaxis. This topic was well covered in a recent review<sup>16</sup>.

The key effector cells are mast cells and basophils. Degranulation can be triggered by specific (IgE and IgG) and non-specific (complement, COX-1, Kinin-Kallikrein system, MRGPRX2 and other receptors) mechanisms. These result in the release of mediators including histamine, proteases, prostaglandin, leukotrienes and platelet activating factor. The clinical features seen are the result of mediator actions.

The diagnosis of anaphylaxis is a clinical one and the treatment is the same regardless of the mechanism. A high index of suspicion by anaesthetists is essential for early recognition and prompt treatment.

Clinical presentation is influenced by patient comorbidities and pharmaceutical treatments, surgical pathology, and surgical and anaesthetic techniques. The evolution of the clinical scenario depends on the physiological reserve of the patient and the effectiveness of the treatment administered.

Perioperative hypersensitivity reactions involve mainly cardiovascular, respiratory and mucocutaneous systems.

#### 4.1 Cardiovascular

Hypotension is the most common presenting feature (46%) and was present at some point in 98.5% of cases in NAP6 (1.5% had bronchospasm as the only feature). It is usually accompanied by tachycardia (effect of histamine on cardiac H<sub>2</sub> receptors, endogenous catecholamine effects on cardiac beta receptors and reflex sympathetic activation) although bradycardia may be more common in severe anaphylaxis. Often cardiac output is (at least initially) maintained or increased.

Hypotension is usually due to circulatory failure rather than myocardial dysfunction. Circulatory failure is caused by decreased preload and decreased intravascular volume resulting in decreased cardiac output.

Myocardial dysfunction may occur due to hypoperfusion secondary to hypovolaemia and increased oxygen demand secondary to tachycardia. This is more common in patients with pre-existing cardiac disease.

**Adequate and early volume replacement is essential.** Intraoperative echocardiography in cases of anaphylaxis typically shows hyperdynamic left and right ventricles with low end systolic volumes.

**Adrenaline (epinephrine)** is the mainstay of pharmacological management and is recommended in all published guidelines. It is both an alpha and beta agonist and beneficial actions include vasoconstriction which transiently increases venous return/preload, reduction in capillary blood flow leading to reduced leakage, positive inotropy with enhanced cardiac output due to increased contractility, bronchodilatation, and inhibition of mast cell and basophil mediator release.

## 4.2 Respiratory

Many patients presenting for surgery have a predisposition to bronchospasm due to asthma, which may be poorly controlled or even undiagnosed, chronic obstructive pulmonary disease, smoking and intercurrent viral respiratory tract infections. Anxiety, irritant volatile anaesthetics, airway instrumentation and histamine releasing drugs may trigger bronchospasm. Anaphylaxis is not the most common cause of perioperative bronchospasm. When anaphylaxis does occur bronchospasm is triggered by the actions of degranulation products including histamine, leukotriene and PAF which are all potent bronchoconstrictors. Histamine is also a potent vasodilator of the tracheobronchial circulation causing submucosal swelling.

Pulmonary oedema is a rare complication of anaphylaxis.

## 4.3 Mucocutaneous

Urticaria occurs due to vasodilatation, increased blood flow and increased capillary leakage in the superficial dermis.

Angioedema (non-pitting, non-gravity-dependent, transient swelling of the skin or mucous membranes) is due to the same pathophysiological process but occurs in the deeper tissues. It may occur as part of anaphylaxis (histaminergic) but may also be bradykinin or complement mediated (non-histaminergic).

Airway swelling is an uncommon feature of perioperative anaphylaxis. In NAP6 it was reported in less than 1% of Grade 3 reactions and in none of the Grade 4 reactions. Bradykinin-mediated angioedema often involves the upper airways and does not respond to treatment with antihistamines, corticosteroids, or adrenaline. It may be triggered by airway manipulation during anaesthesia and is often prolonged.

## 5. How to use the anaphylaxis cards

The cards have been designed for use during an anaphylaxis event with one team member assigned to read the cards and ensure all items have been checked off. The use of cognitive aids and having a 'designated reader' has been shown to increase the number of critical tasks achieved, and improve teamwork and performance<sup>17-19</sup>.

The suggestions below are offered to facilitate effective use of the cognitive aid cards in managing any anaphylaxis emergency<sup>17</sup>. As with any clinical emergency it is recommended that all members of the anaesthesia team are familiar with the cards and their likely roles.

## 5.1 Team structure

It is advisable to send for help early during a suspected perioperative anaphylaxis, due to the potential for multiple simultaneous tasks. A consultant anaesthetist should be present or notified.

The following suggestions as to the roles acknowledges the variability of resources and, consequently, no absolute allocations have been made. The anaesthesia team for anaphylaxis management has at least three team members with specific roles:

- 5.1.1 Team leader** – usually the most senior anaesthetist. This person has the overall view of the situation and coordinates tasks. This person should refrain from any technical tasks if at all possible.
- 5.1.2 Card reader** – this role does not require specific anaesthesia expertise and therefore, may be performed by an anaesthetic technician, a nurse, a second anaesthetist, an anaesthesia trainee, or a surgeon. The role of the card reader is to call out the required actions on the cards to the team and to verify and communicate with the team leader. It is important the cards are not paraphrased or skipped through to ensure all the items have been addressed<sup>18</sup>.
- 5.1.3 Person administering adrenaline (epinephrine)** – this is usually a second anaesthetist, an anaesthesia trainee, or an experienced nurse who is responsible for intravenous (IV) and intramuscular (IM) adrenaline administration, and delegating preparation of the adrenaline infusion.

### **Additional roles if resources allow:**

**Fluid management** – Observation of teams managing anaphylaxis has identified that fluid resuscitation is commonly inadequate during these events.

**Cannulation** – intravenous and intra-arterial access

### **Scribe**

**Cardiopulmonary Resuscitation (CPR)** - In cases of Grade 4 anaphylaxis (cardiac arrest) several people will be required to perform chest compressions. These may be additional clinical staff attending during the cardiac arrest or if limited staffing is available consider using other allied health, clerical, orderly or other staff with basic life support skills.

