PERIOPERATIVE ANAPHYLAXIS

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STAFF ANAESTHETIST
TQEHW
• Anaphylaxis is a life-threatening syndrome triggered by a wide range of antigens and involve multiple organ systems.

• The term ‘anaphylaxis’ is derived from the Greek ‘ana’ means without and ‘phylaxis’ meaning protection.

• The first report of anaphylaxis was described in hieroglyphics in 2640 BC when an Egyptian pharaoh died after a wasp sting.
• Anaesthetists are involved in adverse drug reactions more commonly than most other clinicians.

• Adverse reactions to drugs can be classified as predictable or unpredictable.

  Predictable reactions are usually dose dependent, reproducible and are often expected side-effects of the drug. e.g. hypotension after injection of propofol

  Unpredictable drug reactions may be anaphylactic or anaphylactoid and are dose independent.
Hypersensitivity reactions

Set of undesirable reactions produced by the normal immune system

<table>
<thead>
<tr>
<th>Hypersensitivity Reaction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Bee stings</td>
</tr>
<tr>
<td>IgE-mediated; quick onset after exposure</td>
<td>Latex</td>
</tr>
<tr>
<td>Allergic</td>
<td>Certain medications (e.g. Penicillin)</td>
</tr>
<tr>
<td>Type II</td>
<td>Hemolytic reactions</td>
</tr>
<tr>
<td>Cytotoxic/antibody-mediated</td>
<td>Goodpasture syndrome</td>
</tr>
<tr>
<td>Cytotoxic</td>
<td>Hyperacute graft rejection</td>
</tr>
<tr>
<td>Type III</td>
<td>Hypersensitivity pneumonitis</td>
</tr>
<tr>
<td>Immune complex/IgG/IgM mediated</td>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Immune complex deposition</td>
<td>Polyarteritis nodosa</td>
</tr>
<tr>
<td>Type IV</td>
<td>Serum sickness</td>
</tr>
<tr>
<td>Delayed or cell-mediated</td>
<td>Chronic graft rejections</td>
</tr>
<tr>
<td>Delayed</td>
<td>PPD test</td>
</tr>
<tr>
<td></td>
<td>Latex</td>
</tr>
<tr>
<td></td>
<td>Nickel</td>
</tr>
<tr>
<td></td>
<td>Poison ivy</td>
</tr>
</tbody>
</table>

Mnemonic: “ACID”
Anaphylactic reaction

- Type 1 hypersensitivity reaction
- IgE mediated
- After initial exposure to an antigen, IgE antibodies are produced which binds to mast cells and basophils.
- If there is further exposure, the antigen binds with IgE antibodies and results in the release of mediators including histamine, slow-reacting substances-A (SRS-A), leukotrienes, tryptase and prostaglandins.
- These substances increase mucous secretion, bronchial muscle tone and vascular permeability, causing airway oedema, bronchospasm and hypotension.
Anaphylactic Reaction

1. Antigen/Allergen
2. B-cell
3. IgE bind to the surface of mast cell or basophil
4. Antigen triggers production of IgE antibodies
5. Subsequent exposure to the same antigen
6. Antigen bridges the gap between two antibody molecules, degranulation of the cell and release of histamine and other mediators
7. Histamine increases the permeability and distension of blood capillaries
Anaphylactoid reaction

- Clinically indistinguishable from anaphylactic reactions
- Not IgE mediated nor do they involve previous exposure to the antigen
- Underlying mechanisms include the release of vasoactive substances (e.g. histamine) from the mast cells or compliment activation.
- Most commonly seen in reactions to contrast media
<table>
<thead>
<tr>
<th></th>
<th>Anaphylactic Reactions</th>
<th>Anaphylactoid Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is sensitization required?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Can reaction occur on first exposure?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>How much exposure is needed to elicit reaction?</td>
<td>Very little</td>
<td>Usually more than for anaphylaxis</td>
</tr>
<tr>
<td>Is reaction predicted by allergy skin tests?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

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Epidemiology

• In Australia, the incidence of anaphylaxis is between 1 in 10,000 and 1 in 20,000 with a 3:1 female preponderance.

