

Special Article

Australian and New Zealand Anaesthetic Allergy Group/ Australian and New Zealand College of Anaesthetists Perioperative Anaphylaxis Management Guidelines

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Summary

Anaphylaxis is an uncommon but important cause of serious morbidity and even mortality in the perioperative period. The Australian and New Zealand College of Anaesthetists (ANZCA) with the Australian and New Zealand Anaesthetic Allergy Group (ANZAAG) have developed clinical management guidelines that include six crisis management cards. The content of the guidelines and cards is based on published literature and other international guidelines for the management of anaesthesia-related and non-anaesthesia-related anaphylaxis. The evidence is summarised in the associated background paper (Perioperative Anaphylaxis Management Guidelines [2016] www.anzca.edu.au/resources/endorsed-guidelines and www.anzaag.com/Mgmt%20Resources.aspx). These guidelines are intended to apply to anaphylaxis occurring only during the perioperative period. They are not intended to apply to anaphylaxis outside the setting of dedicated monitoring and management by an anaesthetist. In this paper guidelines will be presented along with a brief background to their development.

Key Words: anaphylaxis, perioperative medicine, adrenaline, resuscitation

Introduction

Anaphylaxis is an uncommon but potentially life-threatening and occasionally lethal event in the perioperative environment. In the last two ‘Safety of Anaesthesia’^{1,2} reports for Australia and New Zealand, anaphylaxis was the cause of about a third of deaths classified as Category One (where it is “reasonably certain” that the cause of death is directly related to the anaesthesia or other factors under the control of the anaesthetist). The recommendation from the 2014 report¹ was that “anaphylaxis remains one of the less preventable causes of anaesthesia-related deaths, but early diagnosis and appropriate crisis management with escalating doses of adrenaline and aggressive fluid replacement are paramount”. The diagnosis and management of anaphylaxis

in the perioperative setting can be confounded by altered conscious state, cardiovascular and respiratory function due to underlying patient pathology and the effects of anaesthesia.

Four key steps to effectively manage perioperative anaphylaxis are: 1) timely diagnosis, 2) early administration of recommended doses of adrenaline (epinephrine), 3) aggressive administration of intravenous fluids, and 4) escalation of therapy where the clinical response to initial therapy is inadequate. Unfortunately, some episodes of anaphylaxis are resistant to conventional treatment, due to the severity of the anaphylaxis and/or the underlying patient comorbidities. In these situations refractory management strategies will be required as well as a systematic approach to ensure alternative diagnoses have not been overlooked.

This paper presents the Australian and New Zealand College of Anaesthetists (ANZCA) with the Australian and New Zealand Anaesthetic Allergy Group (ANZAAG) co-badged Perioperative Anaphylaxis Management Guidelines, which were launched at the ANZCA Annual Scientific Meeting in May 2016.

Guideline Development

In 2013, ANZAAG developed and published management guidelines online that were also endorsed by ANZCA. The

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Table 1

Levels of evidence (based on NHMRC levels)

Level of evidence	Description
Level 1	Systematic reviews, meta-analyses, 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, National Health and Medical Research Council.

purpose was to facilitate the timely diagnosis and effective management of perioperative anaphylaxis.

Following the introduction of the guidelines, their utility was assessed by ANZAAG through observations made during simulation, feedback from anaesthetists after management of episodes of intraoperative anaphylaxis, and from the many anaphylaxis emergency response workshops conducted throughout Australasia. Research was also conducted on the guidelines in two separate simulation environments in Australia³.

In 2015–16 the initial guidelines were revised and redesigned cognitive aids were developed in a further collaboration between ANZAAG and ANZCA.

There are no randomised controlled trials of sufficient quality on which to prepare evidence-based guidelines for the management of perioperative anaphylaxis^{4–10}. The content of the guidelines is consequently based upon a review of the literature focusing on management of anaesthesia-associated anaphylaxis^{11–14} as well as non-anaesthesia-related anaphylaxis^{6–10,15,16} (see Tables 1 and 2). A detailed review of the guidelines is available in the background paper, which can be accessed from the ANZCA or ANZAAG websites (www.anzca.edu.au/resources/endorsed-guidelines; www.anzaag.com/Mgmt%20Resources.aspx).

