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Anaphylaxis Guidelines

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Anaphylaxis Guidelines

1. Introduction

Anaphylactic reactions are fortunately very uncommon, however when they do occur it is often unexpected and it is necessary for healthcare professionals to know what to do. Anaphylaxis is an emergency situation that requires quick and appropriate action.

A patient group direction is not required for the administration of adrenaline for the emergency treatment of anaphylaxis.

Anyone suspected of having an anaphylactic reaction to a substance must be offered a referral to a specialist allergy clinic. Anyone prescribed AAI should be offered a referral to a specialist allergy clinic

2. Scope

The following guidance applies to all healthcare professionals.

It clarifies roles and responsibilities in the management of anaphylaxis, aims to set out a plan of action in the case of anaphylaxis and examines different adrenaline auto-injector devices (AAIs) and the quantities for prescribing.

3. Guidance Statement

All healthcare professionals/ clinical staff who come into direct contact with patients should be able to competently:

- Recognise the signs and symptoms of an anaphylactic reaction.
- Ensure access to advanced life support by calling 999.
- Instigate early supportive measures using the Resuscitation Council guidelines UK 2008 (updated 2012 with links to NICE guidance) and in line with current training.

4. Responsibilities

All clinical staff:

- Must ensure they have a working knowledge of and comply with the guidelines.
- Have responsibility for ensuring that knowledge regarding drug dosage used in the treatment of anaphylaxis is current.
- Must attend training sessions which cover the subject of anaphylaxis at least annually.

5. Training

Current guidelines on the emergency treatment of anaphylaxis can be found on the Resuscitation Council (UK) website.

It is the responsibility of the healthcare professional to keep themselves informed and their training regularly updated.

This can be achieved by attending anaphylaxis training events and by following the guidance of their regulatory body:

- The General Medical Council
- The Nursing and Midwifery Council
- The General Pharmaceutical Council

6. What is anaphylaxis?

Anaphylaxis is a sudden severe life-threatening generalised or systemic hypersensitivity reaction following exposure to a substance to which a person is sensitive. It is characterised by rapidly developing life-threatening problems involving: the airway (pharyngeal or oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia).

In most cases there are associated skin and mucosal changes. The reaction can range from a mild response which disappears without treatment, to death. The reaction may occur immediately following exposure to the antigen or may be delayed for several hours.

7. Causes of Anaphylaxis

Anaphylaxis can be triggered by a broad range of triggers, but those most commonly identified include food, drugs and venom.

- The food allergens that most commonly resulted in anaphylaxis are cow's milk (29%), hen's egg (25%), hazelnut (5%), peanut (4%), kiwi (163, 4%), walnut (4%), pine nut (5/163, 3%), fish (3%), wheat(2%), soy (2%), shrimp (2%),apricot (2%) and sesame (2%)
- Insect stings are a recognised risk (in particular wasp and bee stings).
- Medicinal products particularly associated with anaphylaxis include blood products, vaccines, hyposensitising (allergen) preparations, antibacterials, aspirin and NSAIDS, heparin, anaesthetic drugs and contrast media.
- Anaphylactic reactions may also be associated with additives and excipients in foods and medicines. Refined arachis (peanut) oil, which may be present in some medicinal products, is unlikely to cause an allergic reaction – nevertheless it is wise to check the full formula of preparations which may contain allergenic fats or oils.
- It is important to note that in many cases, no cause can be identified. A significant number of cases of anaphylaxis are idiopathic .

8. Symptoms of Anaphylaxis

Anaphylaxis is typically rapid and unpredictable; it may be rapid, slow or (unusually) biphasic with variable severity and clinical features. There are a range of signs and symptoms, none of which are specific for anaphylactic reaction.

