

Australian and New Zealand College of Anaesthetists (ANZCA) and Australian and New Zealand Anaesthetic Allergy Group (ANZAAG)

Perioperative Anaphylaxis Management Guidelines

Background Paper

PURPOSE

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

This background paper reviews the evidence for 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 are used in this background paper and are described at the end of the document. The levels of evidence and grades of recommendations shown through this document are taken from published reviews and other guidelines for the management of anaphylaxis.

The significant difference between the ANZAAG-ANZCA guidelines and other published anaphylaxis management guidelines is the presentation in a format applicable to crisis management in the perioperative setting. (See cards presented as Appendices 1 – 6 of the ANZAAG-ANZCA guidelines.)

BACKGROUND

The recommendations in the guidelines were originally a consensus statement by the Australian and New Zealand Anesthetic Allergy Group (ANZAAG). As there were no randomised controlled trials of sufficient quality on the management of anaphylaxis, the recommendations in the original document were based upon a review of the literature. The intent was to optimise the management of perioperative anaphylaxis with the provision of a cognitive aid for use during crisis management.

The Australian and New Zealand College of Anaesthetists (ANZCA) then endorsed the document in February 2013.

Due to the need to review the presentation of the guidelines as well as the content it was agreed that the 2015/2016 review would be the result of collaboration between ANZAAG and ANZCA to produce a co-badged document.

ANZAAG has continued to assess the utility of these guidelines since their introduction including research conducted on the guidelines in two separate simulation environments in Australia¹. The second edition of the guidelines has been modified to address

observations made during simulation, feedback from anaesthetists after management of episodes of intraoperative anaphylaxis and from the many anaphylaxis workshops that have been conducted since the initial guidelines were introduced throughout Australasia.

There has been limited improvement in the evidence base for anaphylaxis management in the literature during the intervening three years. There are still no randomised controlled trials of sufficient quality on which to prepare evidence-based guidelines for the management of intraoperative anaphylaxis²⁻⁹. This document and anaphylaxis management cards are based upon a review of the literature focusing on guidelines for management of anaesthetic anaphylaxis¹⁰⁻¹³ as well as general guidelines for the management of anaphylaxis^{5-8, 14, 15}. The following recommendations and the revised guideline and cards are consensus statements by ANZAAG and ANZCA aimed at optimising the management of perioperative anaphylaxis by anaesthetists.

The key changes in the 2016 co-badged guidelines are:

- The development of two paediatric cards to cover the Immediate and Refractory Management of anaphylaxis in children. This allows for age specific recommendations and simplifies information on the adult cards.
- Introduction of cardiac arrest recommendations at the top of the Immediate Management cards.
- Increased emphasis on rapid, large volume fluid resuscitation based on the simulation observations that this step is frequently insufficient.
- Emphasis on the cessation/removal of possible triggers on the Immediate Management and Refractory Management cards. This is based on the observation that the previous cards did not promote this step.
- 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. In line with the United Kingdom's approach, a dual naming strategy is recommended to avoid confusion but maintain international consistency. For ease of reading, the dual nomenclature will be restricted to headings in most instances.

HOW TO USE THE ANAPHYLAXIS CARDS

This background paper is not designed for use during an emergency but for planning prior to an event and for protocol development. It is strongly suggested that institutions consider how the guidelines are enacted in the context of the resources available. In situ simulation is ideal for this purpose but not always feasible.

The cards have been designed for use during an anaphylaxis event with one team member assigned to reading the cards and ensuring all the items have been checked off. The use of a 'designated reader' has been shown to improve the effectiveness of teams in crises^{16, 17}.

A series of suggestions are given below to facilitate effective use of the cards during an emergency¹⁶. As with any clinical emergency it is recommended that all members of the anaesthetic team are familiar with the cards and their likely roles during an emergency.

1. TEAM STRUCTURE

Suggestions are made as to who might take each role during the crisis however as resources are often variable in nature, no absolute allocations have been made. The anaesthetic team for anaphylaxis management has at least three team members with specific roles:

- 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.
- 1.2. **Card reader**¹⁷ – this may be a nurse or second anaesthetist. In some cases a surgeon may fulfil this role. 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.
- 1.3. **Adrenaline (epinephrine)** – this is usually a second anaesthetist or experienced nurse. They will prepare the Adrenaline for intravenous (I.V.) and intramuscular (I.M.) boluses and delegate the making up of an adrenaline infusion.