A noteworthy difference between these Perioperative Anaphylaxis Management Guidelines and others is their presentation as six management cards serving as cognitive aids for crisis management. These include a suggested team structure as summarised below.

Scope

These guidelines are intended to apply to anaphylaxis occurring during the perioperative period. They are not intended to apply to anaphylaxis outside the setting of dedicated monitoring and management by an anaesthetist. Alternative guidelines should be utilised outside this setting¹⁶.

Table 2

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.

NHMRC, National Health and Medical Research Council.

Use of the ANZAAG–ANZCA anaphylaxis management cards

The cards have been designed for use during an anaphylaxis event with one team member assigned to read the cards and ensure all the items have been checked off^{17,18}.

The team for anaphylaxis management should have at least three members with specific roles: Team Leader, Card Reader and Adrenaline (epinephrine) Preparation. It may be necessary to enlist the assistance of other trained staff members.

It is recommended that all members of the anaesthesia team are familiar with the cards and their likely roles during an emergency.

For the immediate and refractory management phases, separate adult and paediatric cards are provided. The differential diagnosis card and post crisis cards can be used for either adult or paediatric patients.

Anaphylaxis Box

It is recommended that an Anaphylaxis Box is prepared and available to complement the introduction of the anaphylaxis management guidelines.

The box should include laminated anaphylaxis management cards, local infusion protocols for adrenaline (epinephrine), noradrenaline (norepinephrine), vasopressin and salbutamol, as well as collection tubes for measuring serum 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. There are six cards for the diagnosis and treatment of anaphylaxis, including two for paediatric use.

Diagnosis of anaphylaxis

1. Early recognition and prompt management of anaphylaxis is essential^{6,7,16,19,20}.
2. Anaphylaxis should be considered if skin signs co-exist with bronchospasm or hypotension.
3. Hypotension or tachycardia alone, especially where this is unresponsive to vasopressors or is unanticipated should

raise suspicion. Bradycardia may also be a presenting sign of anaphylaxis^{21,22}.

4. Bronchospasm or difficulty with ventilation may be a feature of anaphylaxis or the sole presenting feature in some cases²³.
5. The absence of skin signs does not rule out the diagnosis, as skin signs may not appear until the circulation is restored²³.
6. Mild reactions, Grade 1, which include mucocutaneous signs only, such as erythema, urticaria, and peripheral angioedema do not warrant immediate treatment with adrenaline (epinephrine)²⁴, but rather close observation and escalation of therapy if severity worsens (Grade D recommendation).

Severity of anaphylaxis

1. A critical step once the provisional diagnosis of anaphylaxis has been made is the grading of the severity of anaphylaxis in order to administer the recommended initial dose of adrenaline (epinephrine).
2. The Perioperative Anaphylaxis Management Guidelines use a four level anaphylaxis grading scale outlined on card 5, Differential Diagnosis Card²⁵ (see Figure 5).