Anaphylaxis is likely however when the following criteria are met:

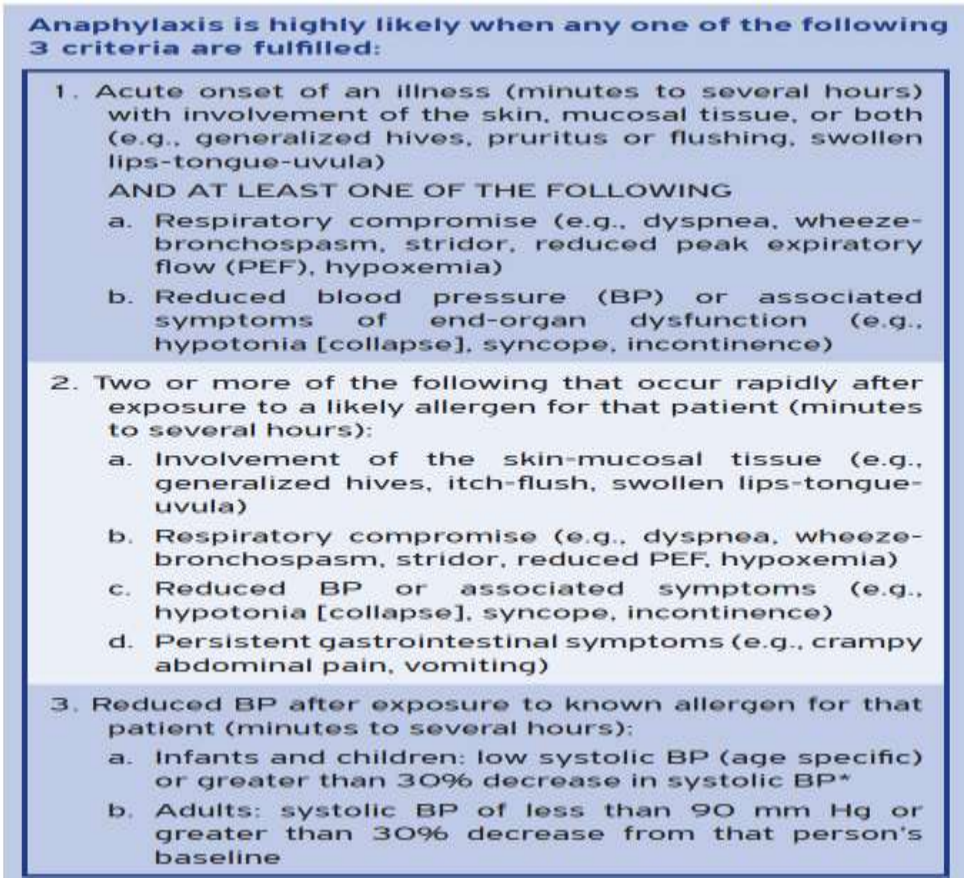
- Sudden onset and rapid progression of symptoms
- Life threatening Airway and/or Breathing and/or Circulation problems
- Skin and/or mucosal changes (flushing, urticaria, angioedema)

The following supports the diagnosis:

- Exposure to a known allergen for the patient
- Hypotension alone after exposure to **known allergen for that patient** (minutes to hours)

1. Infants and children: low systolic BP (age-specific) or >30% drop in systolic BP*,
2. Adults: systolic BP <100 mm Hg or >30% drop from their baseline

- As a general rule, the sooner the symptoms occur, the more severe the reaction and symptoms will be.
- Rarely manifestations may be delayed by a few hours (adding to diagnostic difficulty) or persist for more than 24 hours.
- Diagnostic problems have risen particularly in children.
- The risk of systemic reactions increased when atopic disease co-exists: seasonal allergic rhinitis , perennial rhinitis, food allergy , physician-diagnosed asthma , and any atopic disease



8.1 Symptoms Suggestive of ANAPHYLAXIS (onset 0-72 hours)

Airway problems: Throat and tongue swelling, difficulty breathing and swallowing**,** hoarseness, stridor and feeling of the throat closing up.
Breathing problems: Rapid breathing, wheeze, fatigue, cyanosis, SpO_2 <92% and confusion.
Circulation problems: Pale, clammy, low blood pressure, increased pulse rate, faintness, drowsiness, loss or reduction in consciousness and cardiac arrest.
Skin problems: Erythema, urticaria and peripheral oedema.
An **A**irway, **B**reathing, **C**irculation, **D**isability and **E**xposure approach should be used to assess and treat the patient (the ABCDE).
If airway, breathing and circulation criteria above are met an anaphylaxis reaction is likely and early treatment with adrenaline should be initiated (refer to **Treatment of Anaphylaxis**).

