Health Professional Information Paper

Anaphylaxis

September 2013

This Health Professional Information Paper complements ASCIA anaphylaxis e-training for health professionals. The main purpose of this document is to provide an evidence based, ‘quick reference guide’ to assist primary health care physicians including general practitioners, paediatricians and nurses, in the management of patients with severe allergy (anaphylaxis).

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1. What is allergy and anaphylaxis?
Over the last decade, allergy and risk of anaphylaxis has become an increasing health burden. Common causes of anaphylaxis include foods, insect stings and medications. Effective strategies for primary prevention of allergy are currently limited and secondary prevention is restricted to strategies to prevent exposure to known allergens.

1.1 Allergen sensitisation
Allergen sensitisation is a process in which a normally harmless protein (allergen) leads to the production of a specific type of allergy antibody (IgE). IgE antibodies are produced by plasma cells (mature B cells) in response to exposure to the allergen. IgE attaches to tissue mast cells in the skin, gastrointestinal tract, and/or respiratory system and peripheral blood basophils. In the absence of further contact with the allergen, binding of IgE to mast cell receptors produces no symptoms.

1.2 Mechanisms of an allergic reaction
Subsequent exposure to the allergen with cross-linking of IgE antibodies can cause rapid mast cell activation in some individuals. This results in the release of histamine and other inflammatory mediators. Multiple inflammatory mediators cause increased vascular permeability, smooth muscle spasm, mucosal oedema and inflammation. This results in clinical effects such as urticaria, angioedema, bronchospasm and anaphylaxis.

1.3 Definition of anaphylaxis
Anaphylaxis is the most severe form of allergic reaction requiring urgent medical treatment. There are a plethora of definitions for anaphylaxis within the literature. For the purposes of recognition and emergency treatment, ASCIA defines anaphylaxis as:

Any acute onset illness with typical skin features (urticarial rash or erythema/flushing, and/or angioedema), PLUS involvement of respiratory and/or cardiovascular and/or persistent severe gastrointestinal symptoms.

OR
Any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present.

1.4 Signs and symptoms of allergic reactions
The following signs and symptoms are as stated on the ASCIA Action Plans:

Mild or moderate reactions
- Swelling of lips, face, eyes
- Hives or welts
- Tingling mouth
- Abdominal pain, vomiting (these are signs of a severe allergic reaction to insects)

Anaphylaxis
Watch for any one of the following signs of anaphylaxis:
- Difficult/noisy breathing
- Swelling of tongue
- Swelling/tightness in throat
- Difficulty talking and/or hoarse voice
- Wheeze or persistent cough
- Persistent dizziness or collapse
- Pale and floppy (young children)

NOTE: Urticaria, erythema and angioedema may be transient, subtle and easily overlooked. In 1 out of 6 fatal food induced anaphylaxis cases, severe cardiovascular symptoms developed without skin or respiratory symptoms.
2. Triggers of anaphylaxis
Less common causes include latex, exercise (with or without food), cold temperature, immunisation (rare) and unidentified (idiopathic).

2.1 Food allergy
Whilst 90% of food allergic reactions are caused by egg, cow’s milk, peanut, tree nuts, wheat, fish, shellfish, sesame and soy, any food may cause an allergic reaction. It is important to note that not all patients with food allergy are at risk of anaphylaxis.

Food allergy affects 10% of infants <1 year, 4-8% of children <5 years and up to 2% of the adult population in Australia. It is important to note that food allergy can develop at any age not just in childhood. The most common food allergens are:
- Egg, peanut and cow’s milk in children.
- Tree nuts and seafood in adults.

Small amounts of food can cause anaphylaxis in some very sensitive individuals. Touching or smelling may trigger an allergic reaction but it is unlikely to cause anaphylaxis as the food allergen usually needs to be ingested.

2.2 Allergies to stings and bites
The major causes of sting anaphylaxis are honeybees, wasps, Jack Jumper (“hopper”) ants and related ant species. Anaphylaxis to tick bites is rare outside of endemic coastal areas in Eastern Australia. Allergies to stings and bites are rarely inherited and do not commonly coexist with other allergies.
Most reactions to bites and stings are local swellings that are not life-threatening.
Refer to Appendix C for further information on management of severe insect allergy.

2.3 Drug allergy
Adverse reactions to drugs are a significant problem, however allergic reactions (IgE mediated) are rare. Drug allergy is not more common in those with other allergies and rarely runs in families.

<table>
<thead>
<tr>
<th>NSAIDS</th>
<th>Majority of reactions are not IgE mediated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occurs in approximately 1% of general population; 10% in those with asthma</td>
</tr>
<tr>
<td></td>
<td>IgE mediated reactions to NSAID are characterised by urticaria, angioedema or anaphylaxis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Uncommon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occurs in approximately 1/10,000 courses of penicillin</td>
</tr>
<tr>
<td></td>
<td>Testing is only available for a limited range of antibiotics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>General anaesthetics</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occurs in approximately 1/5,000 – 1/10,000</td>
</tr>
<tr>
<td></td>
<td>Specialised testing required</td>
</tr>
</tbody>
</table>

| Vaccines                    | Anaphylaxis to vaccines is rare, occurring in approximately 1/250,000 doses |
|------------------------------| IgE mediated reactions are often due to vaccine components rather than the vaccine material itself |
|                              | Symptoms of IgE mediated allergic reactions to vaccines are similar to other IgE mediated allergic reactions and should be treated the same |
|                              | Symptoms usually appear within 5-30 minutes, but delayed reactions can occur |

| Others                       | Rare - local anaesthetics (vasovagal reactions are common) and herbal remedies, x-ray contrast agents, patent blue dye (used in sentinel node biopsies in breast cancer surgery, gelatin colloids |

Ref: Up-to-date, 2010
2.4 Risk factors for fatal anaphylaxis
Whilst mild, moderate and even severe allergic reactions are common, deaths from anaphylaxis are rare. However, several factors increase the risk of fatal anaphylaxis:

- Delayed or no administration of adrenaline
- Upright posture during anaphylaxis
- Asthma
- Food allergic individuals eating away from home
- Age:
  - Teenagers and young adults (food allergy)
  - Adults (insect and drug allergy)
- Initial misdiagnosis
- Systemic mastocytosis

Previous mild or moderate reactions do not rule out the possibility of subsequent severe or fatal reactions.