Anaphylaxis during Anaesthesia		 ANZAAG Anaphylaxis & Resuscitation Association, Emergency Group					
Immediate Management		 ANZCA ANZCA ANZCA SOCIETY OF ANAESTHETISTS					
Adults 12+							
IF Adult CARDIAC ARREST Pulseless Electrical Activity, PEA		• ALS GUIDELINES for non-shockable rhythms • 1 mg I.V. Adrenaline, Repeat 1 - 2 minutes pm • Immediately start CPR. Elevate legs. 2 L Crystalloid					
DR	Danger and Diagnosis Response to stimulus	• Unresponsive hypotension or bronchospasm • Remove triggers e.g. chlorhexidine, synthetic colloid • Stop procedure. Use minimal volatile if GA					
S	Send for help and organise team	• Call for Help and Anaphylaxis box • Assign a designated Leader and Scribe • Assign a Reader of the cards					
AB	Check/Secure Airway Breathing - 100% oxygen	• Consider early intubation: airway oedema • Confirm FIO₂ 100%					
C	Rapid fluid bolus Plan for large volume resuscitation	• If hypotensive: Elevate legs • Bolus 2L Crystalloid, Repeat as needed • Large bore I.V. access. Warm I.V. fluids if possible					
D	Adrenaline Bolus Repeat as needed Prepare Infusion	Initial I.V. Adrenaline Bolus (Adult) Dilution 1 mg in 10 mL = 100 mcg/mL • Give dose below every 1-2 minutes pm • Increase dose if unresponsive					
I.M. Adrenaline (Adult) No I.V. access or haemodynamic monitoring OR awaiting Adrenaline Infusion 1:1000 1mg/mL 500 mcg lateral thigh Every 5 minutes pm		<table><tr><td>Moderate (Grade 2)</td><td>Life Threatening (Grade 3)</td></tr><tr><td>20 mcg = 0.2 mL</td><td>100-200 mcg = 1-2 mL</td></tr></table>		Moderate (Grade 2)	Life Threatening (Grade 3)	20 mcg = 0.2 mL	100-200 mcg = 1-2 mL
Moderate (Grade 2)	Life Threatening (Grade 3)						
20 mcg = 0.2 mL	100-200 mcg = 1-2 mL						
Adrenaline INFUSION (Adult) >3 boluses of Adrenaline start infusion Can be administered peripherally		3 mg Adrenaline in 50 mL saline Commence at 3 mL/hr = 3 mcg/min Titrate to max. 40 mL/hr = 40 mcg/min (infusion rate 0.05 - 0.5 mcg/kg/min)					
If NOT RESPONDING see 'Refractory Management'							

Appendix 1 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzaag.edu.au and www.anzcaa.com © Copyright 2016 - Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 1: Adult Immediate Management Card. Reproduced with permission.

3. The Immediate Management Card also has the words 'Moderate' and 'Life Threatening' as descriptors of 'Grade 2 and 3' respectively in the 'Initial IV Adrenaline Bolus' section.
4. Since clinically grading anaphylaxis in the perioperative environment is complex, four members of ANZAAG published a new grading scale, the *Perioperative Anaphylaxis Grading System* (PAGS) with the aim of guiding initial anaphylaxis management and facilitating research²⁶. This system defines three grades of anaphylaxis: A. Moderate, B. Life Threatening, and C. Cardiac Arrest.
5. The descriptor words on the Immediate Management Card enable PAGS to be applied to the Perioperative Anaphylaxis Management Guidelines. With PAGS 'Life Threatening Anaphylaxis' can be distinguished from 'Moderate Anaphylaxis' in an adult by the presence of any one of these signs:
 - systolic blood pressure of <60 mmHg
 - life-threatening tachy- or bradyarrhythmia
 - oxygen saturation <90%
 - inspiratory pressures of >40 cmH₂O

Anaphylaxis during Anaesthesia

Immediate Management

IF Paediatric CARDIAC ARREST Pulseless Electrical Activity, PEA

- ALS GUIDELINES for non-shockable rhythms
- 0.1 mL/kg of 1:10,000 (10 mcg/kg) I.V. Adrenaline
- Repeat 1-4 minutes pm
- Immediately start CPR. 20 mL/kg Crystalloid

DR

Danger and Diagnosis
Response to stimulus

- Unresponsive hypotension or bronchospasm
- Remove triggers e.g. chlorhexidine, synthetic colloid
- Stop procedure. Use minimal volatile if GA

S

Send for help and
organise team

- Call for Help and Anaphylaxis box
- Assign a designated Leader and Scribe
- Assign a Reader of this card

AB

Check/Secure Airway
Breathing - 100% oxygen

- Intubate early: airway oedema
- CVS/Respiratory compromise
- Confirm FiO_2 100%