## 5.2 Anaphylaxis box

Institutions should consider assembling an Anaphylaxis Box in accordance with the accompanying guideline. The box should include the laminated anaphylaxis management cards, local infusion protocols for adrenaline, noradrenaline, vasopressin, and salbutamol and collection tubes for tryptase. The box may also contain patient form letters, patient information brochures and ANZAAG referral forms which can be found on the ANZAAG website at [www.anzaag.com](http://www.anzaag.com).

## 5.3 Departmental anaphylaxis lead

NAP6 recommended that all anaesthetic departments should have a departmental lead for perioperative anaphylaxis acting as a point of contact to ensure that all cases are optimally managed, investigated and followed up. ANZCA, in collaboration with ANZAAG, is setting up a network of anaphylaxis leads in ANZCA accredited training hospitals.

## 5.4 Severity of anaphylaxis

In conscious or minimally sedated patients, anaphylaxis may also have additional respiratory, gastrointestinal, or central nervous system symptoms and signs in addition to itching or flushing. These include rhinorrhoea, cough, dyspnoea, circumoral tingling, difficulty swallowing, nausea, abdominal pain, irritability, confusion, or a sense of impending doom<sup>20</sup>.

Clinical manifestations of intra-operative reactions may not be obvious, as patients are often covered in drapes and unconscious, making them unable to communicate. Moreover, simultaneously administered medications may alter the expression and degree of clinical manifestations<sup>21</sup>.

The severity of anaphylaxis is dependent on the progression and severity of signs and symptoms. For the purposes of the accompanying guideline and management cards, the following Ring & Messmer grading scale for severity of anaphylaxis is used.

**5.4.1 Mild (Grade 1) hypersensitivity** is typified by *mucocutaneous signs only*, such as erythema, urticaria, and peripheral angioedema. These reactions do not usually require treatment with adrenaline. Although the focus of these anaphylaxis management resources is on moderate to severe anaphylaxis, mild anaphylaxis (Grade 1) should also be recognised and monitored carefully in order to promptly detect progression to a higher grade triggering treatment with adrenaline.

**5.4.2 Moderate (Grade 2) hypersensitivity** has *multi-organ manifestations* typically mucocutaneous signs combined with hypotension and/or bronchospasm. Diagnosis of anaphylaxis over other causes of moderate hypotension and/or bronchospasm is facilitated in the presence of mucocutaneous signs, which are more likely to arise in Grade 2 anaphylaxis than Grade 3.

Hypotension is a common event during anaesthesia, especially post-induction, and can be attributed to many other causes than anaphylaxis. The diagnosis of anaphylaxis should be considered where hypotension is unexplained and out of proportion to that which could be expected on basis of patient factors (age, comorbidities) and stage of the operation and/or where there has been a lack of sustained response to usual restorative measures. While tachycardia is common it can be masked by concomitant  $\beta$ -blocker use, and bradycardia may be observed in some patients<sup>21</sup>.

The diagnosis of anaphylaxis should be suspected where bronchospasm and difficulty with ventilation are resistant to commonly employed treatment manoeuvres.

**5.4.3 Life-threatening (Grade 3) anaphylaxis** presents as severe *hypotension and/or severe bronchospasm*. Airway pressures are elevated to levels where oxygenation and ventilation are rapidly compromised. Immediate treatment is required in this situation in order to avoid progression from inadequate tissue perfusion to significant hypoxia or to cardiac arrest. Unlike Grade 2 anaphylaxis, urticaria is not a common presenting feature and skin signs may only appear after resuscitation.

In NAP6 the commonest presenting features of life-threatening anaphylaxis were hypotension (46%) followed by bronchospasm (18%) and tachycardia (9.8%). Hypotension occurred in all patients at some point during the anaphylactic episode followed by flushing/non urticarial rash (56%), bronchospasm (49%), tachycardia (46%), oxygen desaturation (41%) and a reduced or absent capnography trace

(30%). A small number of patients presented with isolated cardiovascular (5.6%) or isolated respiratory features (1.5%).

**5.4.4 Cardiac arrest (Grade 4) anaphylaxis** is discussed further in section 5.1.

## 5.5 Adult immediate management

The card for immediate management has been designed as a cognitive aid for use during a crisis. The main points of managing the crisis are listed on the left-hand side of the card, whereas the right-hand side gives more detailed instructions. Actions are listed in order of priority with the most important at the top.

### 5.5.1 Cardiac arrest: Grade 4 anaphylaxis

Anaphylaxis in the setting of anaesthesia may present as or progress to cardiac arrest, most commonly pulseless electrical activity (PEA). In this circumstance good quality cardiopulmonary resuscitation should commence immediately. NAP6 included 40 cases of cardiac arrest. Of these, 34 were PEA (often preceded by bradycardia), 4 were VF/VT and 2 were asystole. Nine of these patients (22.5%) died and 31 survived (77.5%).

The guideline for in-hospital cardiac arrest recommends starting CPR in any patient who is unresponsive, has abnormal breathing and/or their carotid pulse is absent<sup>6</sup>. Almost all anaesthetised patients are unresponsive with varied patterns of breathing and therefore, initiation of chest compressions relies almost exclusively on cardiovascular assessment. This may include arterial blood pressure, pulse waveform and oximetry, capnography, ECG and measurements of cardiac output. Pulse palpation (peripheral or central) is unreliable even when performed by trained clinicians. One of the recommendations from NAP6 was that CPR should be initiated at a systolic blood pressure of less than 50mmHg (described as profound hypotension). The rationale behind the recommendation is discussed in an editorial by Harper et al<sup>23</sup>. This recommendation was endorsed by the ISPAR group and has been incorporated in several resuscitation guidelines including those from the UK Resuscitation Council, AAGBI and the Brazilian Society of Anesthesiology.

