FIRST TYPE HYPERSENSITIVITY REACTIONS. ANAPHYLACTIC SCHOCK

Assoc. Prof. Vanya Tsvetkova PhD

Important Items

Atopy - genetic predisposition of an individual to produce high quantities of IgE in response to allergens in the environment

Allergic and atopic disorders involve exaggerated immune responses to foreign antigens

Important Items

Type I reactions (immediate hypersensitivity) are IgE-mediated

Antigen binds to IgE that is bound to tissue mast cells and blood basophils, triggering release of preformed mediators and synthesis of other mediators

These mediators cause vasodilation, increased capillary permeability, mucus hypersecretion, smooth muscle spasm, and tissue infiltration with eosinophils, type 2 helper T (T_H2) cells, and other inflammatory cells.

Type I reactions underlie atopic disorders

Allergic asthma

Allergic rhinitis

Allergic conjunctivitis

Anaphylaxis

Angioedema

Urticaria

Conclusion

All atopic disorders are type I hypersensitivity disorders

Type I reactions develop < 1 h after exposure to antigen.

Genetic factors

Familial inheritance of disease

Association between atopy and specific HLA loci

polymorphisms of several genes:

- high-affinity IgE receptor β-chain,
- IL-4 receptor α-chain,
- metalloprotease domain 33 (*ADAM33*)