8.2 Symptoms suggestive of SYNCOPE or PANIC ATTACK (onset 0-1 hour)

- **General**: Sweating, nausea, dizziness, tinnitus, dimmed vision, weakness, choking, difficulty in breathing, hyperventilation leading to paraesthesia and spasms of hands.
- **Cardiovascular (CVS)**: Hypotension,(rarely as bad as in anaphylaxis-see cut off value for anaphylaxis) bradycardia. Strong carotid pulse persists.
- **Neurological**: Rare. Transient jerking movements and eye rolling.

Notes: Recovery from syncope should be rapid. Patient should regain consciousness in 1-2 minutes and any abnormal CVS signs should revert within a few minutes.
Sudden loss of consciousness in the very young, without a carotid pulse, should be assumed to be an anaphylactic reaction rather than syncope or convulsion.

9. Prevention of an Anaphylactic Reaction
Healthcare professionals have a responsibility where possible to prevent anaphylaxis. This can be achieved by a detailed assessment of previous drug and vaccine reactions, other contraindications and by fully recording anaphylactic reactions caused by drugs. Proper dietary advice along with written individualized allergy action plan from a trained HCP is essential in preventing food anaphylaxis in children.

9.1 History

The following can be used as a framework to discover a patient's risk of anaphylaxis:

Q1. Have you ever had a reaction to any drug, injection, insect bite or sting before?

If the patient answers 'yes' then ask precisely what happened. The patient may describe mild, localised reactions. However, the knowledge is still important because the repeated exposure to an antigen increases the likelihood of a more severe reaction.

Q2. What was the name of the drug you reacted to?

If the patient does not know, then ask what he or she was being treated for at the time.

Q3. Are you allergic to anything else?

If the patient answers 'yes' then continue with the question below. If the patient answers 'no' then proceed to Q5.

Q4. How do you know you are allergic to this? The question is important because people sometimes think they are allergic to drugs falsely.

Q5. Have you ever had any respiratory problems such as asthma or hay fever; or skin problems such as eczema?

It is important to ask this as a history of allergies may make a person more susceptible to other problems though this is not always inevitable. This will help to clarify if there are any predisposing conditions/problems.

Q6. Are you currently taking any tablets, medicines or use recreational substances?

Medication such as non-selective beta-blockers (e.g. propranolol) and tricyclic antidepressants (e.g. amitriptyline) interact with adrenaline. Need to review treatment.

Cocaine sensitises heart to adrenaline and may induce a life-threatening arrhythmia, or myocardial ischemia in users with underlying myocardial and vascular pathology.

The patient needs to fully understand why these questions are being asked.

Please note that only in the event of a severe reaction, i.e. previous collapse or severe untreated atopic illness, would you not administer the medicine or vaccine.

Currently in clinical practice it is important to start with a safe dose, call 999, monitor the response and give further doses if a greater response is needed.

If you don't have full medical history then it is advised that you administer the full age appropriate dose of adrenaline as detailed in **10.1 Adrenaline Dose**

10. Treatment of Anaphylaxis

Intramuscular (IM) adrenaline is generally the only drug available for use in the community.

It is anticipated however, that patients who have had this first line treatment will be transferred rapidly to hospital where any necessary further measures can be taken and where replacement auto injectors can be provided.