Living with the risk of anaphylaxis can impair quality of life (QOL), induce great anxiety and lead to significant social and family disruption. The QOL of a child with severe food allergy has been reported as being worse than a child with diabetes. Insect sting anaphylaxis may lead to fear of being outdoors.

3. Diagnosis of allergy and risk of anaphylaxis

3.1 Clinical history and allergy testing
Clinical history along with allergy testing is used in the identification of allergen triggers. Tests to identify IgE sensitisation to an allergen include skin prick testing and serum specific IgE (formerly known as RAST). Medically supervised allergen challenges may also be undertaken to confirm a diagnosis or determine if a patient has outgrown an allergy. Skin prick testing and allergen challenges should be conducted by specialists with allergy training in an environment with the ability to resuscitate if required.

Testing for allergen specific IgE food mixes is not recommended as it does not indicate which foods from the mix the patient is allergic to and may result in unnecessary avoidance of food/s. Measurements of total IgE are also not useful for diagnosis of food or drug allergy and are not recommended.

Allergen specific IgG testing has no role in the identification of allergic triggers.

3.2 Differential diagnosis of anaphylaxis
The following list has been compiled to assist with differential diagnosis of anaphylaxis versus symptoms due to other conditions that may be mistaken as anaphylaxis.

<table>
<thead>
<tr>
<th>Tissue swelling</th>
<th>Other causes of collapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic urticarial</td>
<td>Vasovagal episodes</td>
</tr>
<tr>
<td>Isolated angioedema</td>
<td>Systemic Capillary Leak Syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conditions mistaken for upper airway oedema</th>
<th>Acute respiratory distress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonic reactions mimicking the sensation of swollen tongue (e.g. anti-nausea medication)</td>
<td>Asthma</td>
</tr>
<tr>
<td>Acute oesophageal reflux (sudden onset of painful throat ‘swelling’, which can trigger laryngospasm)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flushing syndromes</th>
<th>Panic disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptide-secreting tumours (e.g. carcinoid syndrome, VIPomas)</td>
<td>Globus hystericus</td>
</tr>
<tr>
<td>Alcohol related</td>
<td>Laryngospasm (can be triggered by anxiety but more commonly triggered by oesophageal reflux)</td>
</tr>
<tr>
<td>Medullary carcinoma of thyroid</td>
<td>Vocal cord dysfunction</td>
</tr>
<tr>
<td>“Red Man Syndrome” (vancomycin related)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neurological syndromes</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epileptic seizures</td>
<td>Scombroid fish poisoning</td>
</tr>
<tr>
<td>Strokes</td>
<td>Systemic mastocytosis</td>
</tr>
<tr>
<td></td>
<td>Serum sickness</td>
</tr>
<tr>
<td></td>
<td>Phaeochromocytoma</td>
</tr>
</tbody>
</table>
4. Acute management of anaphylaxis

4.1. Essential steps in acute management of anaphylaxis

The cornerstones of acute management of anaphylaxis include:

- Placing the patient in the supine position to improve blood return to the heart, as fatality can occur within seconds if a patient stands or sits upright suddenly\(^\text{17}\). If the patient is having difficulty breathing, allow them to sit, but do not allow them to stand or walk\(^\text{17}\). Patients who are vomiting or pregnant should be placed in the left lateral position\(^\text{18}\).
- Intramuscular injection of adrenaline into the lateral mid thigh (1:1000 or 1mg/mL at a dose of 0.01mg.kg with a maximum dose of 0.5 mg/0.5 mL)\(^\text{19}\). Adrenaline is the first line treatment of anaphylaxis and acts to reduce airway mucosal oedema, induce bronchodilation, induce vasoconstriction and increase strength of cardiac contraction\(^\text{20}\).
- Intravenous fluid resuscitation with saline (20 mL/kg)\(^\text{19}\).
- Airway support and ventilation\(^\text{19}\).
- Supplementary oxygen\(^\text{19}\).

(Adapted from Loh et al, Medicine Today, September 2012.)

If you are unsure if a patient is experiencing severe asthma or anaphylaxis, give adrenaline first, followed by asthma reliever medication and follow the patient’s ASCIA Action Plan. For further information regarding the acute management of anaphylaxis, adrenaline dosage table and ancillary treatment, refer to Appendix A or download from Australian Prescriber website: [www.australianprescriber.com/magazine/34/4/artid/1210](http://www.australianprescriber.com/magazine/34/4/artid/1210)

It is important to note that antihistamines have no role in treating or preventing respiratory or cardiovascular symptoms of anaphylaxis. Oral non-sedating antihistamines may be given to treat itch and urticaria. Oral sedating antihistamines are not recommended as side effects (drowsiness) may be similar to signs of anaphylaxis. Injectable promethazine should not be used in anaphylaxis as it can worsen hypotension and cause muscle necrosis\(^\text{21}\).

4.2. Observation after anaphylaxis

Patients should be observed for at least 4 hours after last the dose of adrenaline. Patients will require overnight observation in hospital if they:

- Had a severe or protracted anaphylaxis (e.g. required repeated doses of adrenaline or IV fluid resuscitation),
- Have a history of asthma or severe/protracted anaphylaxis,
- Have other concomitant illness (e.g. asthma, history or arrhythmia),
- Live alone or are remote from medical care,
- Present for medical care late in the evening\(^\text{20}\).
5. Adrenaline autoinjectors

Adrenaline autoinjectors:
- Are automatic injector devices for emergency first aid treatment of anaphylaxis.
- Contain a SINGLE fixed dose of adrenaline.
- Are designed for self-injection (if patient is well and old enough) or other individuals (medical training is not required).
- Should be injected into the outer mid thigh muscle.
- Can be administered through a single layer of clothing.
- Should be stored in an easily accessible, unlocked location with an ASCIA Action Plan for Anaphylaxis.