Fluid management – an additional role if resources allow. Observation of teams managing anaphylaxis has identified that fluid resuscitation is commonly inadequate during these events.

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.

2. ANAPHYLAXIS BOX

Institutions are recommended to consider the preparation of an Anaphylaxis Box to assist with the introduction of the perioperative anaphylaxis management guidelines. 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 the patient form letters, patient information brochures and ANZAAG referral forms which can be found on the ANZAAG website at www.anzaag.com.

3. SEVERITY OF ANAPHYLAXIS¹⁸

For the purposes of these guidelines and management cards, the following grading scale for severity of anaphylaxis is used.

- 3.1. **Mild (Grade 1) anaphylaxis** is typified by *mucocutaneous signs only*, such as erythema, urticaria, and peripheral angioedema. Although the focus of these anaphylaxis management resources is on moderate to severe anaphylaxis, mild anaphylaxis (Grade 1) must also be recognised and monitored carefully in order to promptly detect the development of any multi-organ manifestations which would then reclassify the reaction to a higher grade and thus warrant treatment with adrenaline.
- 3.2. **Moderate (Grade 2) anaphylaxis** has *multi-organ manifestations* typically mucocutaneous signs combined with hypotension and/or bronchospasm.

Grade 2 anaphylaxis is more likely than Grade 3 anaphylaxis to have mucocutaneous signs facilitating the diagnosis of anaphylaxis over other causes of moderate hypotension and/or bronchospasm. Anaphylaxis during general anaesthesia most commonly presents with hypotension²⁰.

Moderate hypotension is a common sign during anaesthesia and is mostly due to causes other than anaphylaxis. The diagnosis of anaphylaxis should be considered where there is hypotension out of proportion to that which could be expected for the stage of the operation in a particular patient and/or where there has been a lack of response to usual vasopressors and restorative measures. While tachycardia is more common, bradycardia may be observed²¹.

The reported rate of bronchospasm during anaesthesia varies widely and has a reported incidence between 1.7 percent and 16 percent of anaesthetics²². Moderate bronchospasm and/or high airway pressure during anaesthesia are frequently caused by conditions other than anaphylaxis. The diagnosis of anaphylaxis should be suspected where bronchospasm and difficulty with ventilation are resistant to the commonly employed treatment manoeuvres.

Grade 2 anaphylaxis may also have additional respiratory, gastrointestinal or central nervous system symptoms and signs in patients who are conscious or minimally sedated. These include rhinorrhoea, cough, dyspnoea, circumoral tingling, difficulty swallowing, nausea, abdominal pain, irritability, confusion or a sense of impending doom.

3.3. Life threatening (Grade 3) anaphylaxis is a clinical presentation of *life threatening hypotension and/or high airway pressure*. Immediate treatment is required in this situation in order to avoid progression from inadequate tissue perfusion to cardiac arrest or significant hypoxia. The airway pressures are elevated to levels where oxygenation and ventilation are rapidly compromised. In up to 20 percent of patients only one of the signs of anaphylaxis is present²².

Unlike Grade 2 anaphylaxis, cutaneous signs are frequently absent initially due to the low cardiac output and may appear only when circulation is restored.

3.4. Cardiac arrest (Grade 4) anaphylaxis is characterised by *either absence of a palpable central pulse or a grossly inadequate blood pressure* as assessed via direct arterial measurement.

4. 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 down the left-hand side, whereas the right-hand side gives more detailed instructions. Actions are prioritized in order of performance.

4.1. Cardiac Arrest: Grade 4 Anaphylaxis

Anaphylaxis in the setting of anaesthesia may present as cardiac arrest, most commonly pulseless electrical activity (PEA). In this circumstance immediate good quality cardiopulmonary resuscitation should commence. At this time the Australian Resuscitation Council (ARC) and New Zealand Resuscitation

Council (NZRC) recommendations²³ for nonshockable rhythms are 1 mg of adrenaline immediately then repeated every 4 minutes. The 2015 recommendations from the American Heart Association are adrenaline 1 mg every 3 to 5 minutes²⁴.