The Resuscitation Council Guidelines states that the best site for IM injection is the anterolateral aspect of the middle third of the thigh and to repeat the IM adrenaline dose after five minutes (into the opposite thigh) if there is no improvement in the patient's condition.

Patients should always be observed after treatment for anaphylaxis, for at least 6 hours and up to 24 hours in adults and for 12 to 24 hours in children, as symptoms can recur up to 24 hours after the initial reaction.

Administering adrenaline should not do any harm should there have been an incorrect diagnosis. Very few conditions can reasonably be mistaken for anaphylactic shock. **Anaphylaxis can be life threatening therefore it is better to give adrenaline than to not.**

10.1 Adrenaline Dose

The following intramuscular doses are recommended in the Resuscitation Council Guidelines 2008 which are specified as being in the context of administration by a healthcare professional.

Adrenaline Intramuscular doses:

The recommended dose of adrenaline is 10 micrograms/kg bodyweight.

Adults: 0.5 milligram IM (= 500 micrograms = 0.5mls of 1:1000) adrenaline

Children: The scientific basis for the recommended doses is weak. The recommended doses are based on what is considered to be safe and practical to draw up and inject in an emergency.

(The equivalent volume of 1:1000 adrenaline is shown in brackets)

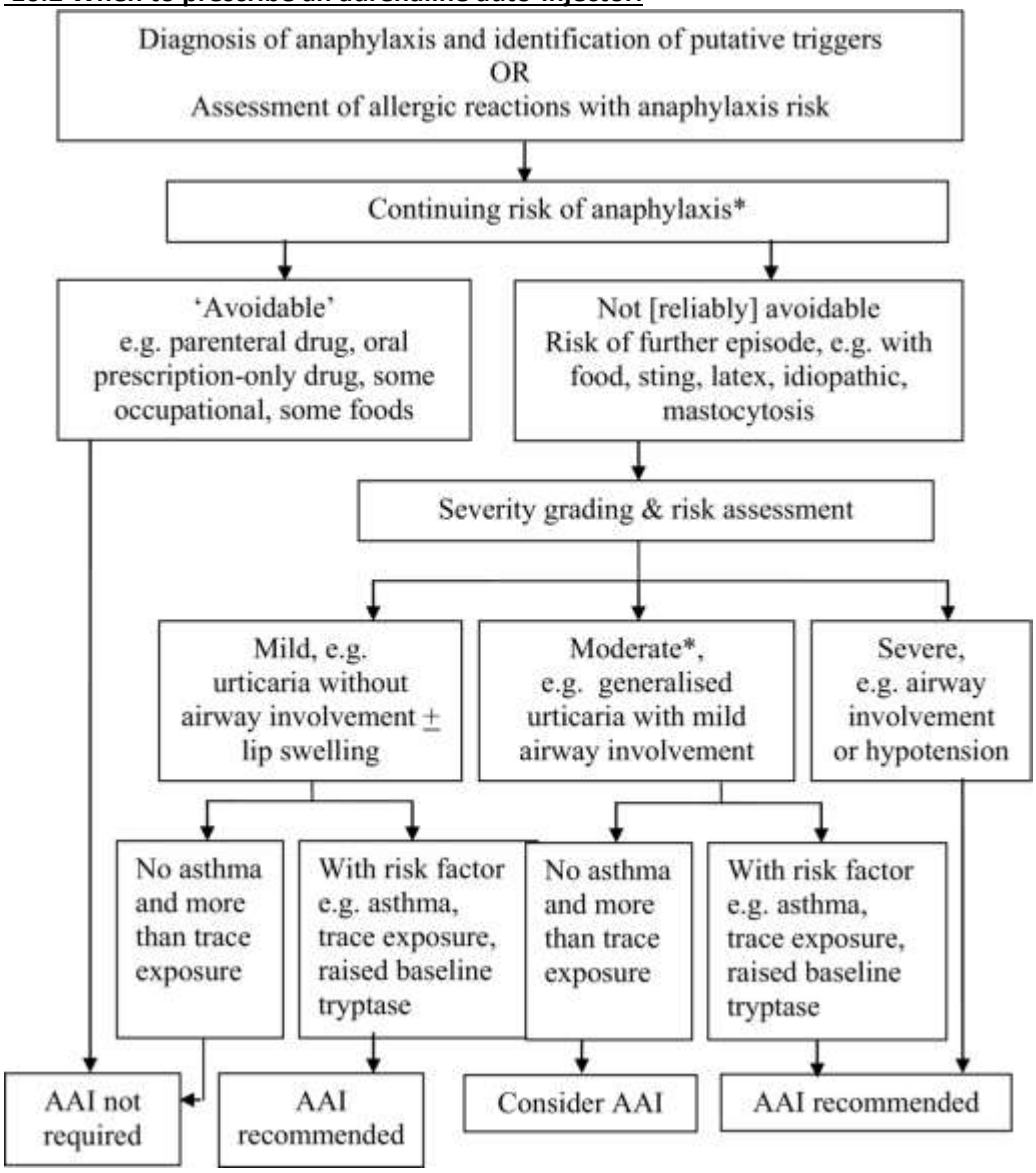
- >12 years: 500 micrograms IM (0.5 mL) i.e. same as adult dose
- 6 – 12 years: 300 micrograms IM (0.3 mL)
- < 6 years: 150 micrograms IM (0.15 mL)

