

ANAPHYLAXIS

Facilitators Guide

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Duration **2 hrs**

Facilitator level **Senior Trainee/ANP and above**

Learner level **Junior Trainee/ Staff Nurse and Senior Trainee/ANP**

Equipment required: **Adrenaline auto-injector if planning a demonstration on model**

OUTLINE (use the sections that are relevant for your learners)

- **Basics (10 mins)**
- **Main session: (2 x 15 minute) case discussions covering the key points and evidence**
- **Advanced session: (2 x 20 minutes) case discussions covering grey areas, diagnostic dilemmas; advanced management and escalation**
- **Sim scenario (30-60 mins)**
- **Quiz (10 mins)**
- **Infographic sharing (5 mins): 5 take home learning points**

We also recommend printing/sharing a copy of your local guideline for sharing admission criteria.

PRE-READING

APLS Anaphylaxis Management

RCPCH Anaphylaxis Pathway

RCH Clinical Practice Guidelines : Anaphylaxis

BASICS (Does not need to be included but for information if it comes up in discussion)

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Anaphylaxis is described as

- Sudden onset and rapid progression of symptoms
- Life-threatening Airway and/or Breathing and/or Circulation problems

Skin and/or mucosal changes (flushing, urticarial, angioedema) are absent 20% of cases

Angioedema is similar to urticaria but involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes in the mouth and throat.

There can also be gastrointestinal symptoms (e.g. vomiting, abdominal pain, incontinence).

Fatality <1%, increased in those with pre-existing asthma. Approximately 20 anaphylaxis-related deaths in the UK every year.

From a case-series (resus council), fatal food reactions cause respiratory arrest typically after 30–35 minutes; insect stings cause collapse from shock after 10–15 minutes; and deaths caused by intravenous medication occur most commonly within five minutes. Death never occurred more than six hours after contact with the trigger.

PATHOPHYSIOLOGY

What is an allergy?

It is the body's response to an external 'allergen'. An unnecessary immune response to an innocuous substance.

Common allergens/triggers include:

- Food: nuts, milk, fish
- Venom: wasp, bee
- Drugs: antibiotics, anaesthetic drugs
- Contrast media
- Latex

Reactions are either delayed type IV or immediate type I. IgE-mediated allergy is broadly characterised as a Type 1 hypersensitivity. Other hypersensitivity reactions (II, III and IV) are mediated by other antibody classes, immune cells or cellular components. Non-IgE mediated reactions typically cause symptoms to appear more slowly, sometimes several hours after exposure.

Allergy is increasing in prevalence. Theories for this include the 'Hygiene Hypothesis', the idea that increased exposure to microorganisms correlates with a decreased tendency to develop allergy and more recently the 'Old Friends Mechanism' which links the tendency to develop allergy to an individual's microbiome (collection of microorganisms living in and on a person's body).

Interestingly kids in developing countries have a decreased allergy prevalence, thought to be because of less sanitation, more exposure to microbes and increased time spent outdoors.

How do we develop allergic reactions?

Part 1: Sensitisation

An allergen enters the body and is captured by an antigen presenting cell, that scoops it up and nicely presents it to immune cells, particularly T cells (in a similar manner as if the allergen was a foreign invading microbe). Through a number of immune interactions between T cells and B cells, B cells produce allergen-specific IgE antibodies. These get released into the blood, where they bind to mast cells (the major allergy immune cell) as well as other friends like basophils. In some individuals, this can cause a 'sensitisation' i.e. the next time their body meets that particular allergen it's going to go on the offensive.

Part 2: Re-exposure

Our patient is now carrying allergen-specific IgE bound mast cells. Upon re-exposure to the offensive allergen binds to IgE, causing the mast cells to initiate an aggressive and immediate immune response.

Mast cells on the attack:

Mast cells are granular cells, containing many secretory granules that all get released on activation. The binding of IgE causes rapid degranulation, and a shower of inflammatory compounds, including histamine. Result?

Local inflammations, and allergy symptoms (see presentation of the patient in anaphylaxis below).