Cases of recovery from anaesthesia related anaphylaxis suggest that higher doses of adrenaline and additional vasopressors may be required before return of adequate cardiac output and blood pressure. As a result, the recommendation in these guidelines is to use 1 mg of adrenaline every 1 to 2 minutes if required initially with rapid administration of adequate volume resuscitation and the early addition of alternative vasopressors when initial therapy is inadequate. The adrenaline dosing is consistent with the recommendations in the French guidelines (Level IV evidence, Grade D recommendation)¹⁰.

4.2. Maintenance of Anaesthesia

Anaesthesia should be maintained with minimal volatile agent until the situation is stabilised. Consider a depth of anaesthesia monitor (e.g. BIS).

4.3. Triggers

Ceasing the administration of triggers should be briefly reviewed at the time of diagnosis to ensure possible allergens such as colloids or drug infusions of possible triggers are ceased (Level V evidence, Grade D recommendation). Muscle relaxants are the most common cause of anaphylaxis during anaesthesia in Australia and New Zealand²⁵⁻²⁹. Antibiotics are also common triggers. Anaphylaxis to chlorhexidine is an emerging concern and further use of this agent should be avoided if it was administered prior to the development of symptoms²⁹⁻³². Chlorhexidine may be present in products including skin preparations and wipes, lubricant gels (e.g. urinary catheters) and some impregnated central venous lines. The anaesthetist needs to 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)⁴ to review and cease possible triggers and remove them from the environment, where practicable, to avoid further administration (Grade D recommendation).

4.4. Check/Secure Airway

In many situations the airway will have been secured as part of the anaesthesia plan. However, in some situations this is not the case, and the anaesthetist will be faced with an evolving clinical picture where airway and cardiorespiratory compromise might develop. It is not possible for these guidelines to provide management plans to cover the variety of clinical situations. It is however vital that prompt management with appropriate doses of adrenaline occurs, as in some situations early administration of adrenaline will avert the need to secure the airway. Where airway oedema is apparent the consideration of early endotracheal intubation is appropriate.

4.5. Position (Level IV evidence)^{8, 10, 15, 33, 34}

Patients should be returned to the supine position as soon as possible where continued resuscitative efforts are required. Where hypotension is a predominant sign leg elevation should be considered (Grade D recommendation).

4.6. Intravenous Access

Large bore intravenous access should be secured as soon as possible. If chlorhexidine has been a possible trigger of the reaction, the anaesthetist is advised to avoid the use of chlorhexidine skin preparation or the placement of a chlorhexidine impregnated central line.

4.7. Fluid Resuscitation (Level IV evidence)^{35, 36}

Along with adrenaline therapy, adequate fluid resuscitation is a critical step in management of hypotension. It has been shown that 35% to 70% of the blood volume may extravasate in 10 -15 minutes³⁵⁻³⁷. This requires aggressive management, and repeated fluid boluses of 20mls/kg may be required (Grade D recommendation). Colloid or crystalloid may be used. Colloid may be more effective during anaphylaxis to restore intravascular volume (Level V evidence)^{10, 38}. The exception to this would be where a synthetic colloid was running at the time of the reaction. In this case, the colloid is a potential culprit and administration should cease and colloid be removed to avoid inadvertent re-connection.

All staff managing anaphylaxis must be aware of the importance of minimising 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.

4.8. Adrenaline (epinephrine) (Level IV evidence)^{4, 5, 9, 39, 40}

Adrenaline is pivotal in the management of anaphylaxis because of its unique pharmacology (Grade C recommendation). In the doses recommended, adrenaline causes vasoconstriction, bronchodilation, increased cardiac output, reduced mucosal oedema and reduced mediator release. Therefore, adrenaline not only treats signs and symptoms but also reduces response amplification^{5, 9}.

International dosing regimens for adrenaline vary, partly because of adrenaline's narrow therapeutic window. For some patients the risks of overdose are higher e.g. extremes of age, patients with hypertension, ischaemic heart disease or hyperthyroidism. In others 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^{39, 41-44}.