Recent international guidelines suggest the following

When **using adrenaline auto-injectors**,

- patients weighing between 7.5-25 kg should receive a 0.15 mg (150 microgram) dose
- Patients weighing between 25-30 Kg should receive 0.3 mg (300 microgram) dose.
- There are no data to inform us which patients should receive a 0.5 mg dose auto-injector, if this is available. The adrenaline dose can be repeated after at least a 5 minute interval .
- Higher dose of 500 microgram is better provided by Health care professionals) .Patients who require repeated intramuscular doses of adrenaline may benefit from an adrenaline infusion
- Adrenaline infusion must be given by those experienced in the use of vasopressors in their daily clinical practice, for example anesthetists, ED and critical care doctors. Intravenous adrenaline in patients with adequate circulation may cause life-threatening hypertension, myocardial ischemia, and arrhythmias.
- Patients who are given intravenous adrenaline should be monitored with continuous ECG, pulse oximetry and requent non-invasive blood pressures.

10.2 When to prescribe an adrenaline auto-injector.



Higher or lower doses may be necessary in some cases depending on weight of child and adolescent.

10.3 Generic Anaphylactic Kits (AKs) / Autoinjectors for practice use

It is each nurses/practices/pharmacists/dentists individual responsibility to ensure that they have an *in date* anaphylactic kit for use in practice, nursing homes, during home visits and other potential emergency locations. The choice of product to be used is at the discretion of the professional but consideration should be given to the ease of access and use in an emergency situation.

Initial stock will need to be purchased, however if the medication is used for a patient then a prescription may be issued to replace stock in the case of an autoinjector.

10.4 Adrenaline Auto-Injectors (AAIs)

There are three licensed devices currently available for the treatment of anaphylaxis with a range of needle length, expiry date and mode of action as detailed in **Table 1** below.

- Prescribe by brand name. Check which AAI was initiated by hospital (the product of choice for BTUH is currently Epipen).
- If clinicians want to switch to an alternative AAI then patients must be shown how to self-inject as devices vary in their mode of action.
- MHRA advice (2017) is that patients carry two AAIs with them at all times in cases of severe anaphylactic reaction or if the first dose is incorrectly administered. This advice is based on the European Medicines Agency review of EU available AAIs (2015).
- For most patients GPs are therefore advised to prescribe two AAIs.
- GPs are currently advised to prescribe a maximum of two AAIs for children.
- Encourage people with allergies and their carers to obtain and practise using a trainer device (available for free from the manufacturers' websites)
- Use the injection as soon as possible if anaphylaxis is suspected.
- Removal of clothing may not be an option. The ideal would be to use on bare skin, but if that is not possible the injection should not be withheld. Evidence has shown that AAIs are not affected by the presence of clothing including jeans.
- There is a risk of overdosing small children with a body weight under 15kg with an auto-injector so this use is unlicensed.
- Auto-injector dose for infants and children