Anaphylactic Shock

Definition

acute potentially life-threatening

rapid in onset

previously sensitized individuals

severe multi-systemic hypersensitivity

Etiology

Drugs

Food

Idiopathic Hormones

Stinging insects

Exercise

Latex –rare

In up to 20%, the elicitor is not identified

Etiology

For ED

- drugs and foods are the most common elicitors of Anaphylaxis

- age-related

Allergy 69 (2014) 1026–1045

Epidemiology

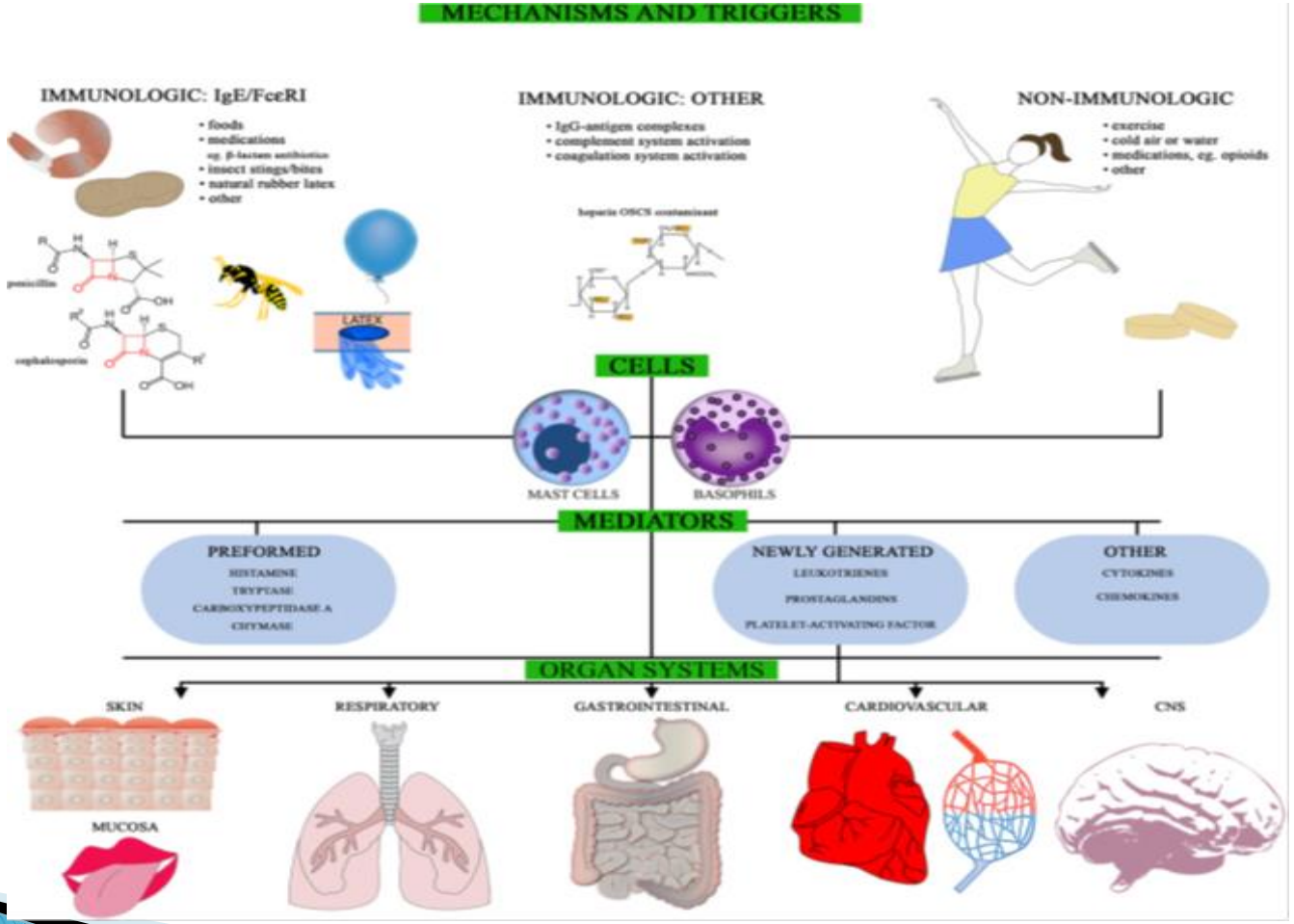
In Europe

1.5–7.9 per 100 000 person-years

Prevalence 0.3%

Foods are the most frequent cause of anaphylaxis in children, with pollen allergy and asthma being important risk factors

Pathophysiology



Risk factors

- Lifestyle factors

physical exertion

alcohol

- Drugs

NSAID

ACE inhibitors

b-blockers

- Patient-specific factors

adolescence, advanced age, and sex

infections

hormonal status

psychogenic stress

- Pre-existing conditions

asthma and other IgE-dependent diseases

mastocytosis and/or increased basal tryptase

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Clinical presentation

Symptoms and signs of anaphylaxis usually occur within 2 h of exposure to the allergen

Median time from symptoms to fatality

- Food 30 min
- Insect venom 15
- Parenteral medication 5 min

Symptoms

Cardiovascular system – drop of blood pressure, week and rapid pulse

Respiratory system – expiratory dyspnea of bronchospasm
inspiratory dyspnea of angioedema

Digestive system - nausea, vomiting, diarrhea, cramps

Skin – hives, itching, angioedema, flushing, swelling – occur in most cases

Symptoms

Eyes – itching, tearing, redness, swelling around eyes

Lung and throat – difficulty breathing, coughing, change in voice, throat swelling and itching

Nose and mouth – sneezing, runny nose, nasal congestion, swelling of the tongue, metallic taste

Nervous system – anxiety, confusion

Clinical Forms

Sudden – 5-10 minutes after allergen exposure

Rapid – 30 minutes after allergen exposure

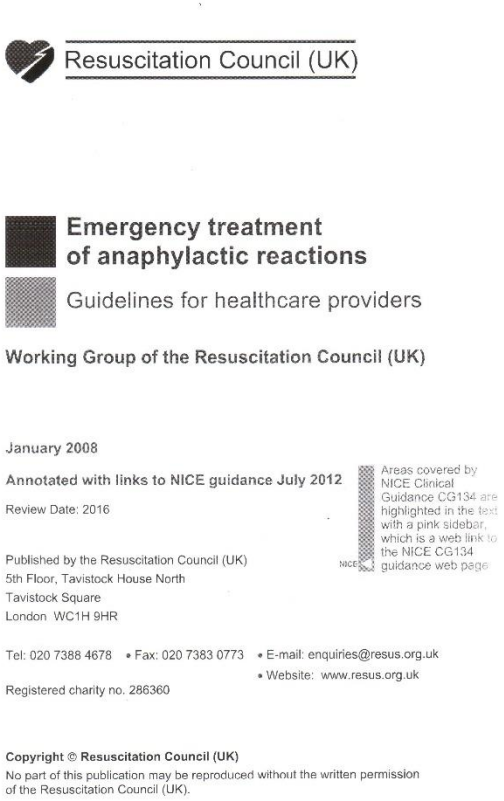
Delayed – several hours after allergen exposure