5.1 Types of adrenaline autoinjectors

<table>
<thead>
<tr>
<th>Feature</th>
<th>EpiPen</th>
<th>Anapen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline dose</td>
<td>Single pre-measured</td>
<td>Single pre-measured</td>
</tr>
<tr>
<td>Colour of 0.15 mg dose device label</td>
<td>Green</td>
<td>Green</td>
</tr>
<tr>
<td>Colour of 0.3 mg dose device label</td>
<td>Yellow</td>
<td>Yellow</td>
</tr>
<tr>
<td>Colour of 0.5 mg dose device label</td>
<td>Not available</td>
<td>Magenta</td>
</tr>
<tr>
<td>Viewing window to check adrenaline for</td>
<td></td>
<td></td>
</tr>
<tr>
<td>discolouration or precipitate</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Availability</td>
<td>S3 (over-the-counter at full price)</td>
<td>S3 (over-the-counter at full price)</td>
</tr>
<tr>
<td></td>
<td>2 devices on PBS authority prescription</td>
<td>2 devices on PBS authority prescription</td>
</tr>
<tr>
<td>Activation of device</td>
<td>Press firmly against outer mid thigh</td>
<td>Depress red button when device on outer mid thigh</td>
</tr>
<tr>
<td>Safety</td>
<td>Blue safety release</td>
<td>Grey safety cap</td>
</tr>
<tr>
<td></td>
<td>Orange needle end automatically extends over needle after use</td>
<td>Black needle shield can be replaced over needle after use</td>
</tr>
<tr>
<td>Trainer devices</td>
<td>Available from distributor of device</td>
<td>Available from distributor of device</td>
</tr>
</tbody>
</table>

(Adapted from Vale et al, Australian Prescriber, 2012)

5.2 Adrenaline autoinjector prescription

Adrenaline autoinjectors are available to patients without prescription from pharmacies at full retail price or on PBS authority prescription in Australia. Purchase of the devices is not currently reimbursed by Pharmac in New Zealand. EpiPen and Anapen have different administration techniques and are NOT brand substitutable and therefore it is important to teach the patient in the use of the device that has been prescribed. Doctors must complete the ASCIA Action Plan for Anaphylaxis that matches the device prescribed for the patient.

PBS authority prescription supply of adrenaline autoinjectors in Australia:
- Maximum of 2 (EpiPen or Anapen) for children or adults (additional devices can be purchased over-the-counter if required).
- Initial supply:
  - When risk and clinical need has been assessed by, or in consultation with a clinical immunologist, allergist, paediatrician or respiratory physician.
  - After hospital or emergency department discharge for acute allergic anaphylaxis treated by adrenaline.
• Continuing supply for anticipated emergency treatment of acute allergic reactions with anaphylaxis, where the patient has previously been issued with an authority prescription.
• In some circumstances, a patient can ask for a general prescription and then claim partial reimbursement from their private health fund.

GPs can consult clinical immunology/allergy specialists regarding PBS prescription for adrenaline autoinjectors by telephone if required.

ASCIA adrenaline autoinjector dose recommendations:
• For children under 10kg (under 1 year) adrenaline autoinjectors are not usually recommended. However, in some circumstances a 150 microgram (0.15 mg) adrenaline autoinjector may be prescribed by a clinical immunology/allergy specialist
• 150 microgram (0.15 mg) adrenaline autoinjectors are for children 10-20kg (aged ~1-5 years)
• 300 microgram (0.3 mg) adrenaline autoinjectors are for adults and children over 20kg (aged over ~5 years)
• 500 microgram (0.5 mg) adrenaline autoinjectors may be prescribed for patients over 60 kg (refer to the ASCIA prescribing guidelines for adrenaline autoinjectors for more information)

Whilst the dose recommendations on the product information leaflet differs, ASCIA recommendations are based on consensus and standard practice by ASCIA members and published in the Australian Medicines Handbook and the National Prescribing Service information on adrenaline autoinjectors.

ASCIA adrenaline autoinjector prescribing guidelines can be accessed from the ASCIA website (http://www.allergy.org.au/health-professionals/anaphylaxis-resources/adrenaline-autoinjector-prescription).

6. Ongoing management of patients at risk of anaphylaxis
Primary care physicians play an important role in the ongoing management of patients at risk of anaphylaxis including:
• Providing updated referral for specialist review when required.
• Checking autoinjector expiry and renewing prescription if required.
• In children, checking that autoinjector dose is appropriate for weight/age.
• Reviewing patient/carer knowledge of adrenaline autoinjector administration using a trainer device.
• Reviewing documentation:
  – Update ASCIA Action Plan.
  – Provide ASCIA Travel Plan as required.
• Reviewing appropriate allergen avoidance measures (refer to Appendices 3 and 4).
• Reviewing and optimising asthma management as poorly managed asthma is a risk factor for fatal anaphylaxis.
• Reviewing and managing other allergic conditions (e.g. allergic rhinitis, atopic dermatitis).
• Providing referral to appropriate allied health practitioners if required (e.g. dietitian).
• Providing resource materials (refer to Appendix 4).
• Complete medical jewellery form (if required).

ASCIA Action Plans for Anaphylaxis are an emergency response plan. They provide patients/carers with guidance on when and how to use the adrenaline autoinjector. Every patient who is prescribed an adrenaline autoinjector should be provided with an ASCIA Action Plan for Anaphylaxis. As a medical document, it is important that the ASCIA Action Plan for Anaphylaxis is completed and signed by the patient’s medical practitioner. It is important to advise patients to keep their ASCIA Action Plan with their adrenaline autoinjector and provide a copy to their school, childcare or workplace.