C

Rapid fluid bolus
Plan for large volume
resuscitation

- If hypotensive: Elevate legs
- Bolus 20 mL/kg Crystalloid, Repeat as needed
- Large bore I.V. Access. Warm I.V. fluids if possible

D

Adrenaline Bolus
Repeat as needed
Prepare Infusion

Initial I.V. Adrenaline Bolus (Paediatric)
Dilution 1 mg in 50 mL = 20 mcg/mL

- Give dose below every 1-2 minutes pm
- Increase dose if unresponsive

I.M. Adrenaline (Paediatric)

No I.V. access or haemodynamic monitoring
OR awaiting Adrenaline Infusion

1:1000 1mg/mL lateral thigh
< 6 years = 0.15 mL (150 mcg)
6-12 years = 0.3 mL (300 mcg)
Every 5 minutes pm

Moderate
(Grade 2)

0.1 mL/kg
2 mcg/kg

Life Threatening
(Grade 3)

0.2-0.5 mL/kg
4-10 mcg/kg

Paediatric Adrenaline Infusion
Commence infusion as soon as possible
Can be administered peripherally

1 mg Adrenaline in 50 mL (20 mcg/mL)
Commence at 0.3 mL/kg/hr (0.1 mcg/kg/min)
Titrate to max. 6 mL/kg/hr (2 mcg/kg/min)

IF NOT RESPONDING see 'Paediatric Refractory Management'

Appendix 2 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzaag.edu.au and www.anzcaa.com © Copyright 2016 - Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 2: Paediatric Immediate Management Card. Reproduced with permission.

- severe difficulty inflating the lungs
- airway angioedema

As a result, the recommended initial intravenous (IV) adrenaline (epinephrine) bolus dose is readily selected from the Immediate Management Card (Grade D recommendation).

Immediate management

Card 1 adult (see Figure 1) and card 2 paediatric, defined as a patient less than 12 years of age (see Figure 2).

1. Adrenaline (epinephrine) is pivotal in management and, in the recommended doses, causes vasoconstriction, bronchodilation, increased cardiac output, reduced mucosal oedema, and reduced mediator release (Level IV evidence, Grade C recommendation)^{7,19}.
2. The mainstay of the management of moderate to life-threatening anaphylaxis during anaesthesia is carefully titrated IV adrenaline with close monitoring of cardiovascular responses (Level IV evidence, Grade D recommendation)¹¹⁻¹⁴.
3. As adrenaline has a narrow therapeutic window clinicians need to be aware of the potential for toxicity including accidental overdose, particularly during crisis management^{24,27-29}.
4. Intramuscular (IM) adrenaline into the lateral thigh should be considered in the initial management of perioperative anaphylaxis where IV 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 (Level I evidence, Grade B recommendation)^{6,7,19,30-33}.
5. After three boluses of adrenaline via either the IV or IM route an adrenaline infusion should be prepared and commenced as early as possible in the clinically appropriate dosage (Level III-3 evidence, Grade D recommendation)^{9,11,34-36}.
6. Aggressive management of fluid resuscitation is a critical step in ensuring blood flow to vital organs. Repeated boluses of 20 ml/kg may be required (Level IV evidence, Grade D recommendation)^{34,37-39}.
7. Large bore IV access should be secured as soon as possible.
8. Patients should be returned to the supine position as soon as possible where continued resuscitative efforts are required (Level IV evidence, Grade D recommendation)^{10,11,15,30,40}.
9. Cessation of the administration of potential triggers should be briefly reviewed at the time of diagnosis to ensure possible allergens such as colloid infusion are discontinued (Level V evidence, Grade D recommendation)⁶. Muscle relaxants are the most common cause of anaphylaxis during anaesthesia in Australia and New Zealand⁴¹⁻⁴⁵. 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 symptoms (Grade D recommendation)⁴⁶⁻⁴⁸.

