

Anaphylaxis: an emergency physician's perspective

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Anaphylactic reaction is a common problem encounter by the emergency physician. Although the drug treatment and management of anaphylaxis had been well published in the literature, the emergency management of anaphylaxis is still unsatisfactory. Severe anaphylactic reaction and death is not uncommonly reported. This article reviews the pathophysiology, aetiology, clinical manifestation, diagnostic approach, management algorithm and prevention of anaphylaxis with particular emphasis on the emergency physician's perspective. The clinical manifestation of anaphylaxis is significantly variable in terms of severity, onset and progression, which imposed a diagnostic challenge to emergency physician. An awareness that severe anaphylaxis can be rapidly fatal is essential for those working in the emergency room. Life threatening clinical features such as laryngeal oedema, bronchospasm and circulatory collapse must be recognize early and treated aggressively as favourable prognosis is well documented. The key to success in managing anaphylaxis emergency depends on the early recognition of anaphylaxis reaction, initial assessment, anticipation of deterioration and finally prompt and aggressive support of airway, oxygenation, ventilation and circulation. Adrenaline is the cornerstone of the treatment modality in anaphylaxis. This is currently underused, although, it is safe and almost always effective. At last prevention of subsequent episode of anaphylaxis should be considered a priority for emergency physician before discharging patient. (*Hong Kong j.emerg.med.* 2002;9:34-41)

Keywords: Anaphylaxis, diagnosis, emergency, management, prevention

Introduction

Anaphylaxis and anaphylactic death is increasingly common over the past few decades. It particularly affect young adults and children. The treatment of anaphylaxis presented a special diagnostic and therapeutic challenge to the emergency physician because of its variable presenting symptoms, its rapid onset and severity. Anaphylaxis is easily treatable provided early recognition and aggressive treatment is implemented. Patient can make a complete recovery even when they present in critical state initially. However, anaphylaxis continues to be poorly managed

even though the drug treatment and management plan had been widely published in the literature. Doctors working in the Accident and Emergency department must know how to deal with anaphylactic emergency and provide advice to prevent further recurrences.

What is the definition of anaphylaxis?

Anaphylaxis and anaphylactoid reactions lack a universally accepted definition. The term anaphylaxis is typically applied to an immediate systemic reaction caused by rapid, IgE-mediated immune release of potent mediators from tissue mast cells and peripheral blood basophils. Anaphylactoid reactions are immediate systemic reaction that mimic anaphylaxis but are not caused by IgE-mediated immune responses.^{1,2} The temporal occurrence of these reactions is usually immediate but may be delayed depending on the route of exposure. The

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manifestations and management of anaphylactic and anaphylactoid reactions are similar so that the distinction is unimportant in relation to the treatment of acute attack. This difference is relevant only when investigations are being considered. For simplicity the term anaphylaxis is used here for both reactions.

Clinically anaphylaxis means a severe systemic allergy reaction, consisting of a constellation of features. Argument arises when considering which are the essential features. Anaphylaxis can present as life threatening airway obstruction and shock. It can also present as minor urticaria and itchiness. Anaphylactic reactions vary in severity and progress may be rapid, slow or biphasic.³ The lack of any consistent clinical manifestation and wide range of possible presentations add diagnostic difficulty when managing patient with acute anaphylaxis. A good working definition is that it involves one or both of two severe features: respiratory difficulty (which may be due to laryngeal oedema or asthma) and hypotension (which can be presented as fainting, collapse, or loss of consciousness).⁴

Epidemiology

The exact annual incidence of anaphylactic reaction in Hong Kong is unknown. In US it is estimated that the annual incidence was 30 per 100,000 population.⁵ A recent study in the United Kingdom reported a frequency of 1 of every 2300 attendees at a hospital emergency department.⁶ The annual international incidence of fatal anaphylactic reactions was about 154 per 1 million hospitalized patients per year.⁷

Pathophysiology

The basic mechanism of allergy reaction is mast cell degranulation and mediators (including histamine, prostaglandin, thromboxane, leukotrienes, etc.) release. The cause of mast cell degranulation include IgE cross-linking, complement activation, nonimmunologic or direct activation, modulation of arachadonic acid metabolism, exercise, catamenial effects and idiopathic cause.⁸ The classical Type I hypersensitivity reaction involved an allergen with

specific IgE antibodies which bound to the Fc receptor on the mast cells and basophils which trigger the rapid synthesis of mediators. These mediators cause capillary leakage and mucosal oedema resulting in shock and asphyxia. The Table 1 summarizes the physiological effect and clinical expression of mediator's release.⁴

Aetiology

A number of allergens had been reported as the cause of anaphylaxis. Foods and additives, drugs and latex rubber are the most common cause of allergy reaction. The Table 2 summarizes the common causes of allergy reaction.