Idiopathic – unknown reason

Prolonged – continuing to more than 24 hours

Biphasic – 4-12 hours after initial improvement-relapse

Emergency treatment of anaphylactic reactions-guidelines



Resuscitation Council (UK)

Emergency treatment of anaphylactic reactions

Guidelines for healthcare providers

Working Group of the Resuscitation Council (UK)

January 2008

Annotated with links to NICE guidance July 2012

Review Date: 2016

Areas covered by NICE Clinical Guidance CG134 are highlighted in the text with a pink sidebar, which is a web link to the NICE CG134 guidance web page

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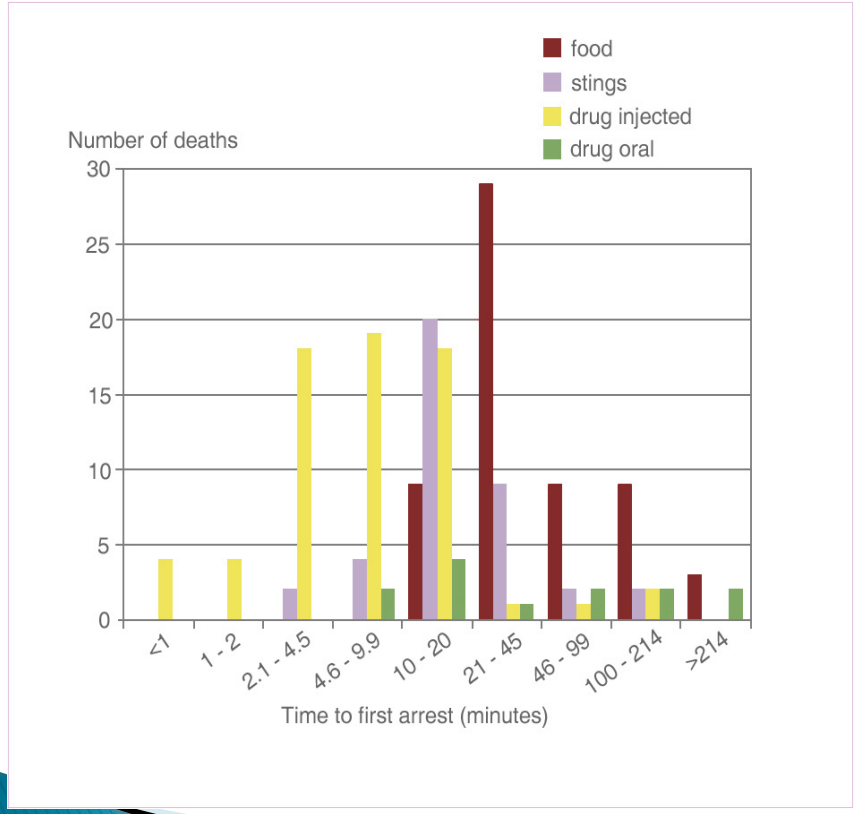
Time to cardiac arrest