10. If airway oedema is suspected then early endotracheal intubation should be considered.
11. 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) recommendations⁴⁹ for non-shockable rhythms are 1 mg of adrenaline immediately then repeated every four minutes. 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, these guidelines recommend administering adrenaline every one to two minutes if required initially with rapid administration of adequate volume resuscitation and the early addition of alternative vasopressors when initial therapy is inadequate (Level IV evidence, Grade D recommendation)¹¹.

Anaphylaxis during Anaesthesia

Refractory Management

Adults 12+

Request more help

- Consider calling arrest code
- May require assistance with fluid resuscitation

Triggers removed?

- Chlorhexidine including impregnated CVCs
- Synthetic Colloid disconnect and remove
- Latex remove from OR

Monitoring

- Consider Arterial line
- Consider TOE/TTE

Resistant Hypotension

- Continue Adrenaline Infusion
- Additional I.V. fluid bolus 50 mL/kg
- Add second vasopressor
- Consider CVC
- Cardiac bypass/ECMO if available

Adult Recommendations

Noradrenaline Infusion 3 – 40 mcg/min (0.05 – 0.5 mcg/kg/min) and/or

Vasopressin bolus 1–2 units then 2 units per hour

If neither available use either

Metaraminol or **Phenylephrine Infusion**

Glucagon 1–2 mg I.V. every 5 min until response

Draw up and administer I.V. (Counteract β blockers)

Resistant Bronchospasm

- Continue Adrenaline Infusion
- Consider:
 - Airway device malfunction
 - Circuit malfunction
 - Tension pneumothorax (decompress)
- Add alternative bronchodilators

Adult Recommendations

Salbutamol

- Metered Dose Inhaler 12 puffs (1200 mcg)
- I.V. bolus 100–200mcg +/- infusion 5–25mcg/min

Magnesium 2 g (8 mmol) over 20 minutes

Consider Inhalational Anaesthetics and Ketamine

Pregnancy

- Manual Left Uterine Displacement
- Caesarean within 4 minutes if arrest or peri-arrest

Consider other diagnoses

See 'Differential Diagnosis Card' in Anaphylaxis Box

Once stable refer to 'Post Crisis Management'

Appendix 3 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzca.edu.au and www.anzaag.com © Copyright 2016 – Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 3. Adult Refractory Management Card. Reproduced with permission.

Anaphylaxis during Anaesthesia

Refractory Management

Paediatric 0-12

ANZAAG
Australian & New Zealand
Anaesthetic Allergy Group

ANZCA
Australian and New Zealand
College of Anaesthetists

Request advice/help	- Contact local/regional paediatric service - Consider calling arrest code
Triggers removed?	- Chlorhexidine including impregnated CVCs - Synthetic Colloid disconnect and remove - Latex remove from OR
Monitoring	- Consider Arterial line - Consider TOE/TTE
Resistant Hypotension - Continue Adrenaline Infusion - Additional I.V. fluid bolus 20 - 40 mL/kg - Add second vasopressor - Consider CVC	Paediatric Recommendations Noradrenaline infusion 0.1 - 2 mcg/kg/min 0.15 mg/kg in 50 mL run at 2 - 40 mL/hr and/or Vasopressin infusion 0.02 - 0.06 units/kg/hr 1 unit/kg in 50 mL 2 mL bolus then 1 - 3 mL/hr Glucagon 40 mcg/kg I.V. to max 1mg
Resistant Bronchospasm - Continue Adrenaline Infusion - Consider: - Airway device malfunction - Circuit malfunction - Tension pneumothorax (decompress) - Add alternative bronchodilators	Paediatric Recommendations Salbutamol - Metered Dose Inhaler (100 mcg/puff) 6 puffs < 6 years, 12 puffs > 6 years - I.V. Infusion as per local paediatric protocol Magnesium sulfate 50% (500 mg/mL) 50 mg/kg to max 2 g over 20 minutes (0.1 mL/kg 50% solution = 50 mg/kg) Aminophylline 10 mg/kg over 1 hour (max 500 mg) Hydrocortisone 2 - 4 mg/kg (max 200 mg)
Consider other diagnoses	See 'Differential Diagnosis Card' in Anaphylaxis Box

Once stable refer to 'Post Crisis Management'

Appendix 4 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzcaa.edu.au and www.anzcaa.com © Copyright 2016 - Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 4. Paediatric Refractory Management Card. Reproduced with permission.