Clinical features of anaphylaxis

The major sites involved in anaphylaxis in the body are cutaneous, respiratory, cardiovascular and

Table 1. Effect of mast cell mediators.

<i>Physiological effect</i>	<i>Clinical expression</i>	<i>Danger</i>
<i>Capillary leakage</i>	Urticaria	
	Angio-oedema	
	Laryngeal oedema	Asphyxia
	Hypotension	Shock
<i>Mucosal oedema</i>	Laryngeal oedema	Asphyxia
	Rhinitis	
	Asthma	Respiratory arrest
<i>Smooth muscle Contraction</i>	Asthma	Respiratory arrest
	Abdominal pain	

Table 2. Common causes of anaphylaxis.

<i>Foods and additives</i>	<i>Drugs</i>
Nuts	NSAID
Shellfish	Antibiotic
Egg	Aspirin
Milk	Intravenous contrast dye
Monosodium glutamine	Intravenous anaesthetic agent
Soybean	
Sesame	<i>Others</i>
Fish	Latex rubber
Peanut	Hymenoptera stings
	Insect parts and molds

gastrointestinal system. The severity of allergy reaction vary from mild to life threatening airway obstruction. Significant variation in the initial symptoms and signs exist. The clinical expression depends on the route, quantity and the rate of antigenic exposure. In general parental antigen exposure results in more rapid onset and progression, more severe reaction than topical and oral exposures. Most anaphylaxis reaction occur within minutes of exposure, however, delay or biphasic reaction had been reported.³

The following is a summary of the clinical feature of anaphylaxis⁹:

Respiratory tract

1. Upper airway

- a) *Laryngeal oedema* – patients complain of difficulty in breathing, throat discomfort, hypersalivation and hoarseness. Examination show stridor and oedema of the supraglottis and glottic region.
- b) *Rhinitis* – symptoms of blocked nose, sneezing and nose itching. Signs include nasal mucosal oedema and rhinorrhoea.

2. Lower airway

- a) *Bronchospasm* – symptoms of coughing, dyspnoea, wheezing and chest discomfort. Signs include respiratory distress, cyanosis, tachypnoea and rhochi.

Cardiovascular system

1. *Cardiovascular collapse* – symptoms of syncope, generalised weakness, dizziness and ischaemic chest pain. Signs include hypotension, tachycardia and shock.
2. *Arrhythmia* – presented with palpitation and syncope. ECG shows atrial fibrillation, tachycardia, non-specific ST change, atrial and ventricle ectopics.
3. *Cardiac arrest* – collapses in cardiac arrest. ECG shows ventricular fibrillation, asystole and pulseless electrical activity.

Cutaneous manifestation

1. *Urticaria* – itchiness, flushing, hive, tingling and warmth. Examination shows diffuse erythema and urticaria.
2. *Angioedema* – periorbital and perioral swelling, non-pruritic extremity. Examination frequently shows asymmetrical nonpitting oedema.

Gastrointestinal system

Symptoms include abdominal pain, nausea, vomiting, diarrhoea and dysphagia.

Others

Anxiety, sense of impending doom, apprehension and confusion.

Differential diagnosis

The diagnosis of anaphylaxis relies on the recognition of the clinical features that occur abruptly after antigen exposure. However, diagnostic difficulties arise when only a portion of full syndrome is present. A list of differential diagnosis according to the presenting symptoms was listed in the Table 3.⁹

Emergency department management of anaphylaxis

The key to success in managing anaphylaxis emergency depends on the early recognition of anaphylaxis reaction, initial assessment, anticipation of deterioration and finally prompt and aggressive support of airway, oxygenation, ventilation and circulation.¹⁰

A. Recognition of anaphylaxis reaction

The clinical manifestation of anaphylaxis reaction is highly variable in the symptoms of presentation, speed of onset, clinical progress and the degree of severity of illness. Anaphylaxis should be always on your list of differential diagnosis when you encounter a critically ill patient. Life threatening feature such as

Table 3. Differential diagnosis of anaphylaxis.