  The BNF lower cut-off for the junior strength auto- injector is a weight of 15 kg, but there are infants < 15 kg at risk of anaphylaxis who require an adrenaline auto-injector. A practical approach taken by specialists is to recommend the junior auto-injector(0.15 mg adrenaline) from age six months. This is supported by Simons, for children weighing > 7.5 kg if there is a high risk of accidental exposure [54]. Below this age, avoidance should be possible and cover most of those at risk. The auto-injector containing 0.3 mg can be used in a child over 30 kg, as well as adults.(BSACI guideline)

10.5 What are the different stages of intervention in anaphylaxis

Recommendation	Evidence level	Grade	Key references
FIRST-LINE INTERVENTION: ADRENALINE			
Adrenaline is potentially life-saving and must therefore promptly be administered as the first-line treatment for the emergency management of anaphylaxis.	IV	C	22, 45, 46, 63, 64
Earlier administration of adrenaline should be considered on an individual basis when an allergic reaction is likely to develop into anaphylaxis.	V	D	Expert consensus
Adrenaline should be administered by intramuscular injection into the mid-outer thigh.	I	B	65, 66
In patients requiring repeat doses of adrenaline, these should be administered at least 5 minutes apart	V	D	66 expert consensus
With inadequate response to 2 or more doses of intramuscular adrenaline, adrenaline may be administered as an infusion by appropriately experienced intensive care, emergency department and critical care physicians, with appropriate cardiac monitoring.	IV	D	64
SECOND-LINE INTERVENTIONS			
Trigger of the anaphylaxis episode should be removed.	V	D	Expert consensus
Help should be called promptly and simultaneously with patient's assessment.	V	D	Expert consensus
Patients experiencing anaphylaxis should be positioned supine with elevated lower extremities if they have circulatory instability, sitting up if they have respiratory distress and in recovery position if unconscious.	V	D	45
High flow oxygen should be administered by face mask to all patients with anaphylaxis.	V	D	Expert consensus
Intravenous fluids (crystalloids) should be administered (boluses of 20 ml/kg) in patients experiencing cardiovascular instability.	V	D	Expert consensus
Inhaled short-acting beta-2 agonists should additionally be given to relieve symptoms of bronchoconstriction.	V	D	22
THIRD-LINE INTERVENTIONS			
Oral H1- (& H2)-antihistamines may relieve cutaneous symptoms of anaphylaxis.	I	B	73, 74
Systemic glucocorticosteroids may be used as they may reduce the risk of late phase respiratory symptoms. High dose nebulized glucocorticoids may be beneficial for upper airway obstruction.	V	D	Expert opinion
MONITORING AND DISCHARGE			
Patients who presented with respiratory compromise should be closely monitored for at least 6-8 hours and patients who presented with circulatory instability require close monitoring for 12-24 hours.	V	D	Expert opinion
Before discharge, the risk of future reactions should be assessed and an adrenaline auto-injector should be prescribed to those at risk of recurrence.	V	D	Expert opinion
Patients should be provided with a discharge advice sheet, including allergen avoidance measures (where possible) and instructions for the use of the adrenaline auto-injector. Specialist and food allergy specialist dietitian (in food anaphylaxis) follow-up should be organized. Contact information for patient support groups should also be provided.	V	D	Expert opinion

10.6 Device failure

If there is failure of the device due to inability to administer, there is no evidence or reason to believe that the patient will be able to correctly administer a second device. Inherent device failure is extremely rare. User error rather than device failure is often to blame and reflects inadequate training. The solution is to train and retrain patients correctly rather than gaining false security by prescribing more devices. Training will increase patient safety.