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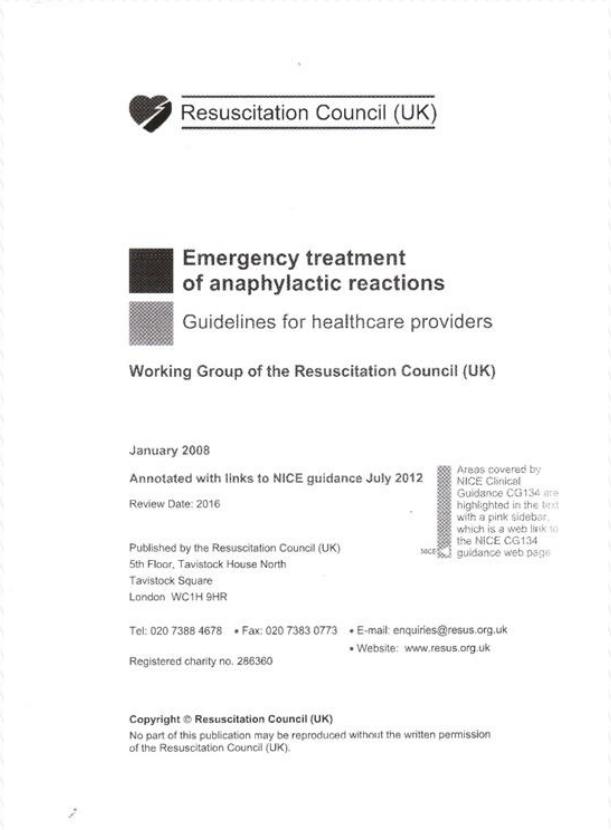
Remember

- Skin or mucosal changes alone are not a sign of an anaphylactic reaction
- Skin or mucosal changes can be subtle or absent in up to 20% of reactions (some patients can have only a decrease in blood

pressure i.e., a circulation problem)

- There can also be gastrointestinal

symptoms (e.g. vomiting, abdominal pain,incontinence)



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Airway problems

- Airway swelling e.g. throat and tongue swelling
- Difficulty in breathing and swallowing sensation that throat is ‘closing up’
- Hoarse voice
- Stridor

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Breathing problems

- Shortness of breath
- Increased respiratory rate
- Wheeze
- Patient becoming tired
- Confusion caused by hypoxia
- Cyanosis (appears blue) – a late sign
- Respiratory arrest

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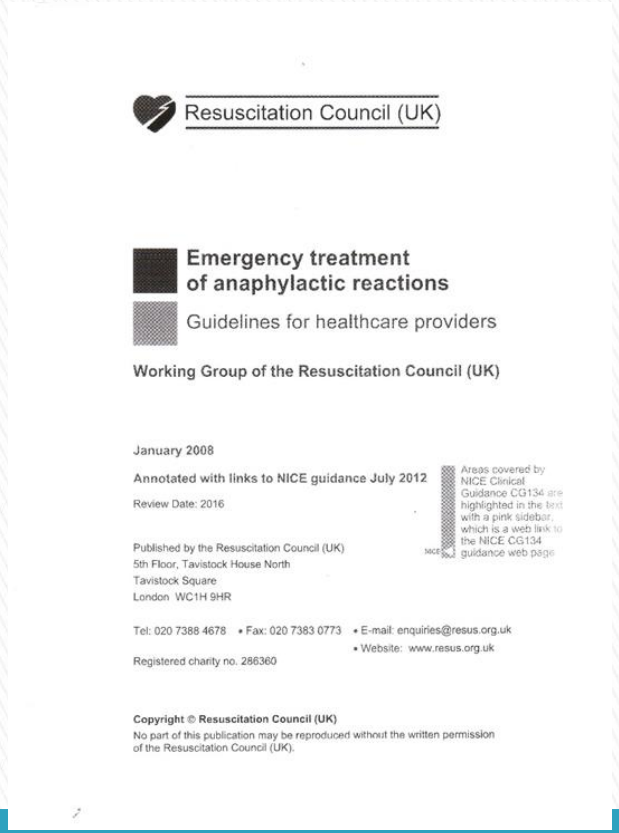
Circulation problems

- Signs of shock – pale, clammy
- Increased pulse rate (tachycardia)
- Low blood pressure (hypotension)
- Decreased conscious level
- Myocardial ischaemia / angina
- Cardiac arrest

DO NOT STAND PATIENT UP



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Disability

- Sense of “impending doom”
- Anxiety, panic
- Decreased conscious level caused by airway, breathing or circulation problem

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Exposure – look for skin changes

- Skin changes often the first feature
- Present in over 80% of anaphylactic reactions
- Skin, mucosal, or both skin and mucosal changes

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Exposure – look for skin changes

- Erythema – a patchy, or generalised, red rash
- Urticaria (also called hives, nettle rash, weals or welts) anywhere on the body
- Angioedema - similar to urticaria but involves swelling of deeper tissues e.g. eyelids and lips, sometimes in the mouth and throat