Refractory management

Card 3 adult (see Figure 3) and card 4 paediatric (see Figure 4).

1. If physiological variables do not stabilise following immediate management then further treatment options should be added.
2. The diagnosis of anaphylaxis should be reviewed to ensure alternative diagnoses with different treatment paths are considered and the most appropriate therapy is administered. Card 5 (See Figure 5) is the Differential Diagnosis Card that lists alternative diagnoses, and relevant therapy.
3. Standard monitoring as recommended by ANZCA PS18 *Guidelines on Monitoring during Anaesthesia* should be utilised throughout resuscitative efforts⁵⁰.
4. An arterial line is highly recommended where possible to aid cardiovascular monitoring, blood sampling and continuous monitoring of adrenaline effects (Grade D recommendation).
5. Transthoracic echo (TTE) or transoesophageal echo (TOE), where available, may allow better targeting of therapy

Anaphylaxis during Anaesthesia

Differential Diagnosis Card

ANZAAG
Australian & New Zealand
Anaesthetic Allergy Group

ANZCA
Australian and New Zealand
College of Anaesthetists

Possible Causes & Actions	
Cardiac Arrest	- Hypoxia - Hypovolaemia - Hypo/hyperkalaemia/metabolic disorders - Hypo/hyperthermia - Tension pneumothorax (Decompress) - Tamponade - Toxins - Thrombosis: pulmonary or coronary
High Airway Pressure/Airway Compromise	Dyspnoea, wheeze, stridor, difficulty inflating lungs - Circuit malfunction → Check using Self Inflating Bag - Misplaced/kinked Airway device → Check with suction catheter/Consider changing device - Tension pneumothorax → Decompress - Exacerbation of Asthma → Treat as per Refractory Management - Foreign Body → Consider bronchoscopy - Acid aspiration → Consider bronchoscopy
Hypotension	- Hypovolaemia - Sepsis - Drug overdose - Vasodilation by drugs - Neuraxial blockade - Embolism: Thrombotic, Air or Amniotic - Vasovagal
Skin and Mucosa Hives, flushing, erythema, urticaria, swelling head and neck or peripheries	- Direct Histamine Release - Venous obstruction - Head down position - C1-esterase deficiency (Angioedema only) - Mastocytosis - Cold induced anaphylaxis
Absence of tachycardia or cutaneous signs does not exclude anaphylaxis Anaphylaxis is usually rapid in onset but is occasionally delayed	
Mild (Grade 1)	Generalised mucocutaneous signs: Erythema, Urticaria +/- Angioedema
Moderate (Grade 2)	Moderate - Multi-organ manifestation may include: - Hypotension, tachycardia - Evidence of bronchospasm, cough, difficult ventilation - Mucocutaneous signs
Life Threatening (Grade 3)	Life Threatening and requiring immediate and specific treatment: - Severe hypotension - Bradycardia or tachycardia, arrhythmias - Severe bronchospasm, and/or airway oedema - Cutaneous signs may be absent, or present only after correction of hypotension
Arrest (Grade 4)	Cardiopulmonary Arrest

Appendix 5 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzcaa.edu.au and www.anzcaa.com © Copyright 2016 - Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 5. Differential Diagnosis Card. Reproduced with permission.

by assessing ventricular function, filling and vasodilation (Grade D recommendation)⁵¹.