Table 1: Comparison of licensed adrenaline auto-injectors

Product	Mode of action	Needle Length (mm)	Expiry Date (months)	Price Sept 2017 (£)	Patient Support
EpiPen® Junior Auto-Injector 0.15 milligram	Swing and jab	13	20 (from manufacturer)	26.45	Expiry date reminder - email/SMS; simulator pen; demonstration video on website; web support
EpiPen®Auto-Injector 0.3 milligram	Swing and jab	16	20 (from manufacturer)	26.45	Expiry date reminder - email/SMS; simulator pen; demonstration video on website; web support
Jext® 0.15 milligram solution for injection in pre-filled pen	Place and press	13	18	23.99	Expiry date reminder - email/SMS; simulator pen; mobile phone app; demonstration video on website; web support
Jext® 0.3 milligram solution for injection in pre-filled pen	Place and press	15	18	23.99	Expiry date reminder - email/SMS; simulator pen; mobile phone app; demonstration video on website; web support
Emerade® 0.15 milligram solution for injection in pre-filled pen	Place and press	16	18	25.99	Expiry date reminder – email; simulator pen; demonstration video on website; web support
Emerade® 0.3 milligram solution for injection in pre-filled pen	Place and press	25	18	25.99	Expiry date reminder – email; simulator pen; demonstration video on website; web support
Emerade® 0.5 milligram solution for injection in pre-filled pen*	Place and press	25	18-	26.99	Expiry date reminder – email; simulator pen; demonstration video on website; web support

**Only licensed 0.5 milligram product*

There are concerns that, owing to the increasing obesity (BMI ≥30) of the population in the UK, the needle lengths in the currently licensed AAIs are not adequate to deliver the dose of adrenaline to the muscle tissue of the thigh. This is a particular problem in females in whom the skin to muscle distance is more frequently longer than the exposed length of the needle of some of the currently available AAIs.

The length of needle and available dose range of Emerade® may provide potential advantages but if a patient is given a new device it is essential that the patient is trained and provided with information on how to use the device. For most of the paediatric patients Epipen with a needle length of 18mm should be adequate.

Patients should only be issued with a different device if their current stock has expired or been used and patients are fully involved in the decision and rationale for changing the device and have demonstrated they can use the new AAI.

10.7 Assessment and Referral after Emergency Treatment

After emergency treatment for suspected anaphylaxis, offer people a referral to a specialist allergy service (age-appropriate where possible) consisting of healthcare professionals with the skills and competencies necessary to accurately investigate, diagnose, monitor and provide on-going management of, and patient education about anaphylaxis.

Practices should also:

- Record as per practice guideline on a Significant Incident (SI) form.
- Record the acute clinical features of the suspected anaphylactic reaction (rapidly developing, life-threatening problems involving the airway [pharyngeal or laryngeal oedema] and/or breathing [bronchospasm with tachypnoea] and/or circulation [hypotension and/or tachycardia] and in most cases, associated skin changes).
- Record the time of the reaction.

- Record the circumstances immediately before the onset of symptoms to help identify the possible trigger.
- Any adrenaline injection and any other treatment that is administered must be entered into the patients' record.
- If a medicine is involved, a yellow card, must be filled in and sent to the Medicines and Healthcare products Regulatory Agency using the online reporting mechanism at: https://yellowcard.mhra.gov.uk/

11. Storage and Handling of Adrenaline

- The expiry dates on adrenaline must be checked regularly. This is printed on the box. If it is out of date it loses its effectiveness.
- Do not break the seal of the pack until you need to use it.
- Order at least 6 weeks prior to expiry dates for anaphylaxis kits – as if not already in stock, it can take that long to get it.
- Anaphylaxis kits are sealed. **If opened, do not use**. Do not add anything to the pack.
- Protect from heat, light and moisture. It is not necessary to store the pack in the refrigerator, but this will cause no harm if it is.
- If it has been left in the heat for a long time, get it renewed before its expiry date (i.e. half way through). If it has been frozen, do not use, return straight away and order a new one.
- Avoid prolonged exposure to raised temperature (e.g. storing the pack in the car boot in the summer).
- Used or expired injections should be disposed of safely:

AK: Remove all ampoules of adrenaline and needles and place into a proper puncture resistant sharps container- the container should be clearly identified and in accordance with BS7320.
AAI: Patient should be advised to return used or expired injections to their pharmacy for safe disposal.