• The mortality rate from perioperative anaphylaxis has recently been quoted in a range between 3-9%.
• The anaphylactic reaction often begins 5-10 min after the start of the anaesthetic, rather than at induction.

• Anaphylactic reactions are also more common when drugs are given intravenously.

• Previous history of drug exposure does not seem necessary, especially with neuromuscular blocking agents.
Signs and symptoms of **Anaphylaxis**

- **Central nervous system**
  - lightheadedness
  - loss of consciousness
  - confusion
  - headache
  - anxiety

- **Respiratory**
  - shortness of breath
  - wheezes or stridor
  - hoarseness
  - pain with swallowing
  - cough

- **Gastrointestinal**
  - crampy abdominal pain
  - diarrhea
  - vomiting
  - Loss of bladder control

- **Heart and vasculature**
  - fast or slow heart rate
  - low blood pressure

- **Skin**
  - hives
  - itchiness
  - flushing

- **Pelvic pain**

- **Swelling of the conjunctiva**

- **Runny nose**

- **Swelling of lips, tongue and/or throat**
Initial presenting feature in anaphylaxis (% of total).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Proportion of patients(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pulse detected, hypotension</td>
<td>28</td>
</tr>
<tr>
<td>Difficulty inflating lungs</td>
<td>26</td>
</tr>
<tr>
<td>Flushing</td>
<td>21</td>
</tr>
<tr>
<td>Coughing</td>
<td>6</td>
</tr>
<tr>
<td>Rash</td>
<td>4</td>
</tr>
<tr>
<td>Desaturation</td>
<td>3</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>3</td>
</tr>
<tr>
<td>Other- ECG change, wheeze, urticaria</td>
<td>9</td>
</tr>
</tbody>
</table>
Table I

Classification of severity of anaphylactic reactions\textsuperscript{20}

<table>
<thead>
<tr>
<th>Anaphylactic grade</th>
<th>Emergency situation</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Local reaction of allergic origin</td>
<td>Localised erythema and swelling</td>
</tr>
<tr>
<td>0/I</td>
<td>Non objective anaphylaxis-associated</td>
<td>Itching, paraesthesia, alteration of sensoric perception, e.g. visual,</td>
</tr>
<tr>
<td></td>
<td>generalized symptoms</td>
<td>acoustic, olfactory</td>
</tr>
<tr>
<td>I</td>
<td>Generalized reaction of the skin and/or oral, nasal</td>
<td>Generalized erythema, urticaria, subcutaneous edema</td>
</tr>
<tr>
<td></td>
<td>or conjunctival membranes</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Pulmonary, cardiovascular and gastrointestinal</td>
<td>Bronchospasm, alteration of pulse and/or tension e.g. dyspnoea, tachycardia,</td>
</tr>
<tr>
<td></td>
<td>reaction of minor severity</td>
<td>hypotension, nausea, abdominal spasms</td>
</tr>
<tr>
<td>III</td>
<td>Pulmonary, cardiovascular and gastrointestinal</td>
<td>Insufficiency of respiration and/or circulation, shock, cyanosis, vomiting,</td>
</tr>
<tr>
<td></td>
<td>reaction of major severity</td>
<td>diarrhoea, loss of consciousness</td>
</tr>
<tr>
<td>IV</td>
<td>Respiratory or circulatory arrest</td>
<td>Absence of respiration and/or circulation</td>
</tr>
</tbody>
</table>
**Anaphylaxis during Anaesthesia**

### Diagnostic Card

Absence of tachycardia or cutaneous signs does not exclude anaphylaxis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Generalised mucocutaneous signs: Erythema, Urticaria+/- Angioedema</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Moderately severe - Multi-organ manifestations including: Mucocutaneous signs, Hypotension, Tachycardia, Evidence of Bronchospasm, cough, difficult ventilation</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Severe-Life Threatening and requiring immediate and specific treatment: Cardiovascular collapse, Bradycardia or Tachycardia, Arrhythmias, Bronchospasm, Cutaneous signs may be absent, or present only after correction of hypotension</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Cardiopulmonary Arrest</td>
</tr>
</tbody>
</table>