Electronic versions of the ASCIA Action Plans with type in fields are available electronically from the ASCIA website www.allergy.org.au/health-professionals/anaphylaxis-resources. To find out how to order hard copies in colour email education@allergy.org.au

For more information about ASCIA Action Plans refer to Appendix B.
Appendix A: ASCIA Acute Management of Anaphylaxis Guidelines

These guidelines are intended for primary care physicians and nurses providing first responder emergency care.

Immediate action

1. Remove allergen (if still present).
2. Call for assistance.
3. Lay patient flat. Do not allow them to stand or walk. If breathing is difficult, allow them to sit.
4. Give INTRAMUSCULAR INJECTION (IMI) OF ADRENALINE without delay using an adrenaline autoinjector if available OR adrenaline ampoules and syringe.
   - 1:1000 IMI into outer mid thigh
   - 0.01mg per kg up to 0.5mg per dose
   - Repeat every 5 minutes as needed.
   - If multiple doses required or a severe reaction consider adrenaline infusion if skills and equipment available.

5. Call ambulance to transport patient if not already in a hospital setting.

If required at any time, commence cardiopulmonary resuscitation.

Supportive management (when skills and equipment available)

- Check pulse, blood pressure, ECG, pulse oximetry, conscious state.
- Give high flow oxygen if available and airway support if needed.
- Obtain IV access in adults and hypotensive children.
- If hypotensive, give IV normal saline 20mL/kg rapidly and consider additional wide bore IV access.

Additional measures - IV adrenaline infusion in clinical setting

If inadequate response or deterioration start IV adrenaline infusion, given by staff who are trained in its use or in liaison with an emergency/critical care specialist.

- Mix 1 mL of 1:1000 adrenaline in 1000 mL of normal saline.
- Start infusion at 5 mL/kg/hour (~0.1 µg/kg/minute).
- Titrate rate up or down according to response.
- Monitor continuously.

IV adrenaline infusions should be used with a dedicated line, infusion pump and anti-reflux valves wherever possible.

CAUTION: IV boluses of adrenaline are NOT recommended without specialised training as they may increase the risk of cardiac arrhythmia.
Additional measures to consider if IV adrenaline infusion is ineffective

| For Upper airway obstruction | • Nebulised adrenaline (5mL i.e. 5 ampoules of 1:1000).
|                            | • Consider intubation if skills and equipment are available
| For persistent hypotension/shock | • Give normal saline (maximum of 50mL/kg in first 30 minutes).
|                            | • Glucagon (1-2mg IMI or IV as starting dose) especially for patients on beta blockers or has heart failure.
|                            | • In adults, selective vasoconstrictors metaraminol (2-10mg) or vasopressin (10-40 units) only after advice from an emergency medicine/critical care specialist.
| For persistent wheeze | Bronchodilators:
|                            | • Salbutamol 8 - 12 puffs of 100µg using a spacer OR 5mg salbutamol by nebuliser.
|                            | • Note: Bronchodilators do not prevent or relieve upper airway obstruction, hypotension or shock
|                            | Corticosteroids:
|                            | • Oral prednisolone 1 mg/kg (maximum of 50 mg) or intravenous hydrocortisone 5 mg/kg (maximum of 200 mg).
|                            | • Note: Steroids must not be used as a first line medication in place of adrenaline.

Antihistamines and corticosteroids

Antihistamines:
• Antihistamines have no role in treating or preventing respiratory or cardiovascular symptoms of anaphylaxis
• Do not use oral sedating antihistamines as side effects (drowsiness or lethargy) may mimic some signs of anaphylaxis.
• **Injectable promethazine should not be used** in anaphylaxis as it can worsen hypotension and cause muscle necrosis.

Corticosteroids:
• The benefit of corticosteroids in anaphylaxis is unproven.
• It is common practice to prescribe a 2-day course of oral steroids (e.g. oral prednisolone 1 mg/kg, maximum 50 mg daily) to hopefully reduce the risk of symptom recurrence after a severe reaction or a reaction with marked or persistent wheeze

Observe patient for at least 4 hours after last dose of adrenaline

Relapse, protracted and/or biphasic reactions may occur.
• Patients will require overnight observation if they:
  – Had a severe or protracted anaphylaxis (e.g. required repeated doses of adrenaline or IV fluid resuscitation), OR
  – Have a history of asthma or severe/protracted anaphylaxis, OR
  – Have other concomitant illness (e.g. asthma, history or arrhythmia), OR
  – Live alone or are remote from medical care, OR
  – Present for medical care late in the evening.

The true incidence of biphasic reactions is estimated to occur following 3-20% of anaphylactic reactions.

Follow up treatment

Adrenaline autoinjector
• If there is a risk of re-exposure (e.g. stings, foods, unknown cause) then prescribe an autoinjector before discharge, pending specialist review
• Train the patient in autoinjector use and give them an ASCIA Action Plan for Anaphylaxis (see ASCIA website www.allergy.org.au)
Allergy specialist referral
• Refer ALL patients who present with anaphylaxis for specialist review
• The allergy specialist will:
  – Identify/confirm cause
  – Educate regarding avoidance/prevention strategies, management of comorbidities
  – Provide ASCIA Action Plan for Anaphylaxis - preparation for future reactions
  – Initiate immunotherapy where available (some insect venoms)

Documentation of episodes
Patients should be advised to document the circumstances of episodes of anaphylaxis to facilitate identification of avoidable causes (e.g. food, medication, herbal remedies, bites and stings, co-factors like exercise) in the 6-8 hours preceding the onset of symptoms. The ASCIA anaphylaxis event record can be used to collect this information (www.allergy.org.au/health-professionals/anaphylaxis-resources/anaphylaxis-event-record).