The World Allergy Organisation has reviewed fatal cases of anaphylaxis and highlighted that administration of adrenaline was often delayed or inadequate^{4, 15, 45}. Diagnosis must therefore be rapid, and adrenaline administered early and in adequate doses to optimise outcome (Level V evidence, Grade D recommendation).

4.8.1. I.M. Adrenaline (epinephrine) ^{4, 5, 9}

World Allergy Organisation guidelines state that the benefits of I.M. adrenaline for the management of anaphylaxis far exceed the risks (Level 1 evidence). Mild anaphylaxis can result in poor outcomes when it is either under-treated or treated with excessive adrenaline doses³⁴. I.M. adrenaline should be considered in the initial management of perioperative anaphylaxis where I.V. access is not yet established or is lost, where haemodynamic monitoring is not in-situ at the start of the reaction, or while awaiting preparation of an adrenaline infusion (Grade B recommendation). Research has shown that I.M. adrenaline provides an effective infusion lasting up to 40 minutes^{46, 47}.

The dose recommendations for I.M. adrenaline are consistent with those recommended by the Association of Anaesthetists of Great Britain and Ireland¹¹. The dose interval of five minutes has been adopted from the European Academy of Allergy and Clinical Immunology, EAACI recommendations (Level V evidence⁴, Grade D recommendation).

4.8.2. I.V. Boluses of Adrenaline (epinephrine) (Level IV evidence⁴)

The mainstay of the management of moderate to severe intraoperative anaphylaxis during anaesthesia is carefully titrated I.V. adrenaline with close monitoring of cardiovascular responses. The guidelines recommend the initial use of I.V. bolus adrenaline in keeping with other international perioperative anaphylaxis management guidelines¹⁰⁻¹³. (Grade D recommendation)

The recommended initial dose of I.V. adrenaline in moderate Grade 2 anaphylaxis, either hypotension or bronchospasm is 20 mcg¹⁰. This is 0.2 ml of adrenaline 1:10,000. Prior to using these guidelines anaesthetists need to consider how they would dilute and administer this dose with accuracy. Some anaesthetists will be familiar with diluting adrenaline to 10 mcg/ml in a 100ml bag of saline. Others might use a 1 ml syringe of 100mcg/ml (1:10,000) solution to accurately administer this dose. An effective safe alternative in this situation is to administer 0.5 mg of I.M. adrenaline into the lateral thigh.

The initial dose of I.V. adrenaline in life threatening Grade 3 anaphylaxis is 100 to 200 mcg of adrenaline and references the French guidelines¹⁰. The dose range is to account for patients in whom adverse effects of I.V. adrenaline are more likely.

Due to the pharmacokinetics of adrenaline and the nature of anaphylaxis repeated boluses of adrenaline may be required. The time interval for repeat boluses is 1 to 2 minutes as required¹⁰.

These recommendations are only intended for use during anaesthesia with an anaesthetist in attendance. They reflect the special circumstances of operative anaphylaxis - higher frequency of sudden onset severe symptoms compared to non-operative anaphylaxis and continuous dedicated monitoring by an anaesthetist. For non-anaesthetic anaphylaxis the Australasian Society of Clinical Immunology and Allergy (ASCI) guidelines entitled *Anaphylaxis: Emergency Management for Health Professionals* should be applied¹⁴.

4.8.3. Adrenaline (epinephrine) Infusion⁴

Adrenaline infusions have been shown to be an effective treatment for anaphylaxis in a non-anaesthetic setting without bolus administration³⁶ (Level III-3 evidence). The use of an adrenaline infusion facilitates ease of titration of dose and effect as compared to a repeated bolus regimen. After three boluses via either the I.V. or I.M. route an adrenaline infusion should be prepared and commenced as early as possible in the clinically appropriate dosage^{7, 10, 36, 48} (Grade D recommendation). The immediate management card outlines a dilution and infusion rate for a 70 kg adult using a syringe driver to facilitate prompt preparation and institution of an adrenaline infusion. The adrenaline infusion can be commenced peripherally and should not be delayed because of the lack of central venous access. The dose ranges recommended here are derived from the French guidelines^{10, 49}.