### Presenting Signs and Symptoms

<table>
<thead>
<tr>
<th>Presenting Signs and Symptoms</th>
<th>Possible Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin and Mucosa</strong>&lt;br&gt;Hives, flushing, erythema, urticaria, Swelling head and neck or peripheries</td>
<td>Direct Histamine Release, Venous Obstruction, Head Down Position, C1-esterase deficiency (Angioedema only), Mastocytosis, Cold induced anaphylaxis</td>
</tr>
<tr>
<td><strong>Airway Compromise</strong>&lt;br&gt;Dyspnoea, wheeze, stridor, difficulty inflating lungs</td>
<td>Direct Histamine Release, Acid aspiration, Exacerbation of asthma, Intubation; Oesophageal intubation, Foreign Body, Difficult airway, Visceral traction, Mastocytosis, Consider: Auto PEEP (disconnect from ventilator), Tension pneumothorax (decompress)</td>
</tr>
<tr>
<td><strong>Hypotension</strong></td>
<td>Direct Histamine Release, Visceral Traction, Vasodilatation by drugs, Central Neural Blockade, Drug Overdose, Vasovagal, Hypovolemia, Mastocytosis, Cold induced anaphylaxis</td>
</tr>
<tr>
<td><strong>Cardiac Arrest</strong></td>
<td>Myocardial ischaemia/Infarction, Electrolyte Abnormality, Sepsis, Blood Loss, Tension Pneumothorax, Cardiac Tamponade, Pulmonary Embolism, Mastocytosis</td>
</tr>
</tbody>
</table>
Differential Diagnosis

- Life Threatening
- Severe Asthma
- Sepsis (SIRS)
- Pulmonary Embolism
- Choking

- Non life-threatening
- Syncope (vasovagal)
- Panic Attack
- Idiopathic Urticaria
- Isolated Angioedema
Causes of life-threatening allergic reactions during anaesthesia

- Neuromuscular blocking agents (70%)
  - steroid based compounds (vecuronium and rocuronium) cause anaphylactic reactions, whereas benzylisoquinolininiums (mivacurium and atracurium) cause anaphylactoid reactions.

- More than half of the reactions occur on first exposure.

- Quaternary ammonium group found in NMB is widely present in other drugs, foods, cosmetics, and hair care products.

- Five to ten times more common in females
• **Latex (12.6%)**
   Increasingly recognized as a cause in abdominal and gynaecological surgery. There is a recognized cross-reactivity between latex and certain foods, bananas, chestnuts and avocado.

• **Colloids (4.7%)**
  Risk is greater with gelatin solutions

• **Induction agents (3.6%)**
  Incidence of severe reactions to thiopental has been reported as about 1 in 14,000. Reactions to propofol are less common.
• **Antibiotics (2.6%)**
  
  Penicillins are most frequently implicated in hypersensitivity reactions. The incidence of cross-reactivity with cephalosporins is about 8%. If there is a history of a severe penicillin reaction, neither cephalosporins nor carbapenems should not be used.

• **Benzodiazepines (2%)**

• **Opioids (2.6%)** - morphine is implicated most commonly.

Reactions to synthetic opioids are rare. Morphine, codeine and pethidine can cause non-immunological cutaneous histamine release.

**Other agents (2.5%)**

Radiocontrast media- can produce hypersensitivity reactions in up to 3% of patients. Reactions can be severe and most occur within minutes of administration.
Anaphylaxis during Anaesthesia

Immediate Management

DR Danger and Diagnosis
Response to stimulus
- Unresponsive Hypotension or Bronchospasm
- Cease triggers including Chlorhexidine & 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 Secure Airway
Breathing - 100% oxygen
- Intubation: airway oedema or compromise
- Confirm FiO₂ is 100%

C Circulation: CPR if no pulse
Give IV fluid bolus
- If no pulse give 1mg Adrenaline IV (Paed 10 mcg/kg) and follow ALS protocol
- IV Fluid: 20mls/kg bolus repeat as required