Preparation: Equipment required for acute management of anaphylaxis

The equipment on your emergency trolley should include:
• Adrenaline 1:1000 (consider adrenaline autoinjector availability in rural locations for initial administration by nursing staff)
• 1ml syringes; 21 gauge needles
• Oxygen
• Airway equipment, including nebuliser and suction
• Defibrillator
• Manual blood pressure cuff
• IV access equipment (including large bore cannulae)
• Pressure sleeve (aids rapid infusion of fluid under pressure)
• At least 3 litres of normal saline

A wall chart has been developed for use by health professionals and published in Australian Prescriber www.australianprescriber.com (August 2011).
Appendix B: ASCIA Advanced Acute Management of Anaphylaxis Guidelines

These guidelines are intended for emergency department staff, ambulance staff, rural and remote GPs and nurses providing emergency care.

Immediate action

6. Remove allergen (if still present).

7. Call for assistance.

8. Lay patient flat. Do not allow them to stand or walk. If breathing is difficult, allow them to sit.

9. Give INTRAMUSCULAR INJECTION (IMI) OF ADRENALINE without delay using an adrenaline autoinjector if available OR adrenaline ampoules and syringe.
   - 1:1000 IMI into outer mid thigh
   - 0.01mg per kg up to 0.5mg per dose
   - Repeat every 5 minutes as needed.
   - If multiple doses required or a severe reaction consider adrenaline infusion if skills and equipment available.

10. Give oxygen (if available).

11. Call ambulance to transport patient if not already in a hospital setting.

Administer intravenous saline (20mL/kg) if hypotensive.

If required at any time, initiate cardiopulmonary resuscitation.

Supportive management (when skills and equipment available)

- Monitor pulse, blood pressure, respiratory rate, pulse oximetry, conscious state.
- Give high flow oxygen (6-8 L/min) and airway support if needed.
- Supplemental oxygen should be given to all patients with respiratory distress, reduced conscious level and those requiring repeated doses of adrenaline.
- Supplemental oxygen should be considered in patients who have asthma, other chronic respiratory disease, or cardiovascular disease.
- Obtain intravenous access in adults and in hypotensive children.
- If hypotensive:
  - Give intravenous normal saline (20 mL/kg rapidly under pressure), and repeat bolus if hypotension persists.
  - Consider additional wide bore (14 or 16 gauge for adults) intravenous access.

DURING SEVERE ANAPHYLAXIS WITH HYPOTENSION, MARKED FLUID EXTRAVASATION INTO THE TISSUES CAN OCCUR: DO NOT FORGET FLUID RESUSCITATION.
Assess circulation to reduce risk of overtreatment

- Monitor for signs of overtreatment (especially if respiratory distress or hypotension were absent initially)—including pulmonary oedema, hypertension.
- In this setting (anaphylaxis) it is recommended that if possible a simple palpable systolic blood pressure (SBP) should be measured:
  - Attach a manual BP cuff of an appropriate size and find the brachial or radial pulse.
  - Determine the pressure at which this pulse disappears/reappears (the "palpable" systolic BP).
  - This is a reliable measure of initial severity and response to treatment
  - Measurement of palpable SBP may be more difficult in children.

If a patient is nauseous, shaky, vomiting, or tachycardic but has a normal or elevated SBP, this may be adrenaline toxicity rather than worsening anaphylaxis.

Additional measures - IV adrenaline infusion

IV adrenaline infusions should only be given by, or in liaison with, an emergency medicine/critical care specialist.

If your centre has a protocol for IV adrenaline infusion for critical care, this should be utilised and titrated to response with close cardio-respiratory monitoring.

If there is not an established protocol for your centre, two protocols for IV adrenaline infusion are provided, one for pre-hospital settings and a second for emergency departments/tertiary hospital settings only.

It is important to note that the two infusion protocols have different concentrations and different rates of infusion.

It is vital that IV adrenaline infusions should be used with the following equipment wherever possible:
  - Dedicated line,
  - Infusion pump,
  - Anti-reflux valves in intravenous line.

Additional measures - IV adrenaline infusion for pre-hospital settings

If there is inadequate response to IMI adrenaline or deterioration, start an intravenous adrenaline infusion. IV adrenaline infusions should only be given by, or in liaison with, an emergency medicine/critical care specialist.

The protocol for 1000 mL normal saline is as follows:

- Mix 1 mL of 1:1000 adrenaline in 1000 mL of normal saline.
- Start infusion at ~5 mL/kg/hour (~0.1 microgram/kg/minute) using a pump.
  - If you do not have an infusion pump, a standard giving set administers ~20 drops per ml; Therefore, start at ~2 drops per second for an adult.
- Titrate rate up or down according to response and side effects.
- Monitor continuously – ECG and pulse oximetry and frequent non-invasive blood pressure measurements as a minimum to maximise benefit and minimise risk of overtreatment and adrenaline toxicity.

Caution - Intravenous boluses of adrenaline are NOT recommended due to risk of cardiac ischaemia or arrhythmia UNLESS the patient is in cardiac arrest.
Additional measures - IV adrenaline infusion for emergency departments and tertiary hospital settings only

This infusion will facilitate a more rapid delivery through a peripheral line and should only be used in emergency departments and tertiary hospital settings.

The protocol for 100 mL normal saline is as follows:

- Mix 1 mL of 1:1000 adrenaline in 100 mL normal saline.
  - Initial rate adjusted accordingly to 0.5 mL/kg/hour.
  - Should only be given by infusion pump.

- Monitor continuously – ECG and pulse oximetry and frequent non-invasive blood pressure measurements as a minimum to maximise benefit and minimise risk of overtreatment and adrenaline toxicity.

