

Allergic Emergencies in the Emergency Room

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Introduction

It is now clear that the prevalence of allergic diseases is increasing everywhere. For example, the cumulative prevalence of allergic diseases places them second as a cause of morbidity in the American population. It has been estimated that 10% of the US population will have asthma or eczema, 10–15% allergic rhinitis, and 10–15% a drug allergy during their lifetimes. Experience in Emergency Departments reflects this trend. The Emergency Room (ER) is frequently a place of recourse for patients having an allergic reaction. Many have consulted a physician or taken an antihistamine before coming to an ER. From the ER physician's point of view, the term "allergy" is often misused by patients, especially when they have a skin problem. For example, patients coming to the ER with a pruritic rash, when questioned commonly say, "It is for an allergy," sometimes reflecting what their physician had previously told them.

The two most important allergic emergencies seen in the ER are anaphylaxis and severe asthma. Since severe asthma is covered in another article in this issue, the present discussion will be limited to anaphylaxis—and its variants—as seen in the ER.

Anaphylaxis, Anaphylactoid, or Pseudoallergic Reactions?

Immediate hypersensitivity (Type I) reactions have, by definition, an immune mechanism. The central feature of this mechanism is the

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production of specific antibodies of the immunoglobulins E (IgE) class. We would also include in the term "allergy" certain other inflammatory conditions, contact dermatitis, for example, which do not involve IgE, but are based on other immune mechanisms, such as serum sickness (Type III) or delayed hypersensitivity (a Type IV reaction). Although conditions of these types are also sometimes seen in emergency departments, they are emergencies and therefore will not be discussed in this article.

Anaphylaxis results from a series of reactions beginning with the reaction between an allergen and cell-bound IgE antibody and leading to the degranulation of mast cells and basophils. The result is the release of preformed (such as histamine) and newly synthesized (such as the leukotrienes) biologically active mediators, which in turn act on vascular tissues, smooth muscle, nerves, and a variety of inflammatory cells (such as eosinophil) to produce the symptoms and signs of an immediate hypersensitivity reaction, including urticaria, angioedema, rhinoconjunctivitis, asthma, and anaphylaxis. There are, however, other pathways leading to mast cell degranulation that do not involve IgE, for example, activation of the complement cascade, direct nonimmune triggers of mast cells and basophils degranulation, enzymatic activation, and so forth. These reactions resemble immediate hypersensitivity reactions, presenting similar signs and symptoms and are usually referred to as anaphylactoid or pseudoallergic reactions. In current ER practice, we do not differentiate them from immediate hypersensitivity reactions, especially when it comes to anaphylaxis-like reactions. The difference is relevant only when subsequent investigation of the reaction is being undertaken.

The definition of anaphylaxis is a clinical one. Some authors restrict the term anaphylaxis to those systemic reactions that are sufficiently severe to be potentially life-threatening, irrespective of their mechanism (1). Others use the term for any clinical condition resulting from mast cell degranulation, from the mildest forms (rhinitis, urticaria) to the most severe episodes (laryngeal edema, shock) (2). In everyday ER practice, an allergic reaction usually means anaphylaxis (which may include airway obstruction), but sometimes it will also be used for some types of delayed hypersensitivity reactions (especially eczema), and although it may have an allergic basis, we tend to place severe asthma in a different category than anaphylaxis. The present article will be limited to anaphylactic reactions that one is likely to encounter in an ER because of their frequency (more than three-quarters of the allergic reactions seen in emergency departments are anaphylactic reactions) and because they are potential life-threatening. In order to be practical, we will adopt the term anaphylaxis as the overall clinical manifestations determined by an intense mast cell and basophil degranulation, whatever the mechanism (3).

What Do We Know About the Epidemiology of Anaphylactic Reactions?

Data on the incidence of anaphylaxis are rare. In the emergency department of the Cambridge Hospital, 1 patient in 1500 presents with an anaphylactic reaction with shock and/or loss of consciousness. This would be equivalent to 1 case/10,000/yr in the population of Cambridge (4). If systemic allergic reactions with respiratory difficulty but without shock are included, the rate is nearly three times higher (1). The difference is also owing to the period of this study (from August through October), when there were eight cases of anaphylactic shock caused by bee or wasp stings.