**The new recommendation in the accompanying guideline is that cardiac compressions should be initiated at a systolic blood pressure of less than 50mmHg in the anaesthetised patient.**

The recently updated recommendations from the American Heart Association, the UK Resuscitation Council and the European Resuscitation Council for non-shockable rhythms are to administer adrenaline 1mg as soon as is feasible and then repeat every 3 to 5 minutes. The ISPAR group recommend following standard ALS guidelines in this circumstance. It is important to note that hypovolaemia (a ubiquitous feature of severe anaphylaxis) is a potential cause of PEA arrest and therefore concomitant aggressive fluid resuscitation is essential.

Excessive use of adrenaline in association with inadequate volume replacement can result in a hyperdynamic underfilled heart and dynamic left ventricular outflow obstruction even in an anatomically normal heart. Continued use of adrenaline in this situation is likely to worsen the condition and may be fatal<sup>24</sup>. Early use of echocardiography (either transthoracic (TTE) or transoesophageal (TOE)) helps optimise therapy by providing information on ventricular function, ventricular filling and vasodilation.

The recommendation in the accompanying guideline is to commence administration of 1mg of adrenaline every 1 to 2 minutes as required, with rapid administration of fluid volume resuscitation and the early addition of alternative vasopressors<sup>25</sup>.

This is intended to apply in circumstances where patients have had a witnessed cardiac arrest from a potentially reversible cause in which prolonged resuscitation may have a good outcome<sup>5,13</sup>.

### **5.5.2 Maintenance of anaesthesia**

Anaesthesia should be maintained with minimal anaesthetic agent until the situation is stabilised. Consider a depth of anaesthesia monitor if this is not already in use (e.g. bispectral index (BIS)).

### **5.5.3 Triggers**

Possible allergens such as colloids and medications should be considered in the context of ceasing administration of potential triggers (Grade D recommendation, Level V evidence).

Muscle relaxants and antibiotics are the most common allergens associated with perioperative anaphylaxis in Australia and New Zealand<sup>26-30</sup>.

Anaphylaxis to chlorhexidine is an emerging concern and further use of this agent should be avoided if administered prior to the development of symptoms<sup>30-33</sup>. Chlorhexidine may be present in products including skin preparations and wipes, lubricant gels (e.g. urinary catheters) and some impregnated central venous lines. Anaesthetists should be aware that these products are sometimes poorly labelled and the number of products containing chlorhexidine is increasing.

Similarly, latex, dyes and colloids utilised prior to the reaction may be overlooked as allergens.

It is particularly important in cases of refractory anaphylaxis (Level V evidence)<sup>34</sup> to review and cease possible triggers and where practicable, remove them from the environment to avoid further administration (Grade D recommendation).

### **5.5.4 Ensure secure airway**

The accompanying guideline is not intended to provide management plans for the variety of clinical situations in which airway and cardiorespiratory compromise may develop. Where airway oedema is apparent early endotracheal intubation should be considered.

### **5.5.5 Position**

Patients in any position other than supine, should be returned to the supine position as soon as possible to facilitate continuing resuscitative efforts should they be required. Where hypotension is a predominant sign leg elevation should be considered (Grade D recommendation, Level IV evidence)<sup>26,35-38</sup>.

### **5.5.6 Intravenous access**

Large bore intravenous access should be secured as soon as possible. If chlorhexidine has been a possible trigger, then anaesthetists are advised to avoid



chlorhexidine skin preparation or placement of any chlorhexidine impregnated central line.

### 5.5.7 Fluid resuscitation

Adequate fluid resuscitation is a critical step in management of hypovolaemia associated with anaphylaxis. It has been shown that 35% to 70% of the blood volume may extravasate in 10 to 15 minutes<sup>39-41</sup>. This requires aggressive management, and repeated fluid boluses may be required (Grade D recommendation, Level IV evidence)<sup>39,40</sup>. Fluid administration was judged to be inadequate in 19% of cases of severe anaphylaxis in NAP6.

A bolus of 20mLs/kg (1400mL in a 70kg patient) was recommended in earlier versions of this guideline. ASCIA recommends a fluid bolus of 20mL/kg “if hypotensive”. The AAGBI guidelines recommend 20mLs/kg bolus repeated “until hypotension resolves”. The ISPAR group recommend an initial fluid bolus of 500mL in Grade 2 and 1000mL in Grade 3 reactions to be repeated if clinical response is inadequate. The UK Resuscitation Council recommends a starting bolus of 500-1000mL in adults with further fluid boluses titrated to response.

**The new recommendation in the accompanying guideline is an initial fluid bolus of 500mL in Grade 2 and 1000mL in Grade 3 reactions, to be repeated as required, and titrated to clinical response. In cases of Grade 4 reactions (cardiac arrest) the recommendation remains for an initial bolus of 2000mL.**

**Echocardiography** (either transthoracic (TTE) or transoesophageal (TOE)) helps optimise therapy by providing information on ventricular function, ventricular filling, and vasodilation<sup>42</sup>. Furthermore, on rare occasions, echocardiography may suggest another diagnosis such as decompensated hypertrophic obstructive cardiomyopathy (HOCM) or Takotsubo cardiomyopathy.

**Crystalloid fluids** are now recommended in all published guidelines<sup>3-6,8,12,13</sup> with the exception of the French<sup>25</sup>. Some guidelines still specifically recommend the use of 0.9% Sodium Chloride (ASCIA, ANZCOR). Large volume resuscitation with 0.9% Sodium Chloride may result in hyperchloremic metabolic acidosis. Therefore, the use of a balanced salt solution such as Plasma-Lyte® is preferred<sup>5</sup>.

Routine use of colloids is no longer recommended. Where synthetic colloid are running at the time of the reaction the colloid is a potential culprit and administration should cease.

All staff managing anaphylaxis need to be aware of the importance of minimising heat loss with patient exposure during resuscitative efforts. Hypothermia has the potential to worsen outcome with increased risk of arrhythmia, cardiac ischaemia and coagulopathy. Warming of intravenous fluids should be performed where practical.