<i>Symptom</i>	<i>Differential diagnosis</i>
Stridor	Foreign body aspiration Epiglottitis Retropharyngeal abscess Quinsy Tumour Hysteria, panic attack
Bronchospasm	Asthma Hyperventilation Vocal cord dysfunction
Syncope	Vasovagal attack Seizure Hypoglycaemia Dysrhythmia
Shock	Septic shock Spinal shock Hypovolaemic shock Cardiogenic shock
Urticaria	Occult infection Mastocytosis
Angioedema	Hereditary angioedema ACEI associated angioedema

laryngeal oedema, bronchospasm and cardiovascular collapse is of great concern to emergency physician although mild reaction such as urticaria and angioedema are more frequent encounters. Symptoms commonly occur within minutes after the patient has been exposed to the causative agents. Generally speaking the more rapid the onset, the more severe the illness.

B. Initial assessment of patients with anaphylaxis

History taking

The good clinical history is essential in determining the nature of clinical event. It help us to construct and analyse a differential diagnosis. It will help us in identifying a specific cause of anaphylaxis.¹¹ The history should concentrate on possible causative agents immediately before the event, the clinical manifestation after the exposure, the time of onset of allergy reaction, past medical and allergy history and current medication. Pre-hospital therapeutic intervention is also important.

Physical examination

It is particularly important for the emergency physician to evaluate the (1) airway patency, (2) effectiveness of ventilation and oxygen saturation, (3) blood pressure, and (4) cardiac status.¹² Assessment of the respiratory system for evidence of laryngeal oedema, inspiratory stridor, dyspnoea, wheezing, cyanosis, apnoea, respiratory effort and oxygen saturation is essential. The peak flow rate should be measured as well. It is essential to obtain vital signs such as blood pressure and pulse and assess the circulatory status of patient especially for any evidence of shock. Documentation of the neurological status and presence of flushing, urticaria, swelling of the lips, tongue and uvula is necessary. The patient may have life threatening symptoms within minutes, or they may develop as the condition progresses and therefore it is important to continue clinical reassessment, monitoring and anticipation of rapid deterioration.

Investigation

Laboratory values have essentially no roles in the emergency care of anaphylaxis patients.

C. Emergency intervention

Advanced life support should be implemented immediately according to the patient's clinical status. Meticulous attention to airway, oxygenation, ventilation and circulatory support is of paramount important. Complete recovery without any neurological deficit had been reported even patient presented with cardiac arrest.⁴ The following is a discussion of the therapeutic options in anaphylaxis.

Adrenaline

Adrenaline is generally agreed to be the most important drugs in the treatment of anaphylactic reaction.¹³ There are two main problems associated with the use of adrenaline in the treatment of anaphylaxis. Firstly, *adrenaline is greatly under utilised* while chlorpheniramine and hydrocortisone injections are more often given. Secondly, there had been an inappropriate use of intravenous adrenaline both by the paramedics and emergency physician, when *adrenaline should be given intramuscularly*.¹⁴ Adrenaline

works best when given early in the course of reaction. Intramuscular injection of adrenaline is extremely safe and adverse effects are rare. There is only one case of acute myocardial infarction reported after intramuscular administration.¹⁵ Intravenous adrenaline is reserved for profound anaphylactic shock and during anaesthesia. Subcutaneous administration of adrenaline may be used but its absorption and maximal plasma concentration may be delayed with shock.¹⁰

Indication: Adrenaline is indicated in the following conditions¹²:

- a) Clinical sign of shock, pronounced tachycardia, decrease capillary filling.
- b) Inspiratory stridor, wheezing, cyanosis and respiratory distress.
- c) When in doubt, remember that give adrenaline is safe, effective and adverse effects are rare.

Action: It acts as an α agonist in reverse the peripheral vasodilatation and reduces oedema. It act as an β agonist to dilate the airways, increase the force of myocardial contraction and suppresses histamine and leukotriene release.¹⁴

*Dosage*¹⁴:

Adult	0.5 ml 1:1,000 solution (500 μ g) intramuscularly (IM)
>11 years	0.5 ml 1:1,000 solution (500 μ g) IM
6-11 years	0.25 ml 1:1,000 solution (250 μ g) IM
2-5 years	0.125 ml 1:1,000 solution (125 μ g) IM
<2 years	0.0625 ml 1:1,000 solution (62.5 μ g) IM

Adrenaline 1-5 ml of 1:10,000 solution (0.1-0.5 mg) given intravenously over 5 minutes is recommended for profound, life threatening manifestation.

The above dosage may be repeated in 5 minutes if no clinical improvement was observed.

Oxygen

Oxygen is indicated in patient with respiratory and cardiovascular compromise. It should be given in high flow.