12. Side-effects

Adrenaline does have side effects, mainly on the heart and include:

- Trembling
- Arrhythmias
- Anxiousness

These are normal effects of adrenaline and soon wear off. Other side-effects include headache, cold extremities; also hypertension (risk of cerebral haemorrhage) and pulmonary oedema (on excessive dosage or extreme sensitivity); nausea, vomiting, weakness, dizziness and hyperglycaemia also reported.

13. Cautions and Contraindications

Adrenaline may be administered in life threatening anaphylactic reactions, even when the following relative contraindications are present: coronary artery disease, uncontrolled hypertension, serious ventricular arrhythmias and second stage of labour.

14. Drug Interactions

- *Beta-blockers* (including eye drops) can antagonise the response to adrenaline and increase the severity of an anaphylactic reaction.

Non selective beta-blockers (i.e propranolol) can markedly increase the hypertensive effects of adrenaline. A severe and potentially life-threatening hypertensive reaction and/or marked bradycardia can develop.

- Patients taking *tricyclic antidepressants* are at an increased risk of hypertension and arrhythmias with adrenaline.
- Patients who are taking *monoamine oxidase inhibitors* are considerably more susceptible to arrhythmias with adrenaline.

15. When to stop adrenaline auto-injector prescription

There are situations when prescription of an AAI is no longer required. This will require explanation with the patient, as this may present difficulties for the patient and doctor. These include the following:

• Resolution, for example, of food allergy;
• After successful venom immunotherapy (maintenance dose tolerated) if no other risk factors;
• When initial prescription was inappropriate;
• When the initial diagnosis has been clarified, and the identified triggers show that an AAI is not Required.

16. Idiopathic anaphylaxis- It is a rare life-threatening disorder with symptoms similar to other forms of anaphylaxis. There is lack of a robust evidence base underpinning the treatment of anaphylaxis and even less so for idiopathic anaphylaxis. Much of the evidence therefore comes from relatively small case series and expert opinion.

It is a diagnosis of exclusion, requiring a thorough history and careful diagnostic work-up investigating possible triggers and underlying predisposing factors. Key diagnostic tests include skin-prick testing, tests for specific-IgE, component-resolved diagnostics, and in some cases for allergen challenge tests.

Other recognized causes of anaphylaxis, such as foods, medications, insect stings, latex, and exercise, should all be considered, as should differential diagnoses such as asthma.

While the cause of idiopathic anaphylaxis remains unknown, prompt treatment with intramuscular epinephrine (adrenaline) is associated with good prognosis. There may also be a role for H1-antihistamines and corticosteroids as second-line agents. Patients need to be carefully monitored for signs of deterioration and/or a possible protracted or biphasic reaction.

Patients with frequent episodes of anaphylaxis (e.g., six or more episodes/year) should be considered for preventive therapy, which may include corticosteroids, H1- and H2-antihistamines, and, in some cases, mast cell stabilizers such as ketotifen.

Alternative immune-suppressants (e.g., methotrexate) and anti-IgE (omalizumab) may rarely also need to be considered. In many cases, the frequency of anaphylaxis declines such that regular use of corticosteroids can be discontinued after 9–12 months. Pediatric patients should be treated with similar regimens as adults, but with appropriate dose adjustments. Patients should carry their self-injectable epinephrine and other emergency medications at all times in order to deal with emergency situations.

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