### 5.5.8 Adrenaline (epinephrine)

International guidelines agree that adrenaline is the first line treatment for anaphylaxis (Level IV evidence)<sup>34,43-46</sup>. The early recognition of anaphylaxis and prompt administration of adrenaline is associated with improved outcomes in perioperative anaphylaxis (NAP6). Adrenaline is pivotal in the management of anaphylaxis due to its unique pharmacology in functionally antagonising the relevant pathophysiological effects of anaphylaxis<sup>47</sup>. In the doses recommended, adrenaline

causes increased cardiac output, bronchodilation, vasoconstriction, reduced mucosal oedema and reduced mediator release. Adrenaline not only treats the clinical manifestations but also reduces response amplification<sup>43,44</sup>, and therefore, cannot be substituted by any other medication<sup>47</sup>.

Although adrenaline is not contra-indicated with any patient co-morbidity, it is worth noting that it has a narrow therapeutic window, and titration of dose according to severity and patient response is essential. International dosing regimens for adrenaline vary for this reason. The risks of overdose are higher in some patients e.g. extremes of age, patients with hypertension, ischaemic heart disease, hypertrophic cardiomyopathy (HOCM) or hyperthyroidism. Consequently, judicious use is advised. In other patients there will be decreased effectiveness of both endogenous and exogenous catecholamines e.g. patients taking  $\beta$ -blockers or angiotensin converting enzyme inhibitors (ACEI). Cocaine and amphetamines in contrast, will sensitise the myocardium to the effects of adrenaline. Despite this, the best available evidence is that adrenaline is key to the management of anaphylaxis. Clinicians need to be aware of the potential for toxicity including accidental overdose, particularly during crisis management<sup>45,47-50</sup>.

The World Allergy Organisation has reviewed fatal cases of anaphylaxis and highlighted that administration of adrenaline was often delayed or inadequate<sup>34,36,51</sup>. It is essential therefore, that diagnosis be rapid, and adrenaline administered early and in adequate doses to optimise outcome (Level V evidence, Grade D recommendation).

#### **5.5.8.1 IM adrenaline (epinephrine)<sup>34,43,44</sup>**

The World Allergy Organisation guidelines state that the benefits of IM adrenaline for the management of anaphylaxis far exceed the risks (Level 1 evidence), and this route of administration is commonplace in all other acute medical disciplines. Due to ease of preparation and administration of IM adrenaline, it should be considered in the initial management of perioperative anaphylaxis in the following circumstances (Grade B recommendation):

- whenever there is an evolving suspicion of moderate (Grade 2) anaphylaxis
- when awaiting assistance
- when IV access is not yet established or is lost
- where haemodynamic monitoring is not in-situ prior to the reaction
- while awaiting preparation of an adrenaline infusion.

Research has shown that IM adrenaline provides an effective infusion lasting up to 40 minutes<sup>52,53</sup>.

This guideline recommends a dose of 500mcg (0.5mg) IM in the lateral thigh repeated every 5 minutes as needed.

This recommendation is consistent with those of the AAGBI, UK Resuscitation Council, European Resuscitation Council, EAACI, ASCIA, and ANZCOR.

#### **5.5.8.2 IV boluses of adrenaline (epinephrine)**

The mainstay of the management of moderate to severe perioperative anaphylaxis is carefully titrated IV adrenaline with close monitoring of cardiovascular responses (Level IV evidence)<sup>34</sup>. This is in keeping with other international perioperative anaphylaxis management guidelines<sup>8-11,25, 54-56</sup> and the recommendations of the ISPAR group (Grade D recommendation).

The dose should be based on the grade of clinical presentation.

Grade 1: no adrenaline required.

Grade 2: 10-20mcg IV adrenaline. Escalate to 50mcg if insufficient response to initial dose. Consider initial IM adrenaline as a safe and effective alternative.

Grade 3: 50-100mcg IV adrenaline. Escalate to 200mcg if insufficient response to initial dose.

Grade 4: As discussed earlier, in PEA arrest 1000mcg (1mg) IV adrenaline immediately and then repeated every 1-2 minutes. For shockable rhythms follow ALS guidelines.

Medication errors are common. They were found to occur in 1 in 133 anaesthetics in a prospective self-reporting study in New Zealand<sup>57</sup>. The risk of a medication error occurring with adrenaline during the management of an episode of anaphylaxis is high due to a number of factors including:

- the availability of two different strengths
- the use of unfamiliar ratio doses (1:10,000 and 1:1,000)
- the potential for two different routes of administration (IV or IM)
- the big variation in dose depending on route of administration and severity of reaction (from 10mcg IV for a Grade 2 reaction up to 1000mcg IV in a cardiac arrest)
- unfamiliarity of the person drawing up and/or diluting the drug
- poor or no syringe labelling due to time pressure and
- poor communication between the person ordering, the person drawing up and the person administering the adrenaline.

Due to the narrow therapeutic window of adrenaline the consequences of any medication error may be severe.

There are a number of ways in which adrenaline may be prepared. This guideline recommends a dilution of 1,000mcg (1mg) in 10mL to yield a concentration of 100mcg/mL. This may be available as a 10mL ampoule of 1:10,000 adrenaline (no dilution required) or it can be made up by adding a 1mL ampoule of 1:1,000 adrenaline to 9mL of diluent. The advantage of this method is that one dilution can be used for both moderate and life threatening reactions. The disadvantage is that the doses recommended for moderate reactions (10-20mcg) require the administration of very small volumes (0.1–0.2mL).

One alternative is to make two dilutions -

- 1mg of adrenaline in a 100mL bag of IV fluid to give a concentration of 10mcg/mL and
- 1mg of adrenaline in 10mL to give a concentration of 100mcg/mL.

The disadvantage of this method is that you have two concentrations of adrenaline which may lead to the wrong dose being delivered. The advantage is that you avoid giving very small volumes when treating moderate reactions.

If the task of drawing up the adrenaline is delegated to another staff member it is very important that clear and detailed instructions are given. Ideally the instructions should be written down as they are on the immediate management cards.

These recommendations are intended for use only in the peri-operative setting. They reflect the special circumstances of peri-operative anaphylaxis where there is continuous dedicated monitoring by an anaesthetist and a higher frequency of sudden onset severe symptoms compared to non-operative anaphylaxis. For non-anaesthetic anaphylaxis the ASCIA guidelines<sup>13</sup> apply.