4.9. Sugammadex

These guidelines do not recommend the use of sugammadex in the situation of anaphylaxis following the administration of rocuronium. There have been a few case reports claiming improved physiological variables temporally related to the administration of sugammadex in patients who have had anaphylaxis after being administered rocuronium. In all these cases conventional resuscitative therapies had also been administered. Despite this, in vitro and in vivo human models of anaphylaxis have not been able to demonstrate immunologically mediated attenuation of established anaphylaxis^{50, 51}. A case-control study from Perth⁵², in patients who were given sugammadex where anaphylaxis followed rocuronium administration, has shown that sugammadex only increased the blood pressure in 46 percent of the 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.

As theorized in the paper from Perth⁵² the therapeutic effect of sugammadex on resuscitation may be to increase muscular tone (and therefore reduced venous capacitance) in circumstances where there is severe distributive shock and inadequate resuscitation. There are potentially significant risks during resuscitation if neuromuscular blockade is reversed. Therefore, the guidelines recommend that all measures on the immediate management card are instituted to maximal levels followed by steps outlined to manage refractory anaphylaxis.

5. PAEDIATRIC IMMEDIATE MANAGEMENT

There is little specific evidence to guide management of perioperative anaphylaxis in the paediatric population available in the literature. Hence, the scientific rationale for the immediate management of anaphylaxis in the paediatric patient is essentially the same as for the adult. The upper limit of age for the paediatric guidelines is unclear. The current ARC/NZRC guidelines for paediatric advanced life support state older children, aged 9 to 14 years, can be treated using adult protocols⁵³. The recommendations for I.M. adrenaline from the AAGBI¹¹ and APLS⁵⁴ recommend adult dosing for children >12 years of age. Taking these precedents into consideration, these guidelines have defined a patient for paediatric management to be less than 12 years of age.

The dilution of adrenaline on the Paediatric Immediate Management card is the same whether preparing bolus I.V. therapy or an infusion. This 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 I.V. bolus doses of adrenaline are based on those recommended in the French and Scandinavian guidelines^{10, 13}. The I.M. dose of adrenaline is recommended by the AAGBI¹¹ and Advanced Paediatric Life Support, APLS⁵⁴. The starting dose for the adrenaline infusion regimen is adopted from the French guidelines¹⁰, with the upper limit within the range recommended in the APLS⁵⁴ formulary for refractory hypotension.

6. ADULT REFRACTORY MANAGEMENT

The immediate management of anaphylaxis necessitates titration of adrenaline, adequate fluid replacement and optimising oxygenation. In some situations these measures, including a maximal adrenaline infusion, may not be adequate. This is known to occur in patients on beta-blockers, ACEI and with spinal blockade. In this scenario, ***all maximal initial measures must be continued*** and specific targeted therapy added in accordance with symptoms and local availability of medications.

6.1. Monitoring

Standard monitoring as recommended by *PS18 Guidelines on Monitoring during Anaesthesia*⁵⁵ 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).

With the increasing availability of point of care ultrasound (transthoracic echo (TTE) or transoesophageal echo (TOE)) better targeting of therapy is possible by assessing ventricular function, filling and vasodilation⁵⁶. This information is likely to be most useful where hypotension is the predominant symptom, 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).

6.2. Resistant Hypotension

Prior to commencing alternative vasopressors the anaesthetist needs to review the adequacy of I.V. fluid resuscitation and ensure that an adrenaline infusion has been instituted. Consider the benefits of inserting a non-chlorhexidine coated CVC, but where resources are limited, the peripheral administration of vasopressors may be appropriate in the short-term. Where it is available cardiac bypass/ECMO⁵⁷ may be considered to re-establish adequate perfusion (Grade D recommendation).

6.3. Alternative Vasopressors (Level V evidence)

The evidence supporting the use of other vasopressors comes from animal models and some case reports of improved clinical variables in refractory anaphylaxis⁵⁸⁻⁶³. Levels of evidence for their use are weaker than for adrenaline and they should only be used following adequate administration of adrenaline and I.V. fluids (Grade D recommendation). Their actions are likely to be more important where cardiac contractility is reasonable, but an adrenaline infusion and fluid boluses are inadequate to maintain adequate perfusion pressures.