Additional measures to consider if IV adrenaline infusion is ineffective

| For Upper airway obstruction | • Nebulised adrenaline (5mL i.e. 5 ampoules of 1:1000).
|                            | • Consider need for advanced airway management if skills and equipment are available (see additional information below). |
| For persistent hypotension/shock | • Give normal saline (maximum of 50mL/kg in first 30 minutes).
|                               | • In patients with cardiogenic shock (especially if taking beta blockers) consider an intravenous glucagon bolus of:
|                               |   • 1-2mg in adults
|                               |   • 20-30 microgram/kg up to 1mg in children
|                               |   This may be repeated or followed by an infusion of 1-2mg/hour in adults.
|                               | • In adults, selective vasoconstrictors metaraminol (2-10mg) or vasopressin (10-40 units) only after advice from an emergency medicine/critical care specialist. Beware of side effects including arrhythmias, severe hypotension and pulmonary oedema.
|                               | • In children, metaraminol 10 micrograms/kg/dose can be used. Noradrenaline infusion may be used in the critical care setting only with invasive blood pressure monitoring. |
| For persistent wheeze | Bronchodilators:
|                      | • Salbutamol 8-12 puffs of 100microgram using a spacer OR 5mg salbutamol by nebuliser.
|                      | • Note: Bronchodilators do not prevent or relieve upper airway obstruction, hypotension or shock.
| | Corticosteroids:
| | • Oral prednisolone 1 mg/kg (maximum of 50 mg) or intravenous hydrocortisone 5mg/kg (maximum of 200 mg).
| | • Note: Steroids must not be used as a first line medication in place of adrenaline. |

Advanced airway management

- Oxygenation is more important than intubation per se
- Always call for help from the most experienced person available
- If airway support is required, first use the skills you are most familiar with (e.g. jaw thrust, Guedel or nasopharyngeal airway, bag-valve-mask with high flow oxygen attached). This will save most patients, even those with apparent airway swelling (these patients have often stopped breathing due to circulatory collapse rather than airway obstruction and can be adequately ventilated with basic life support procedures)
- DO NOT make prolonged attempts at intubation - remember the patient is not getting any oxygen while you are intubating.
If unable to maintain an airway and the patient’s oxygen saturations are falling further approaches to the airway (e.g. cricothyrotomy) should be considered in accordance with established difficult airway management protocols. Specific training is required to perform these procedures.

**Special situation: Overwhelming anaphylaxis (cardiac arrest)**

**Key points:**
- Massive vasodilatation and fluid extravasation.
- Unlikely that IMI adrenaline will be absorbed in this situation due to poor peripheral circulation.
- Even if absorbed, IMI adrenaline on its own may be insufficient to overcome vasodilatation and extravasation.
- Need both IV adrenaline bolus (cardiac arrest protocol, 1 mg every 2-3 minutes) AND aggressive fluid resuscitation in addition to CPR (Normal Saline 20mL/kg stat, through a large bore IV under pressure, repeat if no response).
- Do not give up too soon - this is a situation when prolonged CPR should be considered, because the patient arrested rapidly with previously normal tissue oxygenation, and has a potentially reversible cause.

**Antihistamines and corticosteroids**

**Antihistamines:**
- Antihistamines have no role in treating or preventing respiratory or cardiovascular symptoms of anaphylaxis
- Do not use oral sedating antihistamines as side effects (drowsiness or lethargy) may mimic some signs of anaphylaxis.
- **Injectable promethazine should not be used** in anaphylaxis as it can worsen hypotension and cause muscle necrosis.

**Corticosteroids:**
- The benefit of corticosteroids in anaphylaxis is unproven.
- It is common practice to prescribe a 2-day course of oral steroids (e.g. oral prednisolone 1 mg/kg, maximum 50 mg daily) to hopefully reduce the risk of symptom recurrence after a severe reaction or a reaction with marked or persistent wheeze.

**Observe patient for at least 4 hours after last dose of adrenaline**

Relapse, protracted and/or biphasic reactions may occur.
- Patients will require overnight observation if they:
  - Had a severe or protracted anaphylaxis (e.g. required repeated doses of adrenaline or IV fluid resuscitation), OR
  - Have a history of asthma or severe/protracted anaphylaxis, OR
  - Have other concomitant illness (e.g. asthma, history or arrhythmia), OR
  - Live alone or are remote from medical care, OR
  - Present for medical care late in the evening.

The true incidence of biphasic reactions is estimated to occur following 3-20% of anaphylactic reactions.

**Follow up treatment**

**Adrenaline autoinjector**
- If there is a risk of re-exposure (e.g. stings, foods, unknown cause) then prescribe an autoinjector before discharge, pending specialist review
- Train the patient in autoinjector use and give them an ASCIA Action Plan for Anaphylaxis (see ASCIA website www.allergy.org.au)
Allergy specialist referral
• Refer ALL patients who present with anaphylaxis for specialist review
• The allergy specialist will:
  - Identify/confirm cause
  - Educate regarding avoidance/prevention strategies, management of comorbidities
  - Provide ASCIA Action Plan for Anaphylaxis - preparation for future reactions
  - Initiate immunotherapy where available (some insect venoms)

Documentation of episodes
Patients should be advised to document the circumstances of episodes of anaphylaxis to facilitate identification of avoidable causes (e.g. food, medication, herbal remedies, bites and stings, co-factors like exercise) in the 6-8 hours preceding the onset of symptoms. The ASCIA anaphylaxis event record can be used to collect this information (www.allergy.org.au/health-professionals/anaphylaxis-resources/anaphylaxis-event-record).

Preparation: Equipment required for acute management of anaphylaxis

The equipment on your emergency trolley should include:
• Adrenaline 1:1000 (consider adrenaline autoinjector availability in rural locations for initial administration by nursing staff)
• 1ml syringes; 21 gauge needles
• Oxygen
• Airway equipment, including nebuliser and suction
• Defibrillator
• Manual blood pressure cuff
• IV access equipment (including large bore cannulae)
• Pressure sleeve (aids rapid infusion of fluid under pressure)
• At least 3 litres of normal saline

A wall chart has been developed for use by health professionals and published in Australian Prescriber www.australianprescriber.com (August 2011).
Appendix C: Australian Prescriber Anaphylaxis Wall Chart

Anaphylaxis
Emergency management for health professionals

Clinical features
- Any acute onset of hypotension or bronchoconstriction or other airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present
- Or any acute onset of illness with typical skin features (urticaria, rash or erythema oedematous, and angioedema)
- Plus involvement of respiratory and/or cardiovascular and/or persistent severe gastrointestinal symptoms

1 Immediate action
- Remove victim (if still present)
- Call for assistance
- Lay patient flat. Do not allow them to stand or walk. If breathing is difficult allow them to sit.