#### **5.5.8.3 Adrenaline (epinephrine) infusion<sup>34</sup>**

Adrenaline infusions without bolus administration<sup>40</sup> (Level III evidence) have been shown to be effective in treating anaphylaxis in non-anaesthesia settings and are part of the new ASCIA guidelines for the management of severe refractory anaphylaxis. Use of adrenaline infusions facilitates ease of titrating dose to effect as compared to repeated bolus regimens. After three boluses via either the IV or IM route an adrenaline infusion should be prepared and commenced as early as possible in the clinically applicable dosage<sup>25,40,58,59</sup> (Grade D recommendation). To facilitate prompt preparation and institution of adrenaline infusions using a syringe driver, the immediate management card provides the dilution and infusion rate applicable to a 70kg adult.

Infusions can be commenced with peripheral venous access and should not be delayed because of the lack of central venous access. The dose ranges recommended are derived from the French guidelines<sup>25,60</sup>.

#### **5.5.9 Sugammadex**

The accompanying guideline does not include the use of sugammadex in the treatment of anaphylaxis following administration of rocuronium. There continue to be case reports claiming benefits temporally related to the administration of sugammadex in cases of rocuronium anaphylaxis. In all these cases conventional resuscitative therapies had also been administered. In addition, in vitro and in vivo human models of anaphylaxis have not been able to demonstrate immunologically mediated attenuation of established anaphylaxis<sup>61,62</sup>. A case-control study from Perth<sup>53</sup>, in patients who were given sugammadex following rocuronium anaphylaxis, showed that sugammadex increased blood pressure in 46 percent of these patients. However, with subsequent testing, half of these patients were found not to have had anaphylaxis to rocuronium but to another agent administered during anaesthesia.

The observed therapeutic effect of sugammadex on resuscitation may be to increase muscle tone (and therefore, reduce venous capacitance) in circumstances where

there is severe distributive shock and inadequate resuscitation<sup>16</sup>. The resumption of spontaneous (negative pressure) ventilation after reversal of neuromuscular blockade may also increase venous return<sup>16,63</sup>. There are potentially practical difficulties during resuscitation if neuromuscular blockade is reversed. Therefore, the accompanying guideline recommends that all measures on the immediate management card are instituted to maximal levels followed by steps outlined to manage refractory anaphylaxis.

**The use of sugammadex in resuscitation of suspected anaphylaxis to rocuronium is not recommended.**

## 5.6 Paediatric immediate management

The incidence of paediatric perioperative anaphylaxis is lower than that in adults (2.7 per 100,000 anaesthetics in children as compared to 10 per 100,000 anaesthetics in adults in NAP6). Most bronchospasm in paediatric cases is not due to anaphylaxis but bronchospasm is the most common presenting feature in cases of paediatric anaphylaxis in NAP6 (64%). Hypotension is also very common and was present at some stage in nearly 75% of cases.

There is little specific evidence available in the literature to guide management of perioperative anaphylaxis in the paediatric population. Hence, the scientific rationale for immediate management of anaphylaxis in paediatric patients is essentially the same as for adults. The upper limit of age for paediatric guidelines is unclear. The current Australian Resuscitation Council (ARC) and New Zealand Resuscitation Council (NZRC) guidelines for paediatric advanced life support state older children, aged 9 to 14 years, can be treated using adult protocols<sup>64</sup>. The recommendations for IM adrenaline from the AAGBI<sup>56</sup>, the UK Resuscitation Council, the European Resuscitation Council, ASCIA and APLS<sup>65</sup> recommend adult dosing for children greater than 12 years of age. Taking these into consideration, the accompanying guideline has defined paediatric management to apply to those less than 12 years of age.

The IM dose of adrenaline in this guideline is consistent with that recommended by the AAGBI<sup>54</sup>, UK Resuscitation Council<sup>5</sup> and European Resuscitation Council<sup>6</sup>. Using adrenaline 1mg/mL (1:1,000) concentration the dose varies with age as follows: 6 to 12 years - 300mcg (0.3mL), less than 6 years - 150mcg (0.15mL). This corresponds to the licensed doses used for paediatric adrenaline auto-injectors. This simplified dosing regimen is pragmatic and considered to be safe and practical to draw up and inject in an emergency<sup>66</sup>.

The dilution of adrenaline for bolus IV therapy or infusion on the Paediatric Immediate Management card (1mg in 50mL = 20mcg/mL) is the same. The concentration is more dilute than many infusion regimens but has been chosen to reduce the risk of errors where different dilutions are being prepared during crisis management. Where a prolonged adrenaline infusion is required (e.g. when transferring to ICU) then conversion to a more concentrated local institution regimen should be considered.

The only published recommendations for IV bolus doses of adrenaline for paediatrics are those in the French, Scandinavian and AAGBI guidelines<sup>8,25,56</sup>. Recommended doses range from 1-10mcg/kg depending on the severity of the reaction.

There are no recommendations for the dosing of IV adrenaline infusions in the paediatric population in either the Scandinavian or AAGBI guidelines. The French guidelines recommend starting with a rate of 0.1mcg/kg/minute and titrating up to a maximum of 2mcg/kg/minute.

## 5.7 Adult refractory management

The immediate management of anaphylaxis dictates titration of adrenaline, adequate fluid replacement, and optimisation of oxygenation. In some situations, these measures, including a maximal adrenaline infusion, may not be sufficient. This is known to occur more commonly in patients on beta-blockers, ACEI, and with spinal blockade. In these scenarios, it is essential that *all maximal initial measures be continued* and specific targeted therapy added, in accordance with symptoms and local availability of medications.

### 5.7.1 Monitoring

Standard monitoring as recommended by *PG18(A) Guideline on monitoring during anaesthesia*<sup>67</sup> should be utilised throughout resuscitative efforts. An arterial line is highly recommended where possible to aid cardiovascular monitoring, blood sampling and continuous monitoring of adrenaline effects (Grade D recommendation, Level V evidence).