Information on the incidence of anaphylactic shock occurring outside hospitals is also limited. It appears to be rare, however. A Danish retrospective study in which all cases of anaphylactic shock occurring within a hospital catchment area during a 13-yr period were analyzed found 20 cases, giving a prevalence of 3.2 cases/100,000 inhabitants/yr (5). The responsible allergens were drugs given orally (penicillin in 7 cases, aspirin in 3 cases), hymenoptera stings (8 cases), and foods (2 cases). A multicenter study in France identified food allergy as the cause of anaphylactic shock in 10.2% of cases (6). Other authors have incriminated food allergy in 41% of cases (7).

The rate of anaphylactic shock caused by drugs given in hospital is estimated to be 1 in every 2700 inpatients, and it may account for more than 500 annual deaths in the United States (8). The incidence of anaphylactic shock is considered to be 1/3500–5000 general anesthetics, and a mortality rate of 4–6% is generally accepted (9). Muscle relaxants are the cause in three-quarters of these cases, whereas an increasing number of cases owing to allergy to natural rubber latex (surgical gloves in most cases) has been reported in three multicenter studies, the proportion resulting from this allergy going from 0.5% in 1990 to 12.4% in 1993 and then to 19% in 1995 (10). Systemic reactions associated with allergen immunotherapy or, exceptionally, during skin testing are reported to be infrequent: 155/151,977 injections with 1 case of fatal shock/2,000,000 injections (11).

How to Approach Allergy in the Emergency Department (Fig. 1)

Recognize Anaphylaxis and Exclude Other Diagnoses

From a clinical viewpoint, the diagnosis of an anaphylactic reaction is usually quite evident. Sometimes, however, the cause of an episode or episodes of loss of consciousness with a fall in blood pressure

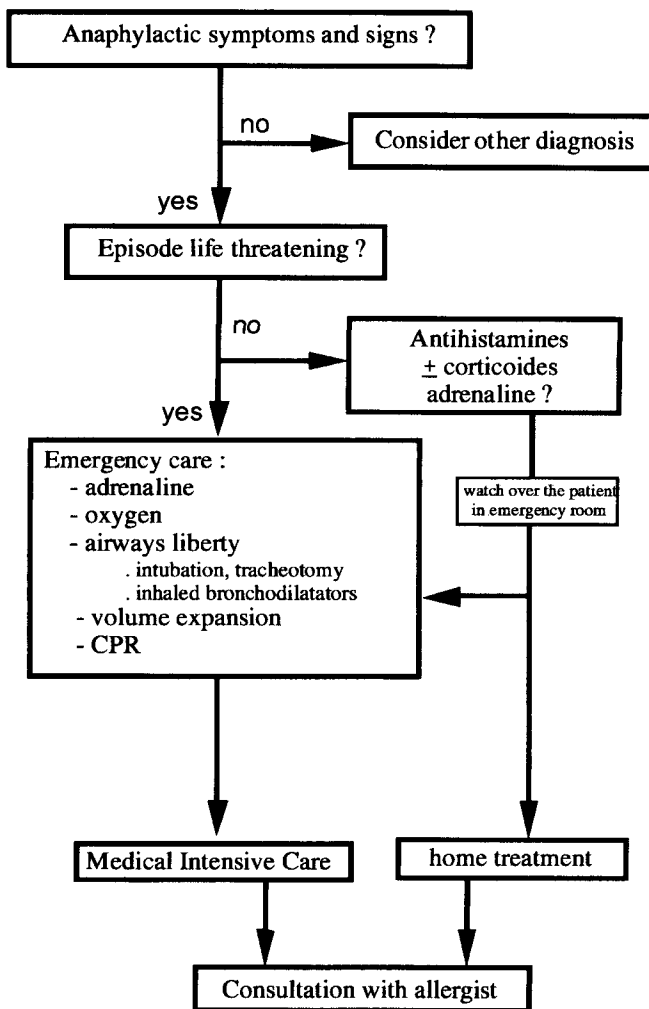


Fig. 1. Anaphylactic reactions: evaluation and management in the ER.

is not evident, for example, until they are found to follow ingestion of bananas in a latex-allergic individual (12).