2 Give INTRAMUSCULAR ADRENALINE into mid-lateral thigh without delay

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Adrenaline volume 1:1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>5-10</td>
<td>0.05-0.1 mL</td>
</tr>
<tr>
<td>1-2</td>
<td>16-40</td>
<td>0.1 mL</td>
</tr>
<tr>
<td>2-3</td>
<td>15</td>
<td>0.15 mL</td>
</tr>
<tr>
<td>4-5</td>
<td>20</td>
<td>0.2 mL</td>
</tr>
<tr>
<td>6-7</td>
<td>30</td>
<td>0.3 mL</td>
</tr>
<tr>
<td>8-10</td>
<td>40</td>
<td>0.4 mL</td>
</tr>
<tr>
<td>&gt;10-12</td>
<td>50</td>
<td>0.5 mL</td>
</tr>
<tr>
<td>&gt;12 and adult</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Autoinjectors
An adrenaline autoinjector (EpiPen or Anapen) may be used instead of an adrenaline ampoule and syringe. For children 18-20 kg (aged 1-5 years) EpiPen Junior or Anapen Junior should be used. Instructions are on device label.

Repeat doses every 5 minutes as needed
If multiple doses required or a severe reaction, consider adrenaline infusion if skills and equipment available (see section 5)

3 Call ambulance to transport patient if required

4 Supportive management
- When skills and equipment available:
  - Monitor pulse, blood pressure, respiratory rate, pulse oximetry
  - Give high flow oxygen and airway support if needed
  - Obtain intravenous access in adults and in hypotensive children
  - If hypotensive, give intravenous normal saline (20 mL/kg/h rapidly) and consider additional large bore intravenous access
For Additional measures see below

5 Additional measures

Adrenaline infusion
If inadequate response or deterioration, start an intravenous adrenaline infusion as follows:
- Give only in liaison with an emergency medicine/critical care specialist. Phone...
- Mix 1 mL of 1:1000 adrenaline in 1000 mL of normal saline
- Start infusion at 0.1 µg/kg/hour (0.1 micromgram/kg/minute)
- Titrated rate according to response
- Monitor continuously

CAUTION: Intravenous boluses of adrenaline are not recommended due to the risk of cardiac arrhythmia

If adrenaline infusion is ineffective or unavailable, consider:
-... and... and...
- If upper airway obstruction:
  - Neutralised adrenaline (5 mL i.e. 5 ampoules of 1:1000)
- Consider intubation if skills and equipment are available

For persistent hypotension/hypovolemia:
- Give normal saline maximum 50 mL/kg is the first 30 min
- In patients with cardiogenic shock (especially leaking aortic or mitral) consider a continuous infusion of dopamine (1-3 µg/kg/min) in adults (30-50 microgram/kg per minute)
- In adults, selective vasoconstrictors metaraminol (0.5-2 µg/kg/min) or vasoconstrictors (10-20 units) only after advice from an emergency medicine/critical care specialist

For persistent wheeze:
- Bronchodilators: Salbutamol 8-12 puffs of 100 microgram using a spacer or 5 mg salbutamol by nebuliser
- Ums prescripción 1 mg/kg (maximum 50 mg) or intravenous hydrocortisone 1 mg/kg (maximum 200 mg)

6 Observation
- Prolonged and biphasic reactions may occur
- Observe patient for at least 4 hours after last dose of adrenaline
- Observe longer (overnight) if patient:
  - Has a severe reaction (hypotension or hypoxia)
  - Required repeated doses of adrenaline or
d  - Has a history of asthma or previous anaphylaxis or
e  - Has other comorbid illness or
  - Lives alone or a remote from medical care

7 Follow-up treatment

Antihistamines
- Antihistamines have no role in treating respiratory or cardiovascular symptoms of anaphylaxis. Oral non-sedating antihistamines may be given to treat itch and urticaria.
- Nebulised promethazine should not be used in anaphylaxis as it can worsen hypotension and cause muscle necrosis.

Corticosteroids
- The role of corticosteroids is unknown. It is reasonable to prescribe a 2-day course of oral steroid (e.g. prednisolone 1 mg/kg per day) to reduce the risk of symptom recurrence after severe reaction or a reaction with marked or persistent wheezing

Adrenaline autoinjector
- Prescribe an autoinjector, pending specialist review. Train the patient into autoinjector use and give them an ASCIA Action Plan for Anaphylaxis (see Australian Society of Clinical Immunology and Allergy website www.allergy.org.au)
- Allergy specialist referred
- Refer patients with anaphylaxis for specialist review

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Appendix D: ASCIA Action Plans and Travel Plan

ASCIA Action Plan for Anaphylaxis (personal)
- Provided to patients at risk of anaphylaxis to any allergen/s.
- These are for individual patients and include personal details and a photo.

ASCIA Action Plans for Anaphylaxis (insect allergy) have been phased out and information relevant to insect allergy is now included in this ASCIA Action Plan.

ASCIA Action Plan for Allergic Reactions
Provided to patients with known mild to moderate allergies (including insect allergy) who have not been prescribed an adrenaline autoinjector because they are considered at relatively low risk of anaphylaxis.

ASCIA Action Plan for Anaphylaxis (general)
- These are posters for general use.
- These Action Plans do not include personal information.
- A copy should be stored with adrenaline autoinjectors in first aid kits.

ASCIA Travel Plan for Anaphylaxis
- Provides documentation for patient to carry adrenaline autoinjector in aircraft cabin.
- Can be printed from the ASCIA website.
- It is important to check the expiry date of adrenaline autoinjectors and review instructions for use before travelling.