Echocardiography (transthoracic (TTE) or transoesophageal (TOE)) helps optimise therapy by providing information on ventricular function, ventricular filling and vasodilation<sup>42</sup>. This information is likely to be most useful where hypotension is the predominant sign, but ultrasound has also been used to assist in the diagnosis of pneumothorax which is a differential diagnosis for high airway pressures (Grade D recommendation).

In very rare situations, HOCM or takotsubo cardiomyopathy may be misdiagnosed as anaphylaxis. In this circumstance, the patient may deteriorate despite appropriate treatment for presumed anaphylaxis. In particular, high-dose adrenaline may be harmful. For a patient who fails to respond to appropriate therapy for presumed anaphylaxis, echocardiography may be helpful confirming the diagnosis of anaphylaxis or suggesting another diagnosis, such as decompensated HOCM or Takotsubo cardiomyopathy. In general, if an alternative diagnosis is considered, additional expertise should be sought to both confirm the diagnosis and to help guide treatment.

### 5.7.2 Resistant hypotension

Prior to commencing alternative vasopressors anaesthetists need to review the adequacy of IV fluid resuscitation and ensure that an adrenaline infusion has been instituted. Consideration should be given to the benefits of inserting a non-chlorhexidine coated central venous catheter, but where resources are limited, peripheral administration of vasopressors is acceptable in the short-term (Level V evidence).

In recent years extracorporeal membrane oxygenation has become increasingly common in the treatment of in-hospital cardiac arrest in non-cardiac surgery patients, as well as in cases of perioperative anaphylaxis refractory to standard treatment<sup>68,69</sup>. This now forms part of many resuscitation guidelines<sup>4-7</sup>.

It is recommended that, where extracorporeal membrane oxygenation (ECMO) is available, it should be considered in the management of perioperative anaphylaxis refractory to maximal standard treatment (Grade D recommendation).

### 5.7.3 Alternative vasopressors

The evidence supporting use of vasopressors comes from animal models and some case reports of improved clinical variables in refractory anaphylaxis<sup>70-75</sup>. Levels of evidence for their use are weaker than for adrenaline and they should only be used following adequate administration of adrenaline and IV fluids (Grade D recommendation, Level V evidence).

In the presence of adequate cardiac contractility as shown on echocardiography, vasopressors may be considered where adrenaline infusions and fluid boluses are inadequate to achieve targeted blood pressure. Noradrenaline and vasopressin dose recommendations are based on the French and Scandinavian guidelines<sup>25,56,60</sup>. Metaraminol and phenylephrine are included to accommodate those environments where alternatives to adrenaline are limited<sup>60</sup>. Noradrenaline, vasopressin and metaraminol are included in the UK Resuscitation Council and AAGBI guidelines for the management of refractory anaphylaxis and their use is suggested by the ISPAR group in this context.

Glucagon is included in the management of resistant hypotension because it may be of benefit for patients on beta blockers<sup>76</sup> (Grade D recommendation). Glucagon is included in the following guidelines: French and Scandinavian<sup>25,56</sup>, the UK Resuscitation Council, ASCIA, AAGBI and the recommendations of the ISPAR group.

It is recommended that institutions place their own infusion regimens in the anaphylaxis box along with the ANZAAG-ANZCA Anaphylaxis Management Cards to enable infusions of the available alternative vasopressors to be readily prepared.

#### 5.7.4 Resistant bronchospasm

High airway pressure is less likely to be the predominant feature of perioperative anaphylaxis but can be problematic where it occurs (Level V evidence)<sup>34</sup>. It is vital that alternative causes of high airway pressure such as oesophageal intubation, airway device or circuit malfunction and tension pneumothorax are sought and eliminated as causes.

Adrenaline remains the first line treatment of bronchospasm in cases of anaphylaxis. Bronchodilators should not be used as first line treatment for bronchospasm due to anaphylaxis as they do not prevent or relieve other manifestations of anaphylaxis such as hypotension<sup>5,13</sup>.

In patients with resistant bronchospasm inhaled bronchodilators such as salbutamol may be used (12 puffs of 0.1mg of salbutamol administered using a metered dose inhaler inserted into the anaesthesia circuit or 5mg of nebulised salbutamol in the awake patient)<sup>4,5,13</sup> (Grade D recommendation). Intravenous salbutamol may be considered for severe persistent bronchospasm<sup>4,5,25</sup>.

Additional treatments for resistant bronchospasm include intravenous magnesium<sup>58</sup>, which needs to be infused slowly due to its potential to cause hypotension (Grade D recommendation), inhalational anaesthetics, and ketamine<sup>4</sup> (Grade D recommendation).

In NAP6 bronchospasm was reported in 48.5% of cases. Specific bronchodilator therapy (excluding adrenaline) was used in 22.2% of all cases. This included inhaled salbutamol (10.2%), IV magnesium phosphate (7.4%), IV salbutamol (4.2%), aminophylline (less than 2%) and ketamine (1.5%).

Clinicians should institute therapy based on the clinical situation including the extent of hemodynamic instability.

### **5.7.5 Pregnancy**

Management of anaphylaxis during anaesthesia in pregnant patients follows the same treatment principles as for non-pregnant patients (Level V evidence). Prompt resuscitation is essential for a good outcome for mother and baby and early treatment with adrenaline is indicated.

The American Heart Association issued a Scientific Statement on Cardiac Arrest in Pregnancy in 2015 and a Cardiac Arrest in Pregnancy In-Hospital ACLS Algorithm in 2020. Specific considerations for pregnant patients from around 20 weeks gestation (when uterus is palpable at or above umbilicus) include positioning to minimise aortocaval compression. This is done by manual left uterine displacement (LUD). Historically left tilt has been used but this is less effective at relieving aortocaval compression than LUD and may make chest compressions less effective<sup>4,5,7</sup>. In the setting of cardiac arrest peri-mortem caesarean delivery (PMCD) should be undertaken if there is no return of spontaneous circulation within 5 minutes. The rationale for PMCD is to facilitate maternal resuscitation and improve maternal and foetal outcomes. Similar recommendations are contained in the UK resuscitation council guidelines and from the ISPAR group.