Noradrenaline and vasopressin dose recommendations are based on the French and Scandinavian guidelines^{10, 13, 49}. Metaraminol and phenylephrine are included as alternatives because in some environments there may be limited alternatives to adrenaline⁴⁹. Glucagon is included in the management of resistant hypotension because it may be of benefit for the patient who is on beta blockers⁶⁴ (Grade D recommendation). The dose recommendation comes from the French and Scandinavian guidelines^{10, 13}.

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.

6.4. Resistant Bronchospasm (Level V evidence)⁴

High airway pressure is less likely to be the predominant feature of perioperative anaphylaxis but can be problematic where it occurs. It is vital that alternative causes of high airway pressure such as airway device or circuit malfunction and tension pneumothorax are sought and eliminated as the cause.

Inhaled bronchodilators are likely to be the first treatment method chosen by anaesthetists in managing bronchospasm. 1200 mcg i.e. 12 puffs of 100 mcg of salbutamol can be administered in an adult using a metered dose inhaler into the anaesthesia circuit⁵⁴ (Grade D recommendation). Intravenous salbutamol may be considered when the predominant symptom is bronchospasm. Dosage recommendations for intravenous bolus and infusion of salbutamol are adopted from the French guidelines¹⁰.

Alternative treatments for resistant bronchospasm include intravenous magnesium⁷ which needs to be infused slowly due to its potential to cause hypotension (Grade D recommendation). Other options to aid bronchial relaxation include inhalational anaesthetics and ketamine (Grade D

recommendation). Clinicians should use the most appropriate therapy based on the clinical situation including the extent of hemodynamic instability.

6.5. Pregnancy (Level V evidence)⁶⁵

Particular issues with anaphylaxis⁶⁶ during anaesthesia in the pregnant patient include positioning to minimise aortocaval compression. This can be achieved using the following methods left lateral position, left tilt, or manual left uterine displacement. The later method is recommended in situations where the uterus is above the umbilicus by The Society for Obstetric Anesthesia and Perinatology⁶⁷ and in the latest recommendations from the 2015 American Heart Association⁶⁵(Grade D recommendation). In the setting of cardiac arrest, despite well conducted maternal resuscitation, peri-mortem caesarean delivery (PMCD) should be undertaken with the aim of incision at four minutes⁶⁵ with delivery of the foetus at five minutes (Grade D recommendation). The rationale for PMCD is to facilitate maternal resuscitation.

7. 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.

7.1. Request advice/more assistance (Grade D recommendation)

Most of the locations where paediatric anaphylaxis occurs will not be tertiary paediatric centres. As a result, requesting advice or assistance from either local paediatric anaesthetists/intensivists or from the nearest paediatric referral centre may provide valuable assistance in a difficult situation.

7.2. Resistant Hypotension

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

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

The infusion rates for noradrenaline⁶⁸ and vasopressin^{69, 79} are referenced from available literature for paediatric therapy in sepsis and prolonged resuscitation.

7.3. Resistant Bronchospasm

Bronchospasm is more likely to be a problem in the paediatric patient due to the increased frequency of bronchospasm and infective processes within the respiratory tract, both upper and lower. As a consequence the guidelines include 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*^{49, 54}.

8. DIFFERENTIAL DIAGNOSIS CARD

Early recognition and prompt management of anaphylaxis is essential^{5, 9}. The differential diagnosis card outlines the classification of severity of anaphylaxis in accordance with the physical signs present¹⁰. 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 stage of operation, should cause anaphylaxis to be considered. Bronchospasm or difficulty with ventilation may be the sole presenting feature in some cases. The absence of skin signs does not rule out the diagnosis of anaphylaxis, as skin signs may not appear until circulation is restored¹⁰. The list of differentials presented on this card is targeted to causes where alternative treatment may be required e.g. needle decompression with a tension pneumothorax. It is particularly important to collect mast cell tryptase levels in cases where the diagnosis is unclear to differentiate anaphylaxis from other causes of perioperative adverse reaction¹⁰.

9. POST CRISIS MANAGEMENT

9.1. Steroids

There is no evidence that administering steroids changes the outcome in anaphylaxis^{4, 10, 71} (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 i.e. only for administration after all acute management has been completed and the patient is stable. They may be useful in cases where there is a protracted reaction or biphasic response^{4, 72} (Grade D recommendation).

The paediatric dosage recommendations for dexamethasone are adopted from APLS guidelines⁵⁴ and for hydrocortisone from the AAGBI¹¹ and APLS⁵⁴.