ASCIA Action Plans and Travel Plan are available from the ASCIA website: www.allergy.org.au/health-professionals/anaphylaxis-resources
Appendix E: Management of severe insect allergy

Treatment of minor reactions including local swelling
• Flicking the bee sting out as soon as possible may reduce venom dose (wasps and bull ants rarely leave their sting in the skin and jack jumper ant stings retract after stinging).
• In the case of tick anaphylaxis, the tick should not be removed outside of a medical facility (see below).
• Cold packs, paracetamol and soothing creams may relieve symptoms.
• Oral antihistamines may be useful for treating itch.
• Immediate application of high potency topical corticosteroid ointment may reduce swelling in some patients.
• Severe large local swelling may require oral corticosteroids.

Severe allergic reactions can be fatal
• Anaphylaxis to stings and bites should be treated as a medical emergency
• Patients who have a history of anaphylaxis should always be:
  - Prescribed an adrenaline autoinjector and be given an ASCIA Action Plan for Anaphylaxis.
  - Educated to always carry the autoinjector with them.
  - Referred to a clinical immunology/allergy specialist for assessment and consideration of immunotherapy.

Venom immunotherapy can reduce the severity of allergy
• Immunotherapy is highly effective at reducing the risk of anaphylaxis to future stings from bees and some wasps.
• Currently there is no commercial allergen extract for immunotherapy to Jack Jumper ants, other species of ants, ticks and some wasps.
• Immunotherapy is not recommended for patients with large local swellings alone.
• Patients should be referred to a clinical immunology/allergy specialist for:
  - Initiating immunotherapy and determining duration. Generally patients undergo immunotherapy for 3-5 years, however this treatment needs to be individualised.
  - Assessing the need for ongoing prescription of adrenaline autoinjector as some patients are at greater risk of anaphylaxis during and after immunotherapy.

Stinging insect allergy: management overview

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Antihistamine</th>
<th>Oral corticosteroid</th>
<th>Adrenaline autoinjector</th>
<th>Immunotherapy/Refer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor local</td>
<td>✓</td>
<td>×</td>
<td>✓</td>
<td>×/×</td>
</tr>
<tr>
<td>Large local</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>×/×</td>
</tr>
<tr>
<td>Systemic – no anaphylaxis</td>
<td>✓</td>
<td>×</td>
<td>?</td>
<td>?/✓</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓/✓</td>
</tr>
<tr>
<td>Serum sickness</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
<td>×/?</td>
</tr>
</tbody>
</table>

Tick reactions
• Anaphylaxis to tick bites is rare.
• In patients with tick anaphylaxis, it often occurs soon after tick removal. In such patients, the adrenaline autoinjector should be close to hand before tick removal is considered.
• Ticks should ideally be freeze dried before removing (e.g. using liquid nitrogen, ether or ether containing products such as Aerostart).
• Currently no allergen extract for treatment is available.
• Confirmatory allergy testing is not yet available, although recent research suggests that most have detectable IgE to a carbohydrate allergen called alpha-galactose, also present in red meat. This is available as a commercial assay from diagnostic pathology laboratories.
Caution:
- If using liquid nitrogen, use caution to prevent burns.
- If using ether containing products, be aware that they are flammable products and should not be used near naked flames or lit cigarettes.

Jack Jumper Ant Allergy
- In areas where Jack Jumper ants are common, 2-3% of people have generalised allergic reactions and approximately half of these reactions can be life threatening.
- Approximately 70% of people with Jack Jumper ant allergy will have another allergic reaction if stung again.
- Specific allergen IgE testing is available through SA Pathology (Flinders Medical Centre, IMVS).
- Skin allergy testing is only available in Tasmania.
- Immunotherapy is only available under research conditions (except in Tasmania).

General strategies to prevent stings and bites
- Cover up with clothing as much as possible:
  - When gardening, wear gloves, long sleeves and pants.
  - Always wear shoes.
  - Wear light coloured clothing, as it is less attractive to bees and wasps (avoid dark and bright coloured clothing).
- Use insect repellent.
- After being outdoors, check for ticks in people who are in endemic areas.
- Do not drink from open drink cans as these attract bees and wasps.
- Have nearby nests (ant, bee, wasp) removed by professionals. This is also relevant to schools and childcare, particularly if they have children enrolled with stinging insect allergy.

Appendix F: Further information and resources for health professionals and patients

Australasian Society of Clinical Immunology and Allergy (ASCIA)
ASCIA is the peak professional body of clinical immunology and allergy specialists in Australia and New Zealand.
www.allergy.org.au

ASCIA e-training for health professionals
- Anaphylaxis, food allergy, allergic rhinitis, immunotherapy.

ASCIA anaphylaxis resources webpage
www.allergy.org.au/health-professionals/anaphylaxis-resources includes links to:
- ASCIA Action Plans, Travel Plans, FAQ, Guidelines, Information for parents and other anaphylaxis related resources.
- ASCIA anaphylaxis e-training for schools and childcare.
- ASCIA e-training for the community.

The ASCIA health professionals webpage
www.allergy.org.au/health-professionals
- Includes links to ASCIA health professional information papers, position papers and guidelines.

ASCIA patients and consumer webpage
www.allergy.org.au/patients/ascia-education-resources
- Includes links to more than 60 topics in the ASCIA Education Resources patient information series including ASCIA infant feeding advice. Most of these documents include allergen minimisation and avoidance strategies.
- ASCIA dietary avoidance information sheets

Patient support organisations
- Allergy & Anaphylaxis Australia
  www.allergyfacts.org.au
  Provides patient resources and phone assistance throughout Australia.

- Allergy New Zealand
  www.allergy.org.nz
  Provides patient resources and phone assistance throughout New Zealand.

Adrenaline autoinjector supplier websites
- EpiClub
  www.epiclub.com.au
  Provides EpiPen expiry date reminder for patients.

- Analert
  www.analert.com
  Provides Anapen expiry date reminder for patients.
Appendix G: References