The 2020 International consensus on CPR and emergency cardiovascular care (ECC) science with treatment recommendations (CoSTR) publication from International Liaison Committee on Resuscitation (ILCOR)<sup>77</sup> suggests delivery of the foetus by perimortem caesarean section for women in cardiac arrest in the second half of pregnancy. They found insufficient evidence to make a recommendation about the use of left lateral tilt or manual left uterine displacement during CPR in the pregnant patient.

**The accompanying guideline recommends that for pregnant patients manual left uterine displacement (LUD) should be performed as part of the management of anaphylaxis, in the presence of hypotension or cardiac arrest.**

**Perimortem caesarean delivery (PMCD) should be undertaken in the setting of cardiac arrest if there is no return of spontaneous circulation (ROSC) in 5 minutes.**

## **5.8 Paediatric refractory management**

The paediatric refractory card follows the same structure as the adult card but acknowledges that the evidence base for this section is even more limited than for immediate management.

### **5.8.1 Request advice/more assistance**

Most locations where paediatric anaphylaxis occurs will not be tertiary paediatric centres. Advice or assistance should be sought from either local paediatric anaesthetists or intensivists, or from the nearest paediatric referral centre as these may provide valuable assistance in difficult situations (Grade D recommendation).

### **5.8.2 Resistant hypotension**



As with adult management, it is important to review the adequacy of the immediate resuscitation with respect to adrenaline and IV fluids and ensure this continues while adding in other therapy where indicated.

Dose regimens for noradrenaline and vasopressin are provided with their applicable dilutions. If alternate infusion regimens are used, then the protocol should be included in the anaphylaxis box.

The infusion rates for noradrenaline<sup>78</sup> and vasopressin<sup>79,80</sup> are referenced from available literature for paediatric therapy in sepsis and prolonged resuscitation.

### 5.8.3 Resistant bronchospasm

Bronchospasm is more likely to be a problem in the paediatric patient due to the increased frequency of irritable airways and infective processes within both upper and lower respiratory tracts. Consequently, the guideline includes more therapeutic options than for the adult (Grade D recommendation). The therapeutic options available will differ and local paediatric infusion protocols should be included in the anaphylaxis box.

Intravenous aminophylline and hydrocortisone have been added to the inhaled salbutamol and intravenous magnesium recommendations present on the Adult Refractory Management Card. The doses of these therapies are derived from the APLS guidelines and Drug Doses<sup>60,65</sup>.

## 5.9 Differential diagnosis card

The differential diagnosis card aims to aid consideration of alternative causes of clinical signs by classifying the common ones with a view to expedite management (e.g. needle decompression to treat tension pneumothorax).

Early recognition and prompt management of anaphylaxis is essential<sup>43,44</sup>. However, as anaphylaxis is a clinical diagnosis and symptoms mimic other perioperative events, diagnosis can be challenging. Anaphylaxis should be considered if skin signs co-exist with bronchospasm or hypotension. Hypotension or tachycardia alone, especially where this is unresponsive to vasopressors or unexpected for the depth of anaesthesia, should trigger anaphylaxis to be an early consideration. Bronchospasm or difficulty with ventilation may be the sole presenting feature in some cases and may be resistant to therapy. Absence of skin signs does not rule out the diagnosis of anaphylaxis, as skin signs may not appear until circulation is restored<sup>25</sup>.

Oesophageal intubation has been added in as a differential diagnosis for refractory bronchospasm in the accompanying guideline. NAP4: Major complications of airway management in the UK<sup>81</sup> identified 9 cases of undetected or prolonged oesophageal intubation resulting in 6 deaths and 1 case of persistent vegetative state. Two of the 9 cases were mistakenly treated as severe bronchospasm due to anaphylaxis. Unfortunately, recent coroners reports from the UK and Australia show that this continues to occur<sup>82,83</sup>. The Royal College of Anaesthetists and the Difficult Airway Society have launched a “No Trace = Wrong Place” educational campaign to try to address this issue<sup>14</sup>. During cardiac arrest and CPR the end-tidal CO<sub>2</sub> trace is attenuated but present. In oesophageal intubation the end-tidal CO<sub>2</sub> trace is a flat line.

Tryptase levels are important in differentiating anaphylaxis from other causes and should be collected when any suggestion of perioperative anaphylaxis is raised.

## **5.10 Post crisis management**

### **5.10.1 Steroids**

There is no evidence that administering steroids changes the outcome in anaphylaxis<sup>25,34,84</sup> (Level V evidence). However, steroids have been of benefit in the management of other allergic diseases. As such they are recommended as part of secondary management, that is for administration only after all acute management has been completed and patients are stable. They may be useful in cases of protracted reactions or biphasic response<sup>34,85</sup> (Grade D recommendation).

Paediatric dosage recommendations for dexamethasone are adopted from APLS guidelines<sup>65</sup> and for hydrocortisone from the AAGBI<sup>54</sup> and APLS<sup>65</sup>.

### **5.10.2 Antihistamines**

Antihistamines do not have a role in the acute phase of anaphylaxis crisis management in the operating theatre<sup>86,87</sup>. Accordingly, the use of antihistamines has been removed from the immediate and refractory anaphylaxis management cards. These drugs are useful for the symptomatic treatment of urticaria, angioedema and pruritus<sup>34</sup> (Level 1 evidence). They have little effect on hypotension and bronchospasm<sup>86,87</sup>. They may be used for mild Grade 1 reactions involving skin signs only (Grade B recommendation). Oral antihistamines such as cetirizine have a better side-effect profile compared to parenteral promethazine. Injectable promethazine should not be used in anaphylaxis as it can worsen hypotension<sup>88</sup> and can cause tissue necrosis (Grade D recommendation).

### **5.10.3 Proceed/Cancel/Postpone surgery**

Any decision whether to proceed with surgery will be determined by the urgency of the surgery, the grade of anaphylaxis and severity of underlying comorbidities (Grade D recommendation). Discussions with the surgeon, other anaesthesia colleagues or intensive care specialists may assist with clarifying the risks and benefits of proceeding or postponing. The risks of proceeding are lower in milder cases. In some situations, it may be necessary to proceed with surgery to facilitate resuscitation despite some persistent instability related to the anaphylaxis.