CASE 1 (15 MINS)

An 8 year old girl presents after collapsing following attendance at a friend's birthday party. She was noted to have been eating a sandwich, then promptly developed respiratory distress. On admission with the ambulance crew she is audibly wheezy, with swelling of the tongue and lips.

How would you assess this child?

What is your immediate management?

How much adrenaline do you give and how?

Any adjunct therapies to consider?

DISCUSSION POINTS: PRESENTATION, ASSESSMENT AND TREATMENT

Usually the parents or child will give a history of exposure to an allergen. This is useful however not essential. If the clinical picture is of anaphylaxis – treat first and seek the provoking agent second!

Life-threatening features of anaphylaxis include:

- Airway: swelling, hoarse voice, stridor
- Breathing: shortness of breath, tachypnoea, wheeze, cyanosis, respiratory arrest
- Circulation: pale, clammy, tachycardia, low blood pressure, shock, cardiac arrest
- Confusion, agitation or decreased level of consciousness can occur due to above problems

Manage according to APLS – remember ABCDE approach

- **Get senior help**
- **Remove the allergen if possible** - remove a stinger, stop IV drugs, but **don't** make a patient vomit if suspected food allergy – risk of aspiration.
- Maintain oxygen delivery 15l via non-rebreather mask
- Get monitoring on – and get a BP early
- If hypotensive then get IV access and bolus 20mls/kg 0.9% sodium chloride

Adrenaline – early and often – delayed administration directly linked with increased morbidity and mortality

- Scientific evidence is weak, instead based on what is considered safe and practical.
- Adrenaline IM – use 1 in 1000 (or 0.1% - 1mg/ml)
- The dose is 0.01ml/kg or 0.01mg/kg. Max dose is 0.5ml.

| Age | Dose |
|------------------|-----------------------------|
| < 6 years old | 150 micrograms IM (0.15 mL) |
| 6 – 11 years old | 300 micrograms IM (0.3 mL) |
| >12 years old | 500 micrograms IM (0.5 mL) |

- Give as an IM injection into the anterolateral thigh. IM provides faster rise in plasma and tissue concentrations than sub-cutaneous route.
- Don't give IV boluses unless there is cardiac arrest.
- Can use the patient's own adrenaline auto-injector if not already used

Why adrenaline?

No RCT, but a logical choice and lots of anecdotal evidence.

Mechanism of action

Alpha receptor agonist

- Reverses peripheral vasodilation
- Reduces oedema

Beta receptor agonist

- Bronchodilation
- Increased force of myocardial contraction
- Suppresses histamine and leukotriene release
- Inhibits mast cells – attenuates severity of IgE-mediated allergic reactions.

What about the side effects?

Normally only occur with IV administration (at which point PICU will be present)

- Arrhythmias
- Hypertension
- Pulmonary haemorrhage
- Intracranial haemorrhage

Duration of action

- Rapid onset – should see improvement in 5 minutes
- Duration of action is 15 minutes – beware of rebound

Can I go again?

- Absolutely – 20% of patients require more than one dose!
- By the third dose please call PICU (just in case)

The patient isn't getting better. What else do I do?

- Adrenaline is the mainstay of treatment – given another dose (call PICU!)
- If concerns about upper airway obstruction consider 5mls of 1:1000 adrenaline neb
- Is the child wheezing? Consider a salbutamol neb 2.5mg/5mg depending on age
- Antihistamines (H1 and H2 blockers) are a second line treatment and should not delay adrenaline administration! Examples such as chlorpheniramine are useful for urticaria, nasal and ocular symptoms
- Steroids – think about steroids. 1mg/kg prednisolone (PO) or 4mg/kg hydrocortisone (IV) – but remember slow onset of action.

Additional points

- Keep patient comfortable and minimise distress
- Ideally have them lying down to aid venous return (hypotension can precipitate cardiac arrest)
- NICE evidence: Limited evidence from systematic review - consider mast cell tryptase investigations only if reaction is thought to be drug, venom or idiopathic

related! Send three timed samples. Immediately after reaction has been treated. 1-2 hours after the start of symptoms. At 24 hours or in convalescence (baseline sample) after the reaction.