9.2. Antihistamines

Antihistamines do not have a role in the acute phase of anaphylaxis crisis management in the operating theatre^{14, 73}. 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 pruritus⁴ (Level 1 evidence). They have little effect on hypotension and bronchospasm^{14, 73}. 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 hypotension⁷⁴ and can cause tissue necrosis (Grade D recommendation).

9.3. Proceed/Cancel/Postpone Surgery

The decision to proceed or abandon surgery will be determined by the urgency of the surgery, the grade of anaphylaxis and the patient's underlying comorbidities (Grade D recommendation). Discussion of the situation with the surgeon, other anaesthetic colleagues or intensive care specialists may assist

with clarifying the risks and benefits of proceeding or postponing. In some situations it is necessary to proceed with surgery to facilitate resuscitation despite some persistent instability related to the anaphylaxis.

9.4. Serum Tryptase Levels

An acute elevation of serum tryptase level is supportive of the diagnosis of perioperative anaphylaxis⁷⁵. The peak level is usually reached 15-120 minutes after onset of the reaction. The tryptase level declines slowly within the following 3-6 hours. The biological half-life for tryptase is approximately two hours. The return to baseline level can be measured 24 hours after the reaction⁷⁶. On this basis, the guidelines recommend timing for the sampling of tryptase to detect the peak level and also the recovery to baseline. It is recommended that each institution contact its local pathology provider prior to introducing these guidelines to ensure the type of collection tube and method of handling meets local requirements.

9.5. Other Investigations

Other investigations should be ordered as clinically indicated. In the setting of an adrenaline infusion, hypokalaemia may develop requiring replacement. 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 TEG or Rotem may be useful adjuncts particularly where there is evidence of bleeding or where surgery must proceed⁷⁷.

9.6. 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 close monitoring is recommended. (Level V evidence, Grade D recommendation).⁴

9.7. Referral

Prior to discharge from hospital patients who have had a suspected anaphylaxis require 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.

The anaesthetic allergy testing centres in Australia and New Zealand are listed on the ANZAAG website. It may assist 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.

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.

LEVELS OF EVIDENCE AND GRADING OF RECOMMENDATIONS

Levels of Evidence (based on NHMRC levels)

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

NHMRC Grades of Recommendation

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

RELATED ANZCA DOCUMENTS

A01 Policy for the Development and Review of Professional Documents

PS02 Statement on Credentialing and Defining the Scope of Clinical Practice in Anaesthesia

PS03 Guidelines for the Management of Major Regional Analgesia

PS06 Recommendations on the Recording of an Episode of Anaesthesia Care

PS07 Recommendations for the Pre-Anaesthesia Consultation

PS09 Guidelines on Sedation and/or Analgesia for Diagnostic and Interventional Medical, Dental or Surgical Procedures

PS18 Guidelines on Monitoring during Anaesthesia

PS53 Statement on the Handover Responsibilities of the Anaesthetist

PS55 Recommendations on Minimum Facilities for Safe Administration of Anaesthesia in Operating Suites and other Anaesthetising Locations

PS60 Guidelines on the Perioperative Management of Patients with Suspected or Proven Hypersensitivity to Chlorhexidine

ANZCA Handbook for Training and Accreditation

ANZCA Handbook for Training and Accreditation in the Affiliated Training Regions

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Australian and New Zealand College of Anaesthetists (ANZCA) and Australian and New Zealand Anaesthetic Allergy Group (ANZAAG)

Perioperative Anaphylaxis Management Guidelines

Background Paper

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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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ANZCA professional documents are reviewed from time to time, and it is the responsibility of each practitioner to ensure that he or she has obtained the current version which is available from the College website (www.anzca.edu.au). The professional documents have been prepared having regard to the information available at the time of their preparation, and practitioners should therefore take into account any information that may have been published or has become available subsequently.

This document has been prepared in collaboration with the Australian and New Zealand Anaesthetic Allergy Group (ANZAAG). Whilst ANZCA and ANZAAG endeavour to ensure that professional documents are as current as possible at the time of their preparation, it takes no responsibility for matters arising from changed circumstances or information or material which may have become available subsequently.

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