In the NAP6 cohort of patients with Grade 3 or 4 anaphylaxis the surgical procedure was postponed or abandoned in two thirds of cases.

### **5.10.4 Serum tryptase levels**

An acute elevation of serum tryptase level is supportive of the diagnosis of perioperative anaphylaxis<sup>89</sup>. Peak levels are usually reached within 15 to 120 minutes after onset of the reaction. Tryptase levels decline slowly within the following 3 to 6 hours. The biological half-life for tryptase is approximately two hours. The return to baseline level can be measured 24 hours after the reaction<sup>90</sup>.

NICE recommends immediate sampling and a second sample within 1 to 2 hours but no later than 4 hours after onset of symptoms. AAGBI guidelines recommend taking a tryptase sample as soon as the patient is stable, at 1 to 2 hours and after 24 hours. NAP6 found that earlier tryptase samples gave higher levels that rapidly fell within 30 minutes.

**The new recommendation in this guideline is that a tryptase sample be taken as soon as possible after the onset of symptoms and then repeated at 1 hour, 4 hours and after 24 hours.**

Serum tryptase elevation is not invariable with anaphylaxis. Discuss the need for referral with your local Anaphylaxis Lead or Testing Centre where clinical presentation suggests anaphylaxis with a normal serum tryptase level.

#### **5.10.5 Other investigations**

Other investigations should be ordered as clinically indicated. In the setting of an adrenaline infusion, hypokalaemia may develop requiring potassium administration. Arterial blood gas (ABG), electrolytes and coagulation screen should be considered if proceeding with surgery. In some locations the availability of point of care assessment of clotting using either thromboelastography (TEG) or rotational thromboelastometry (Rotem) may be useful adjuncts, particularly where there is evidence of bleeding or where surgery must proceed<sup>91</sup>.

#### **5.10.6 Observations**

Most patients who have had a moderate to life-threatening reaction will require admission to an ICU/HDU for monitoring and therapy. Where the reaction has been either a minor Grade 1 reaction, or a moderate Grade 2 reaction that has settled quickly with treatment a minimum six hours with close monitoring is recommended (Level V evidence, Grade D recommendation)<sup>34</sup>.

#### **5.10.7 Referral**

Prior to discharge from hospital patients who have had a suspected anaphylaxis should be provided with a letter that contains a description of the reaction and the agents administered prior to the reaction. A template letter facilitating this is available on the ANZAAG website at [www.anzaag.com](http://www.anzaag.com).

The anaesthetic allergy testing centres in Australia and New Zealand are listed on the ANZAAG website. It may assist the referral if the local testing centre's contact information is attached to the post crisis management card. A downloadable referral form accepted by all ANZAAG centres can also be found on the website.

## **6. Summary**

Anaphylaxis is a life-threatening emergency that requires prompt recognition and institution of life-saving therapy. The Perioperative Anaphylaxis Management Guidelines (including cards) have been developed with the aim of providing anaesthetists with ready access to the best evidence available to manage this potentially life-threatening situation. In view of the difficulty in conducting research into anaphylaxis management the evidence base for all recommendations is weak but based on expert opinion from multiple bodies internationally. ANZCA and ANZAAG will continue to update this resource in line with best international practice.

## Appendix 1

### Levels of evidence and grading of recommendations

#### Levels of evidence (based on NHMRC levels)

| Level of evidence  | Description   |
|--------------------|---|
| <b>Level 1</b>     | Systematic reviews, meta-analysis, randomised controlled trials                                     |
| <b>Level II</b>    | A randomised controlled trial.  |
| <b>Level III-1</b> | A pseudorandomised controlled trial.  |
| <b>Level III-2</b> | A comparative study with concurrent controls (Case-control study)                                   |
| <b>Level III-3</b> | A comparative study without concurrent controls   |
| <b>Level IV</b>    | Descriptive studies that include analysis of outcomes (single subject design, case series)          |
| <b>Level V</b>     | Case reports and expert opinion that include narrative literature, review, and consensus statements |

#### NHMRC Grades of recommendation

| Grade of recommendation | Description  |
|-------------------------|--|
| <b>A</b>                | Body of evidence can be trusted to guide practice  |
| <b>B</b>                | Body of evidence can be trusted to guide practice in most situations                                     |
| <b>C</b>                | Body of evidence provides some support for recommendation(s) but care should be taken in its application |
| <b>D</b>                | Body of evidence is weak and recommendation should be applied with caution                               |

### **Related ANZCA documents**

CP24(G) Policy for the development and review of professional documents (2019)

PS02(A) Position statement on credentialling and defining the scope of clinical practice in anaesthesia (2020)

PG03(A) Guideline for the management of major regional analgesia (2014)

PG06(A) Guideline on the anaesthesia record (2020)

PG07(A) Guideline on pre-anaesthesia consultation and patient preparation (2017)

PG09(G) Guideline on sedation and/or analgesia for diagnostic and interventional medical, dental or surgical procedures (2014)

PG18(A) Guideline on monitoring during anaesthesia (2017)

PS53(A) Position statement on the handover responsibilities of the anaesthetist (2013)

PS55(A) Position statement on minimum facilities for safe administration of anaesthesia in operating suites and other anaesthetising locations (2020)

PG60(POM) Guideline on the perioperative management of patients with suspected or proven hypersensitivity to chlorhexidine (2016)

ANZCA handbook for training (2021)

ANZCA handbook for accreditation (2021)

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## Document development group

Dr Karen Pedersen, FANZCA, (Chair), ANZAAG

Dr Peter Roessler, FANZCA, Director of Professional Affairs (Professional Documents)

Dr Robyn Tran - ANZCA representative

In addition, the following were consulted:

ANZAAG Executive Committee

ANZCA regional and national committees

Faculty of Pain Medicine Board, national and regional committees

ANZCA Safety and Quality Committee

Relevant ANZCA/ASA/NZSA Special Interest Groups

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Promulgated: 2016  
Date of current document: Nov 2022

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