CASE 2 (15 MINS)

A 3 year old presented with a localised erythematous rash after being stung by a bee at a family picnic. His family attended PED where he subsequently developed respiratory distress and he was treated with IM adrenaline. After a couple of hours he was playful and appeared well and his parents want to take him home.

What would you say to the parents?

How would you manage this patient?

What key points make up the discharge planning?

Don't forget oral analgesics (as above) and a full assessment for other injuries. (From DFTB: Wound management)

DISCUSSION POINTS: BIPHASIC REACTIONS

- Occur in 6 – 11% of children
- Usually manifest in the first 8 hours after exposure, but may be delayed up to 72 hours
- NICE evidence: Children who have had emergency treatment for suspected anaphylaxis should be admitted to hospital under the care of a paediatric medical team. No direct evidence from systematic review however in light of risk of biphasic reaction risk, better to keep them in overnight for observation.
- All children with suspected anaphylaxis will require risk planning and allergy avoidance advice
- Corticosteroids have been advocated to prevent protracted and biphasic reactions (no RCT on this). Recent systematic review and meta-analysis (Lee et al) included 27 studies with 4114 anaphylaxis cases, of whom 192 (4.7%) had biphasic reactions.
- Steroid administration did not affect the likelihood of a late phase reaction (OR 1.52, 95% CI 0.96 to 2.43). In fact, there was a non-significant trend towards increased risk, (?because steroid use was more common with severe reactions).
- Biphasic reactions were more common where hypotension was present at initial reaction (OR 2.18, 95% CI 1.14 to 4.15), but this is unusual in food-induced anaphylaxis.

- The median time to onset of biphasic symptoms was 11 (range 0.2–72) hours, that is, 50% of reactions occurred >11 hours after initial reaction. Hence why all children should be admitted.

For the child going home (RCPCH pathway)

- Children and young people at risk of anaphylaxis should be referred to clinics with specialist competence in paediatric allergies.
- Children and young people who are at high risk of an anaphylactic reaction should carry an adrenaline auto-injector and receive training and support in its use.
- They will need 2 auto-injectors – 20% require a second dose
- Medic-alert bracelet and patient education

- Further follow up - the most common way to diagnose an IgE-mediated allergy is through a blood test to identify allergen specific IgE or a skin prick test which results in a local inflammatory reaction after administration of the trigger allergen.
- Oral food challenges – need to have appropriate resus facilities.

- AIT - Allergy immunotherapy or ‘Desensitisation’ works by changing the immune system’s response. These changes may include producing less IgE, producing ‘blocking’ IgG antibodies, and producing more regulatory T cells, promoting tolerance and a less active immune response. However, the exact mechanism behind desensitisation is not yet known and it is likely that different patients exhibit different immune profiles following the treatment. Only available for wasps, bees, dust mites and animal dander. Clinical trials for food allergies are on-going.

Do you know how to administer IM adrenaline?

EpiPen <https://www.youtube.com/watch?v=FXlqSuzzrws> (5 minutes)

ADVANCED DISCUSSION (20 MINS PER CASE)

This is an opportunity to cover grey areas, diagnostic dilemmas and advanced management and escalation if there are more experienced trainees or senior registrars in your group.

ADVANCED CASE 1

A 6 year old spina bifida patient is currently admitted with an LRTI. She has been having a course of amoxicillin for the last week. You are crash bleeped to the ward where she is having her urinary catheter changed by a bank nurse. She is pale and cool to touch, with increased respiratory rate.

What's going on? Is this allergy? Is this anaphylaxis?

How would you treat it?

What allergy avoidance advice do you give?