Position

Victims should be placed in a position of comfort. If hypotension is present, elevate the legs and head down until replacement fluids and vasopressors restore the blood pressure. Patient with respiratory distress should be placed in sitting position.

Antihistamine

It is indicated in all anaphylactic reaction. Its use may be helpful and is unlikely to be harmful. It should be given by slow intravenous injection or by intramuscular route to avoid drug induced hypotension. The dosage for chlorpheniramine in adult and child over the age of 11 is 10-20 mg IM; 6-11 years, 5-10 mg IM; 1-5 years, 2.5-5 mg IM.

Hydrocortisone

It is indicated in severe attacks to help avert late sequelae especially in asthmatic patient who have previously been treated with corticosteroids. Hydrocortisone should be given by slow intravenous or intramuscular injection. Beneficial effects are expected to delay by at least 4-6 hours. The dosage for adult and child age >11 is 100-500 mg; 6-11 years, 100 mg; 1-5 years, 50 mg.

Isotonic solution

Isotonic crystalloid (normal saline) should be given if there is hypotension especially for those do not response rapidly to adrenaline. A rapid infusion of 1-2 litre of crystalloid solution may be needed. For paediatric patient with hypotension, 20 ml/kg crystalloid solution should be infused rapidly, follow by another similar dose if there is no clinical response.

Inhaled bronchodilator

Inhaled β -adrenergic agents are indicated in patients with bronchospasm. Nebulised Ventolin should be given which may be repeated depending on the clinical response. Inhaled ipratropium may be useful for treatment of bronchospasm in patients on β -blocker.

Glucagon

It may be effective for patients who are unresponsive to adrenaline and those receiving β -blocker. The agent

is short acting and dosage is 1-2 mg every 5 minutes intramuscularly or intravenously. Common side effects are nausea, vomiting and hyperglycaemia.

H2 blocker

Administer H2 blocker such as cimetidine may be helpful if only partial response obtained after the above treatment.¹⁶

D. Clinical reassessment and monitoring

After emergency intervention, monitoring with frequent assessment of vital signs is important for the assessment of clinical response to treatment. A good clinical response represents resolution of the allergy reaction. However, if only partial response is achieved or if there is concern about the biphasic anaphylaxis, monitoring should be continued. An awareness that deterioration may occur due to late-phase reaction is necessary.

E. Disposal arrangement

Admission to hospital is recommended for all patients with clinical manifestation of laryngeal oedema or significant hypotension, even if they respond to the initial treatment. Deterioration may occur when the effect of the treatment wears off.

Mild or moderate anaphylaxis which respond to treatment and no complication to treatment can be safely discharged.

All patients with anaphylaxis should be given allergen avoidance advice such as Medic Alert card. Referral to an allergist should be considered if the patient needs further advice.

Prevention

Spending a few minutes with patients before discharge and discussing details of allergy history, offering environmental modification and educating the patient on the initial treatment for subsequent anaphylaxis will decrease the morbidity and mortality of anaphylactic reaction. The following suggestions may reduce the incidence of anaphylaxis or decrease its severity related to the practice of emergency physician.⁹

1. Get through drug allergy and atopic history for every patient you encounter in emergency department.
2. Make sure all the drugs have proper labelling before being dispensed to patients.
3. Whenever possible give drugs orally rather than parentally. If parental route is necessary, try to inject the drugs in via the extremity.
4. It is advisable for patients to wait 30 minutes after parental drug administration in emergency department.
5. For patient with known drug allergy, use unrelated drugs.
6. Make sure that resuscitation equipment is available when administering antigenic compound.
7. When antiserum is essential, always use human if available. Always perform pretest before heterologous serum is administered.
8. For contrast radiological investigation, pretreat with antihistamine and steroid if patient is susceptible.
9. Advise patient to avoid known antigens, for example, antibiotics, foods, insect and sting.
10. Predisposed patient should carry warning identification for example Medic-Alert.
11. Predisposed patients should be taught self-injection of adrenaline pen, they are advised to carry the treatment kit at all times.
12. It is recommended appropriate patients should be referred to an allergist who can give more advice on avoidance and prevention of further attack. Skin test and hyposensitization immunotherapy should be considered when appropriate.

Summary

The Figure 1 summarizes the acute treatment of anaphylaxis in the emergency department.