Systemic allergic reactions can involve the cutaneous, respiratory, cardiovascular, and/or gastrointestinal systems. The clinical features vary from simple pruritus to life-threatening manifestations. The range of signs and symptoms is listed in the Table 1. The onset of an anaphylactic reaction is usually within a few minutes of exposure to the responsible allergen, but it may be delayed for up to a few hours. In general, the sooner it occurs, the more severe it will be. The symptoms usually reach their peak within several minutes and may persist for several hours afterward. In the following section, the clinical features that will be described will be those that are most frequent,

Table 1
Features of Anaphylaxis

Manifestations	Symptoms	Clinical signs
Erythema	Pruritus	Erythematous macules and/or papules
Urticaria	Itching, redness	Edematous papules
Angioedema	Nonpruritic tingling Sense of tension	Swelling of lips, eyelids, hand No sensation of warmth, no erythema
Laryngeal edema	Hoarseness, pruritus of palate Dysphagia, foreign body sensation Dyspnea Hypersalivation Sudden death	Stridor Intercostal and supraclavicular retraction Cyanosis Edema of lips, tongue, uvula Subglottic edema
Bronchospasm	Cough Dyspnea Sense of chest tightness	Wheezing Respiratory failure Respiratory muscular retraction
Hypotension	Fainting, lightheadedness Loss of consciousness Confusion, convulsion Sense of impending doom	Hypotension, tachycardia Oliguria "Hot shock"
Rhinitis	Nasal congestion and tingling Sneezing, nasal blockage Sometimes epistaxis, even hyposmia	Edema of nasal mucous membrane Watery rhinorrhoea
Conjunctivitis	Watering Tingling Foreign body sensation	Conjunctival injection Edema of eyelids Chemosis
Gastroenteritis	Cramps Diarrhea, vomiting Hematemesis	Normal examination

where a differential diagnosis is necessary and where there is a high risk of death.

Mucocutaneous Manifestations

Maculopapular rashes, urticaria, and angioedema are allergic manifestations currently seen in emergency departments. Acute urticaria, with a cumulative prevalence of 10–20% (13), represents 35% of skin disorders presenting in the ER (14). Because of different etiologic factors and emergency management, acute urticaria and/or angioedema has to be differentiated from chronic forms. Chronic urticaria

and/or angioedema is defined by convention as the occurrence of daily or almost daily symptoms during at least 6 wk (15). In acute episodes, an allergen, such as a food or a drug, or a physical factor is often found to be the cause, whereas with chronic urticaria, an IgE-dependent allergy cannot be demonstrated in a majority of patients.

Maculopapular Eruptions

Numerous cutaneous drugs reactions are morbilliform or maculopapular exanthems, but only 10% of them have an allergic origin. Many viral (picornavirus, parvovirus, cytomegalovirus) or bacterial (rickettsia, syphilis) illnesses should be included in the differential diagnosis. Maculopapular rashes owing to ampicillins occur frequently when these antibiotics are given in the course of various viral diseases, and they are almost constant in the course of the mononucleosis. In these cases, continuation of ampicillin treatment is usually well tolerated.

Urticaria

Urticaria is a strictly clinical diagnosis. It is characterized by labile, pruritic, firm-or-elastic to the touch, erythematous, or whitish-yellowish plaques with normal overlying epidermis. Urticarial lesions can vary in size and shape from small papular lesions to giant annular lesions with serpiginous, raised erythematous borders, and central clearing. The individual urticarial lesions usually appear brutally, persist for some minutes or hours, usually do not last longer than 24 h, and they disappear without leaving a trace. The lesions are migratory and may appear in different areas of the body for up to 2 wk. They are more often localized on the trunk and members than on the face. Urticaria is rarely associated with significant morbidity or mortality, except in patients with hereditary angioedema and in patients with cold urticaria after sudden generalized cold exposure.

A first step in diagnosis is to identify those patients with urticaria provoked at the sites of a physical stimulation, such as stroking the skin (dermographism), cooling the skin (cold urticaria), or sun exposure (solar urticaria). Cholinergic urticaria, a widespread transitory pruritic rash following exercise, emotion, or heat, also falls into this category. To confirm these conditions requires only challenge testing, such as with a dermographometer, an ice cube test, a solar simulator, or brisk exercise, respectively.