D Drugs: Adrenaline
IV Bolus, repeat if needed
- Prepare Infusion

IV Adrenaline BOLUSES
- Draw up 1mg in 10ml
Adrenaline (1:10,000) = 100mcg/ml
Give dose below every 1-2 minutes prn:

<table>
<thead>
<tr>
<th>Grade 2 – Moderate Hypotension or Bronchospasm</th>
<th>Grade 3 – Severe Hypotension or Bronchospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult 5-20 mcg = 0.05 - 0.2 ml</td>
<td>Adult 100-200 mcg = 1 - 2 ml</td>
</tr>
<tr>
<td>Child 1 - 5 mcg/kg = 0.01 - 0.05 ml/kg</td>
<td>Child 5 - 10 mcg/kg = 0.05 - 0.1 ml/kg</td>
</tr>
</tbody>
</table>

No IV access or haemodynamic monitoring:
Consider IM Adrenaline
1:1000 (1mg/ml) into lateral thigh
- Adult = 0.5ml (500mcg)
- <12 years = 0.3ml (300mcg)
- <6 years = 0.15ml (150mcg)

Adrenaline INFUSION If requiring repeated doses of Adrenaline prepare and start infusion:
- Adult 0.05 to 0.4 mcg/kg/min
- Child 0.1 to 5 mcg/kg/min

Example Infusion 3mg/50mls = 60mcg/ml with 1ml/hour = 1mcg/min (70 kg Adult 3.5 – 28 ml/hour)

If NOT RESPONDING see ‘Refractory Management’
Anaphylaxis during Anaesthesia

**Refractory Management**

- **Ensure possible triggers removed**
  - Chlorhexidine including impregnated CVCs
  - Colloid stop if running at time of reaction
  - Latex none in theatre

- **Consider other diagnoses**
  - See ‘Diagnostic Card’ in Anaphylaxis Box

- **Monitoring**
  - Consider Insert Arterial line and CVC
  - Consider TOE/TTE to assess filling

- **Request more help if required**
  - Consider calling arrest code

- **Resistant Hypotension**
  - Continue Adrenaline and IV fluid bolus 50 ml/kg
  - Noradrenaline infusion 0.1mcg/kg/min
  - Metaraminol infusion if noradrenaline not available
  - Vasopressin bolus 1-2 units (0.03units/kg)
    then infusion 2 units per hour
  - Glucagon 1-5mg over 5 min (βblocker reversal)
    (Child 20-30mcg/kg to max 1mg)
  - Consider cardiac bypass where available

- **Resistant Bronchospasm**
  - Salbutamol IV bolus 100-200mcg
    +/- Salbutamol infusion 5-25mcg/min
    (Child 5mcg/kg/min for 1 hour
    then run infusion at 1-2mcg/kg/min)
  - Consider:
    - Auto PEEP (disconnect from ventilator)
    - Tension pneumothorax (decompress)

- **Pregnancy**
  - Lateral tilt
  - Caesarean section if arrest or peri-arrest

**Once stable refer to ‘Post Crisis Management’**
## Anaphylaxis during Anaesthesia
### Post Crisis Management

### Once Situation is Stabilised

| Consider Steroids     | Dexamethasone 0.1-0.4 mg/kg  
|                       | Hydrocortisone 2-4 mg/kg     |
| Consider ORAL Antihistamines | Consider Oral 2\textsuperscript{nd} Generation Antihistamines when patient able to take oral medications |
| Parenteral Antihistamines | NOT RECOMMENDED               |

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

### Investigations
- Tryptase at 1 hour, 4 hours and $>$ 24 hours
- Tryptase unstable in whole blood: send promptly to laboratory for processing
- Use Plain, serum or EDTA tube
- ABG as required
- Electrolytes, FBE, Coagulation Screen

### Observations
- Monitor closely for 6 hours
- Consider 24 hours ICU/HDU if moderate to severe (up to 20% incidence of biphasic reactions)
- Anaphylaxis may last up to 32 hours despite aggressive treatment

### Letter with Patient: Reaction Description + Agents Used

Refer Patient for Testing and Allergy Assessment

For a referral form & to locate your nearest testing centre go to [www.anzaaq.com](http://www.anzaaq.com)
THANK YOU