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Diagnosis

Based upon multi-system symptoms occurring suddenly after exposure to a potential trigger

Target organs involved: skin, respiratory tract, gastrointestinal tract, heart and vasculature, CNS

Laboratory findings: histamine, increased serum tryptase during the first three hours

Differential Diagnosis

- Skin or mucosal

chronic remittent or physical urticaria and angioedema

pollen food syndrome

- Respiratory diseases

acute laryngotracheitis

tracheal or bronchial obstruction (e.g., foreign substances,

vocal cord dysfunction)

status asthmaticus (without involvement of other organs)

- Cardiovascular diseases

vasovagal syncope

pulmonary embolism

myocardial infarction

cardiac arrhythmias

hypertensive crisis

cardiogenic shock

Allergy 69 (2014) 1026–1045

Differential Diagnosis

- **Pharmacological or toxic reactions**

Ethanol histamine, e.g. scombroid fish poisoning

opiates

- **Neuropsychiatric diseases**

hyperventilation syndrome

anxiety and panic disorder

somatoform disorder (e.g., psychogenic dyspnea, vocal cord dysfunction)

dissociative disorder and conversion (e.g., globus hystericus)

epilepsy

cerebrovascular event

psychoses

artifact (factitious disorder)

- Hoigne's syndrome
- Coma, e.g. metabolic, traumatic

Allergy 69 (2014) 1026–1045

Differential Diagnosis

- **Endocrinological diseases**

hypoglycemia

thyrotoxic crisis

carcinoid syndrome

vasointestinal polypeptide tumors

pheochromocytoma

Allergy 69 (2014) 1026–1045

Differential Diagnosis

Acute generalized hives

Severe asthma attack

Heart attack

Panic attack

Food poisoning

Cerebrovascular events

Fforeign body aspiration

Acute generalized hives

An itchy rash which can affect any area of skin

Small raised areas called wheals - 1-2 cm

Each wheal is usually red surrounded by red area called – flare

The wheals are often circular

Severe asthma attack

A sudden worsening of asthma symptoms caused by bronchospasm

Difficult breathing

Wheezing

Coughing

Acute exacerbations of asthma require urgent treatment to prevent a serious outcome

Heart attack

Usually occur as a result of coronary heart disease

Due to atherosclerosis

Severe spasm of coronary artery

Can lead to heart failure or life-threatening of arrhythmias

Panic attack

A sudden outburst of anxiety and fear

Often, there is no clear reason for the attack

A panic attack may be a one-time occurrence, but many people experience repeat episodes

Food poisoning

Reasons

Bacteria	**Parasites**	**Viruses**
E. Coli	Toxoplasma	Norovirus
Listeria Salmonella		Sapovirus
		Rotavirus
		Astrovirus

Food poisoning

Symptoms

abdominal cramps
diarrhea
vomiting
loss of appetite
mild fever
weakness
nausea
headaches

Cerebrovascular events

"Brain attack" is an acute CNS injury due to reduction or absence of perfusion to a territory of the brain

Ischemic stroke

Hemorrhagic stroke

Transient ischemic attack

Foreign body aspiration

In infants

One of the most important clinical causes of dyspnea

Symptoms

Hurried respiration

Progressive swelling of face, neck, and anterior chest wall

Tachypnea

Cough

Patient-specific risk factors

Age related factors

Infants

Teenagers and young adults

Pregnancy

Elderly

Patient-specific risk factors

Comorbidities

Vision or hearing impairment

Neurologic disorders, psychiatric disorders, autism

Severe allergic rhinitis and eczema, asthma, chronic obstructive pulmonary disease

Other respiratory diseases, cardiovascular diseases

Patient-specific risk factors

Concurrent medications

diphenhydramine, chlorpheniramine

b-adrenergic blockers, angiotensin-converting enzyme inhibitors

Various

exercise, exposure to extremes of temperature or humidity

acute infection, emotional stress, aspirin or other nonsteroidal anti-inflammatory medications

Emergency management

First-line intervention

Adrenaline

Second-line interventions

- Trigger of the anaphylaxis episode should be removed

- Patients should be positioned supine with elevated lower extremities- Trendelenburg position