Urticaria regarded as a symptom justifies a complete clinical examination to exclude nonallergic diseases. Several dermatologic disorders, erythema multiforme, dermatitis herpetiformis, or bullous pemphigoid, for example, may have urticarial lesions as part of their clinical presentation. Various infectious diseases, including parasitic (ascaris, filariasis, trichinosis) and viral diseases (the preicteric phase of hepatitis B, infectious mononucleosis, others viral infections in children) are

frequently accompanied by urticaria. Hypersensitivity vasculitis may present with urticarial lesions and be misdiagnosed as a simple urticaria (15). The lesions of this condition have some differentiating clinical signs: painful or burning sensation of the urticarial wheals rather than pruritus, lesions lasting longer than 24 h, a purpuric component of the skin lesions, modification of the skin pigmentation, lesions more prominent on the lower extremity than on the trunks or arms, and an association with constitutional symptoms (arthralgia, fever). Serum sickness is a particular case of hypersensitivity that is accompanied by urticaria.

Angioedema

Angioedema is characterized by acute subdermal swelling that is firm to the touch, without erythema or pruritus. It is localized mainly in the loose subcutaneous tissues, notably on the face (lips, eyelids) and genital organs, and more rarely on the extremities and zones of pressure (palms and soles). It may also involve the mucous membranes, especially of the upper respiratory tract, which is why it can be very serious. Abdominal pains, vomiting, and/or diarrhea is the result of edema in the mucosa of the gastrointestinal tract. Angioedema occurs in about 50% of cases of urticaria although it can occur alone.

When there is acute edema of the face, the physician must first exclude an infectious disease. The exceptional case of staphylococcal infection of the face and erysipelas has to be suspected when fever and shaking chills are associated with inflammatory lesions of the face. Bilateral maxillary sinusitis may be accompanied by erythematous edema of the cheeks, with sharp facial pain and fever. The palpebral edema of trichinosis may be associated with urticaria. Acute eczema of the face is a frequent cause of consultation in the ER, with intense pruritus and erythema accompanied by microvesicles occurring 8–24 h after contact with the allergen. Subcutaneous emphysema of the face is easily recognized by its crepitation to the touch and by the circumstances of its occurrence (acute asthma, injection of air into a dental root, and so on). The superior vena cava syndrome, hypothyroidism, and nephrosis can be misdiagnosed as allergic edema of the face. Patients with hereditary angioneurotic edema (HAE; a C1 esterase inhibitor deficiency) may experience laryngeal edema without urticaria, and this is frequently accompanied by severe abdominal pain. Most patients with HAE will report a family history of the disease, although acquired forms do exist.

The Oral Allergy Syndrome (OAS) (Lessof's Syndrome)

The OAS, also called the fruit-vegetable syndrome, is a clinical particularity. It can also be induced by foods other than fruits or vegetables, e.g., shrimp (16). The patients complain of tingling and pruritus of

the lips, tongue, and/or other mouth parts. Angioedema of the lips appears in half of the cases, and pharyngeal involvement is possible. Typically, the patients describe the onset of symptoms within 5 min of contact with the allergenic food, and almost all develop symptoms within 30 min; the symptoms usually disappear within 90 min. Other symptoms of immediate hypersensitivity may follow the oropharyngeal symptoms. OAS is often associated with allergic rhinitis and asthma in patients who are allergic to tree, grass, or weed pollens.

Upper and Lower Airway Manifestations

Upper airway obstruction is the major cause of death in anaphylaxis. First, it is necessary to search systematically for any clinical signs or symptoms of oropharyngeal or laryngeal edema and, if they are found, to treat them vigorously. Other conditions that may be confused with anaphylactic upper airway obstruction include simulated laryngeal edema, which occurs without edema of the face, a panic attack, infectious laryngitis or epiglottitis, a laryngeal foreign body in children, a laryngeal tumor in adults, and, finally, isolated stridor in Münchausen's syndrome.

Lower respiratory tract involvement in anaphylaxis is primarily manifested by dyspnea and wheezing, typical of an acute asthma attack, without general signs or painful manifestations. Isolated cough, typically spasmodic and often nocturnal, may be considered as an asthmatic equivalent. Nocturnal asthma should make one search for allergy to house dust mites and cockroaches, chronic sinusitis, or gastroesophageal reflux. Some irritants and toxic products may produce symptoms resembling asthma, and these need to be distinguished from allergic asthma. The hyperventilation syndrome, like laryngeal edema, may also simulate asthma.