DISCUSSION POINTS

- Initial management: Observations and assess (BP)
- Initial presentation of anaphylaxis – high safety margin for IM adrenaline
- Hypotension as a warning sign (absence of a rash) – is it fluid responsive? May require large volumes of fluids. No evidence for crystalline vs colloid. Give 0.9% or Hartmanns.
- Explore medical history for triggers, explore unusual or uncommon triggers (e.g. exercise as a trigger, consider co-existing triggers e.g. prawns and exercise)

Risk factors for latex allergy:

- Repeated bladder catheterisation
- Neural tube defects: Spina bifida
- Cloacal abnormalities
- Multiple surgical procedures, especially as a neonate
- Atopy and multiple allergies
- Food allergies: fruit and vegetables including bananas, celery, fig, chestnuts, avocados, papaya and passion fruit are most significant.
- Children with a strong or confirmed allergy to banana should be considered allergic to latex and managed accordingly.

Patient education

- Cross reactivity between certain allergens
- What is this most common food trigger for fatal anaphylaxis?

The most common food trigger for fatal anaphylaxis in children in the UK is milk, followed by peanut and tree nuts. While there is broad public recognition of the risks posed by nuts, cow's milk allergy is often perceived as being less se-

vere. However, milk allergy persisting into school age is often associated with other coexisting atopies (such as asthma) and more severe reactions, particularly in the 30%–40% of milk-allergic children who are unable to tolerate milk in well-baked foods (such as biscuits or cakes). Such exposure often results in delayed reactions which mimic asthma; under such circumstances, it may not be obvious that the child has been exposed to milk. Therefore, always consider anaphylaxis in someone with a known food allergy who has sudden breathing difficulty.

ADVANCED CASE 2

An 8 year old girl presents after collapsing following attendance at a friend's birthday party. She was noted to have been eating a sandwich, then promptly developed respiratory distress. She has had 2 epipens with the ambulance crew, and a further dose in PED. You are called as senior support. Her sats are dropping and she is becoming bradycardic.

If the patient isn't improving after IM adrenaline, what are your next management plans?

How do you prepare for intubation?

What do you do next?

(From DFTB: Procedural sedation)

Nitrous oxide

Nitrous oxide provides anaesthesia, anoxiolysis and some mild amnesia but offers limited analgesia. Administration of analgesic supplements is recommended. Many papers including the FAN study demonstrate the safety and efficacy of co-administering intranasal fentanyl. Other analgesics can also be safely used.

There are 2 methods of delivering nitrous oxide, piped nitrous oxide and Entonox. Piped nitrous oxide can provide variable concentrations and can be titrated to response whereas entonox is a fixed 50/50 mix of nitrous and oxygen and comes in canisters. The canister is set up with a demand valve that needs to be overcome with a deep breath; this can be difficult for under 5's.

You should see onset of effect in 30-60 seconds with the peak effect at 2-5 minutes. Offset of effects is similar at 2-5minutes, 100% oxygen should be applied during this time post procedure to avoid diffusion hypoxia.

Advanced management of anaphylaxis

- Ensure the most senior people are present
- Contact retrieval services early

Does this child need to be intubated?

- How would you determine this?
- Airway obstruction/cardiovascular collapse
- Who should be involved in the conversation? Who should perform the intubation?
- Most senior anaesthetist, ideally with ENT support
- What do you do whilst prepping
- Continue adrenaline – IM and nebulised whilst prepping for intubation
- What sedation would you use?
- Choose cardiovascular stable drugs – a drop in BP at this stage can precipitate cardiac arrest. Consider ketamine, fentanyl and rocuronium in 1:1:1 ratios.
- What equipment would you use?
- Have advance and difficult airway trolley prepped and ready
- What settings would you use?
- **Ventilate as for air trapping/bronchospasm**
- Pressure control (aim PIP <35 cm H₂O)
- Slow respiratory rate (e.g. 10-15 bpm)
- Long expiratory time (e.g. I:E 1:2)
- Permissive hypercapnia (aim pH >7.2)
- PEEP 5 – 10 cm H₂O to overcome intrinsic PEEP
- Consider manual decompression
- Muscle relax
- Regular chest physiotherapy and suction for mucus plugging
- Treat bronchospasm as per asthma guidelines (CATS or local)
- Watch for pneumothoraces
- Consider IV adrenaline infusion
- Consider NaHCO₃ for profound/refractory acidosis

Use of IV adrenaline

- Might need to escalate to IV adrenaline infusion – prescription calculation available on CATS website - 'in a hurry' drug chart (see appendix)
- UK Resus council: No evidence to base a dose recommendation – the dose is titrated to response. Can titrate in presence of continued haemodynamic monitoring. Consider arterial line to enable continuous monitoring.
- A child may respond to a dose as small as 1microgram/kg. This requires very careful dilution and checking to prevent drug errors.