- High-flow oxygen should be administered by face mask– 4-6 l/min

- Intravenous fluids (crystalloids) should be administered (boluses of 20 ml/kg) in patients experiencing cardiovascular instability

- Inhaled short-acting beta-2 agonists should additionally be given to relieve symptoms of bronchoconstriction

Emergency management

Third-line interventions

- Oral H1- (and H2)-antihistamines
- Systemic glucocorticosteroids to reduce the risk of late-phase respiratory symptoms
- High-dose nebulized glucocorticoids for upper airway obstruction
- Monitoring and discharge:

Patients who presented with respiratory compromise should be closely monitored for at least 6–8 h

Patients who presented with circulatory instability require close monitoring for 12–24 h

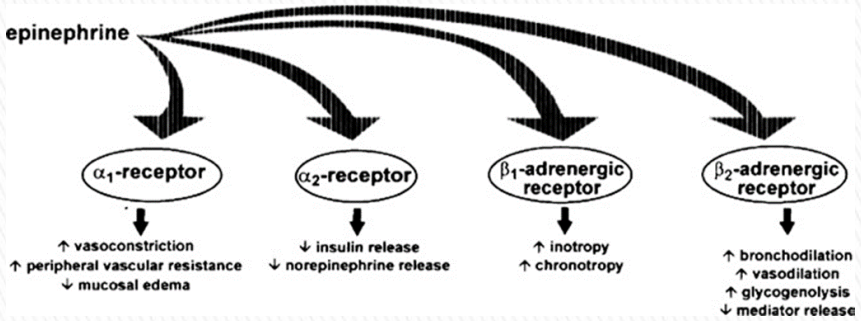
- Before discharge, the risk of future reactions should be assessed and an adrenaline auto-injector should be prescribed to those at risk of recurrence

Anaphylaxis: guidelinesfrom the European Academy of Allergy and Clinical Immunology. Allergy 2014; 69: 1026–1045.

Adrenaline

A drug with combined a and β agonist actions which result in

- peripheral vasoconstriction, thereby reversing hypotension and mucosal edema
- increased rate and force of cardiac contractions, thereby reversing hypotension
- reversal of bronchoconstriction and reduction in the release of inflammatory mediators



Adrenaline

There are no absolute contraindications to treatment with adrenaline in a patient experiencing anaphylaxis

Benefits outweigh the risks in the elderly and patients with pre-existing cardiovascular disease

Adrenaline should be given by intramuscular injection into the mid-outer thigh

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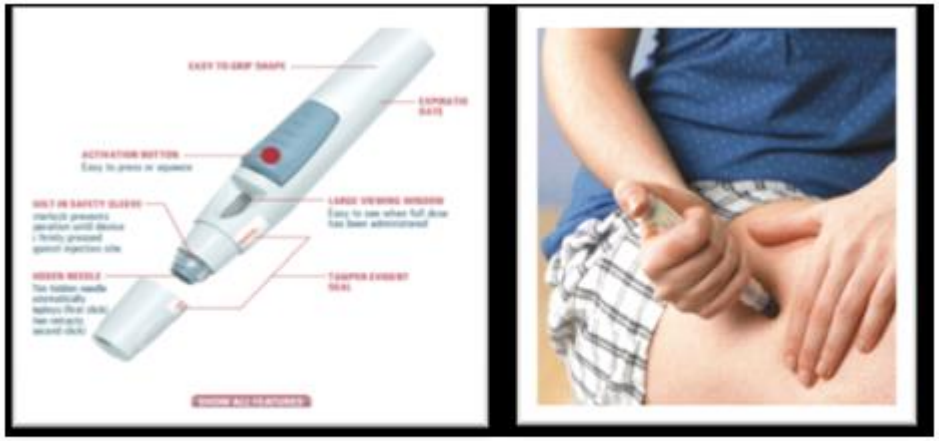
Adrenaline