6. In the setting of resistant hypotension alternative vasopressors have been used⁵²⁻⁶¹. They should be used only after recommended doses of adrenaline and IV fluid volumes have been administered. The adrenaline should be continued even when these agents are added (Level V evidence, Grade D recommendation).
7. Where it is available cardiac bypass/extracorporeal membrane oxygenation (ECMO) may be considered to re-establish adequate perfusion⁶² (Grade D recommendation).
8. High airway pressure is less likely to be the predominant feature of anaphylaxis. Alternative treatments for resistant bronchospasm may be used where clinically indicated^{9,33}. Alternative causes of high airway pressure such as airway device or circuit malfunction and tension pneumothorax should be sought and eliminated as the cause (Level V evidence, Grade D recommendation).
9. Management of perioperative anaphylaxis in the pregnant patient includes manual left uterine displacement

Anaphylaxis during Anaesthesia

Post Crisis Management

Once Situation is Stabilised

Consider Steroids	Dexamethasone 0.1 - 0.4 mg/kg (Paediatric maximum 12 mg) Hydrocortisone 2 - 4 mg/kg (Paediatric maximum 200 mg)
Consider ORAL Antihistamines	Consider Oral non-sedating Antihistamines when patient able to take oral medications
I.V./I.M. Antihistamines	NOT RECOMMENDED

Consider: Proceed/Cancel/Postpone Surgery
Postoperative ICU/HDU monitoring

Investigations	• Trypsase at 1 hour, 4 hours and > 24 hours • Send to laboratory for processing ASAP • If > 1 hour to laboratory then refrigerate • Use serum (SST) or plain tube • Other investigations as clinically indicated • Coagulation screen if proceeding with surgery
Observations	• Monitor closely for 6 hours • Consider 24 hours ICU/HDU if moderate to severe • Anaphylaxis may persist for >24 hours despite aggressive treatment

Letter with Patient: Reaction Description + Agents Used
Refer Patient for Testing and Allergy Assessment
For referral form & to locate nearest testing centre go to www.anzaag.com

Appendix 6 ANZAAG-ANZCA Perioperative Anaphylaxis Management Guidelines version 2 May 2016. The scientific rationale and evidence base for the recommendations on this card is explained in more detail at www.anzaag.com and www.anzca.edu.au © Copyright 2016 – Australian and New Zealand College of Anaesthetists, Australian and New Zealand Anaesthetic Allergy Group. All rights reserved.

Figure 6. Post Crisis Management Card. Reproduced with permission.

to minimise aortocaval compression. Peri-mortem caesarean delivery may be required in order to facilitate resuscitation of the mother (Level V evidence, Grade D recommendation)^{5,63-64}.

Post crisis management

Card 6 (see Figure 6):

1. Steroids have been of benefit in the management of other allergic diseases and they are recommended as part of secondary management. They may be useful in cases where there is a protracted reaction (Level V evidence, Grade D recommendation)^{6,11,65,66}.
2. Oral antihistamines are useful for the symptomatic treatment of urticaria, angioedema and pruritus (Level 1 evidence, Grade B recommendation)^{15,67,68}.
3. The decision to proceed with or abandon surgery will be determined by the urgency of the surgery, the grade of anaphylaxis, the response to treatment and the patient's underlying comorbidities.
4. An acute elevation of serum tryptase level is supportive of the diagnosis of perioperative anaphylaxis.

5. Serum tryptase levels are recommended to be collected at 1, 4 and 24 hours^{69,70}.
6. Most patients who have had a moderate to life-threatening reaction will require admission to an intensive care unit/high dependency unit for around 24 hours. Where the reaction has been either minor or moderate and settled quickly with treatment, a minimum of six hours close monitoring is recommended (Level V evidence, Grade D recommendation)⁶.
7. 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.
8. Referral to an anaesthetic allergy testing centre is required to investigate the reaction. The anaesthetic allergy testing centres in Australia, New Zealand, Hong Kong and Malaysia are listed on the ANZAAG website—www.anzaag.com.

Conclusion

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 to assist anaesthetists in managing 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 is based on consensus expert opinion from multiple bodies internationally. ANZCA and ANZAAG will continue to update this resource in line with best international practice.

Conflict of interest

No conflict of interest with any of the authors.

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