Conclusion

Anaphylaxis is a clinical syndrome that can involve multiple organ systems, with variable severity and course. An awareness that anaphylaxis can present as

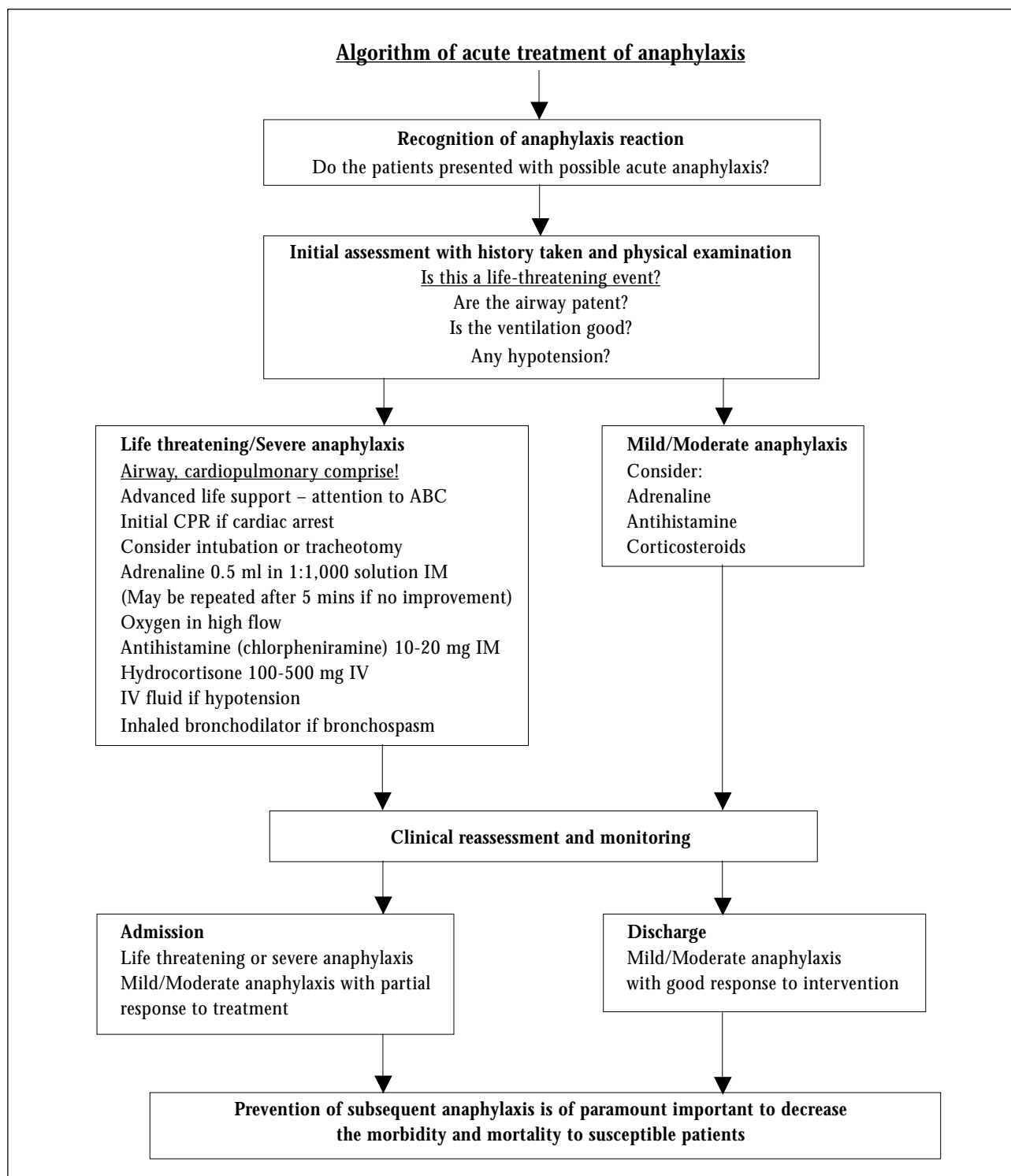


Figure 1. Acute treatment of anaphylaxis in the emergency department.

laryngeal oedema, bronchospasm and circulatory collapse, which are fatal if unattended immediately is of paramount importance to emergency physician. Early recognition of anaphylactic reaction, anticipation of deterioration and early aggressive emergency care of airway, breathing and circulation is the key to success in acute management of anaphylaxis. Adrenaline is the cornerstone of the treatment modality in anaphylaxis; it is currently underutilized. Intramuscular injection of adrenaline is safe, side effects are rare and the most important is that it almost always works when given early. In summary anaphylaxis is easily treatable and patients can make a complete recovery. At last prevention of subsequent episode of anaphylaxis should be considered a priority for emergency physician before patient discharge.

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