Reporting of reaction

All adverse drug reactions should be reported to the Medicine and Healthcare products Regulatory Agency (MHRA) using the “Yellow Card” scheme (found in BNF and MIMS).

The patient must be referred to an allergist in a defined Regional Allergy Centre. All fatal cases of suspected anaphylaxis should be discussed with the coroner.

SIMULATION (30-60 MINS)

Anaphylaxis sim by Optimus Bonus: Practice made perfect?

QUIZ QUESTIONS (10 MINS)

Question 1.

What dose of adrenaline would you give to a 5 year old presenting in suspected anaphylactic shock?

- | | |
|--|--|
| A 150 micrograms IM (0.15 mL) of 1:1000 | C 300 micrograms IV (0.15 mL) of 1:1000 |
| B 150 micrograms IM (0.15 mL) of 1:10000 | D 300 micrograms IM (0.15 mL) of 1:10000 |

IM is always preferred in children owing to its broad safety profile. 1:1000 is the correct concentration. 1ml/kg of 1:10000 IV is the cardiac arrest dose. If the child does arrest then stop using IM and move to the standard APLS arrest dose as per protocol.

Question 2.

In order to diagnose anaphylaxis there must be a rash

- | | |
|------------------|-------------------|
| A True | B False |
|------------------|-------------------|

Cutaneous symptoms (most commonly urticaria or ‘hives’) are absent in around 10-20% of anaphylaxis reactions and where present may be delayed in onset. This is consistent with a case series of six paediatric fatalities due to food anaphylaxis, where only one child had evidence of skin involvement: the lack of skin signs may have delayed diagnosis and appropriate treatment with epinephrine, contributing to the fatal outcome.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) recently

issued new guidelines, which define anaphylaxis as:

- Any acute onset illness with typical skin features (urticarial rash or erythema/flushing, and/or angio-oedema), 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.

These criteria better reflect increasing recognition that cutaneous manifestations are often absent or appear late in near-fatal and fatal anaphylaxis.

Question 3.

Antihistamines can be used to treat anaphylaxis initially; epinephrine is only needed if symptoms worsen

A

True

B

False

Histamine is only one of many inflammatory mediators released during anaphylaxis. Oral antihistamines take around 30 min for onset of effect; intravenous chlorphenamine has a faster onset, but can cause hypotension. Antihistamines are not effective against anaphylaxis: their prophylactic use during controlled immunotherapy does not prevent anaphylaxis, and any apparent response during acute management of reactions is most likely due to the patient's own endogenous epinephrine. Antihistamines have now been relegated to third-line therapy in international guidelines; their use is limited to the relief of cutaneous symptoms and should never delay the administration of epinephrine or fluid resuscitation during patient stabilisation.

Finish-infographic of the take home tips (5 minutes)

- 1 Recognise broad presentation of anaphylaxis
- 2 Can be life-threatening– get senior help, get IV access
- 3 IM adrenaline – early and often
- 4 Biphasic reactions – consider when to discharge
- 5 Unusual allergens – latex

REFERENCES

Allergy

Emergency treatment of anaphylactic reactions:
Guidelines for healthcare providers

Pedemorsels: anaphylaxis

Anaphylaxis Q+A

http://site.cats.nhs.uk/wp-content/uploads/2018/01/cats_anaphylaxis_2018.pdf

<http://site.cats.nhs.uk/in-a-hurry/drug-calculator/>

Allergy care pathway for anaphylaxis

Anagnostou et al. Myths, facts and controversies in the diagnosis and management of anaphylaxis.
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Lee et al. Time of onset and predictors of biphasic anaphylactic reactions: a systematic review and meta-analysis of the literature. *Ann Emerg Med* 2014;64:S13

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