Design of auto-injector

Administration of auto-injector

Adrenaline – Intra-muscular

- IM doses of 1:1000 adrenaline (repeat after 5 min if no better)
- Adult or child more than 12 years: 500 micrograms IM (0.5 mL)
- Child 6 -12 years: 300 micrograms IM (0.3 mL)
- Child 6 months - 6 years: 150 micrograms IM (0.15 mL)
- Child less than 6 months: 150 micrograms IM (0.15 mL)

- Adrenaline can be repeated every 5 minutes if required. The initial dose for adults is 0.25-0.5 ml i.m. for those weighing less than 50 kg and 0.5 ml for those weighing more than 50 kg

- In case of treatment refractoriness – adrenaline 1

ml, 0,1% in saline - 500 ml -intravenously

For use by experts only Monitored patient

- IV fluids to rise blood pressure – 1500 ml

Fluids

Once IV access established

- 500 – 1000 mL IV bolus in adult
- 20 mL/Kg IV bolus in child
- Monitor response - give further bolus

as necessary

- Colloid or crystalloid (0.9% sodium chloride or Hartmann's)
- Avoid colloid, if colloid thought to have caused reaction

Second line drugs

Methylprednisolone 1-2 mg/kg every 6- 8 hours

H1 antagonist - intravenously every 8 hours

H2 antagonist- intravenously every 8 hours

Glucagon- patients who are unresponsive to adrenaline, particularly in those taking beta-blockers

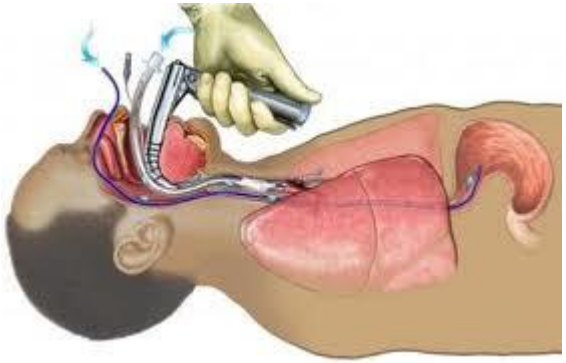
Auto-injectors

- For self-use by patients or carers
- Should be prescribed by allergy specialist
- For those with severe reactions and difficult to avoid trigger
- Train the patient and carers in using the device
- Practice regularly with a trainer device
- Rescuers should use these if only adrenaline available

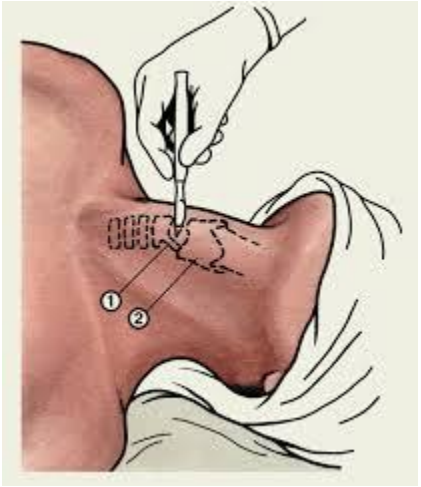
Monitoring of vital signs

Next steps

Intubation



Crycothyrotomy



Blood pressure remains low – dopamine (dobutamine) – 15-20 mcg/min/kg

Patients treated with beta blockers – glucagon 1-3 mg intravenously

Six hours later – CS, H1 and H2 blockers again to escape symptom recurrence

Prevention

Avoid the responsible allergen

Keep an adrenaline kit and H1 antagonist at all times

Wear medic alert bracelets

Venom immunotherapy is highly effective in protecting insect-allergic patients

Prophylaxis

Scratch tests before treatment with antibiotics

Scratch tests with anesthetics and myorelaxants prior to surgery

Scratch tests with contrast media in case of X-ray investigation of patients reporting iodine allergy

Immunotherapy with specific allergens to insects, indoor allergens and pollens

How should be treated atopic patients before surgery or X-Ray investigation

Prior to general anaesthesia: H1 blocker for 48-72 hours per os
1 tablet daily with/without CS – 40 mg/day

Methylprednisolone – 40-100 mg intravenously two hours before surgery/contrast application

H1 blocker – 1 amp. Intramuscular 1 hour before surgery/contrast application

Thank you