Anaphylactic Shock

The development of anaphylactic shock is stereotypic. Within minutes following the allergen exposure by a parenteral route or within 2–3 h by the oral route, the patient notices a sensation of heat and then pruritus of the palms and soles, sometimes with axillary tingling that generalizes. This may be followed by urticaria with or without angioedema or diffuse erythema, epigastric pain, and tachycardia. In the first minutes, the blood pressure is normal or even raised. In a period that varies according to the allergen, its route of introduction, and the patient's underlying disease, more serious symptoms may appear: laryngeal edema, bronchospasm, diarrhea and vomiting, hypotension, loss of consciousness, convulsions, rhythmic or conduction cardiac anomalies, and cardiac arrest that is sometimes

the first and only manifestation of the reaction. With well-timed, adequate treatment, the response is rapid, and there should be no sequelae after an anaphylactic episode. In about 5% of cases, however, there can be a relapse after an initial or incomplete improvement (biphasic anaphylaxis) (17). Nevertheless, the victim may die very rapidly before any medical intervention is available, or the course may be irreversible in spite of adequate treatment or because of delay in its administration.

Anaphylactic shock must be differentiated from shock owing to other causes: staphylococcal toxic shock syndrome with erythema, vasovagal syncope, toxic drug reactions (e.g., massive injection of an anesthetic agent with extravasation), or the toxic effect of multiple hymenoptera stings (vomiting, diarrhea, hypotension, convulsion, rhabdomyolysis). It can triggered by the ingestion of a very large amount of histamine (e.g., scombroid poisoning), pheochromocytoma, or carcinoid syndrome. On rare occasions, patients with systemic mastocytosis may experience symptoms of anaphylaxis. The so-called Chinese restaurant syndrome, consisting of a flushed sensation, sweating, headache, chest tightness, nausea, and sometimes asthma, shortly after ingesting monosodium glutamate may be confused with a systemic allergic reaction.

What About Laboratory Tests?

Laboratory tests are rarely necessary in the acute phase of an anaphylactic reaction, but can be useful in the search for an allergic etiology. A complete blood count and erythrocyte sedimentation rate may sometimes help to distinguish allergy from infectious, hematologic, and inflammatory diseases. If specimens are required for laboratory tests, in no case should the antiallergic treatment be changed while awaiting the results. Some typical findings: the hematocrit and the hemoglobin levels can be raised secondary to the loss of intravascular fluids, and leukocytosis with neutrophilia is usual after the administration of adrenaline. Chest X-ray, which should be ordered systematically in the case of severe asthma or laryngeal edema, can show hyperinflation and atelectasis owing to mucus obstruction of the airways. An electrocardiogram may show anomalies owing to arterial hypotension or hypoxia or because of the adrenaline use in the treatment of the anaphylactic episode.

The plasma histamine level can be elevated in anaphylaxis, but it is measured except for research purposes because its increase is of short duration (<30 min after the beginning), and it is not available in most clinical laboratories. The increase of plasma tryptase, a neutral protease that is secreted when mast cell degranulate, is more readily seen since it is prolonged (lasting from 30 min to 6 h), with a peak

being reached at 60–90 min after the onset of the reaction. Its measurement postmortem (and also that of specific IgE) can be useful in confirming the activation of mast cells (18). When food is suspected of being the triggering allergen, then any remaining portion should be recovered, deep-frozen, and tested for allergenic activity against the patient's serum.

Emergency Care of Anaphylaxis

Estimation of the Initial and Potential Severity

Except for certain allergies, food and latex allergy in particular or a previous history of anaphylaxis to a given substance, there are no characteristics that allow one to identify those patients who are at risk for anaphylaxis. Of all the routes of exposure to an allergen, a reaction following exposure by the parenteral route is usually the most immediate and most severe. Anaphylactic reactions can be more serious in patients with hereditary angioedema, in patients treated with β -blockers (including eye drops), or angiotensin-converting enzyme inhibitors, and these with nonspecific bronchial hyperresponsiveness.

In the course of any anaphylactic reaction, even if the episode seems moderate and limited at first, collection of a few simple clinical data provides a rapid evaluation. Initial evaluation should be focused on the state of consciousness (reduced alertness, confusion, stupor, loss of consciousness, seizures, coma), the respiratory system (respiratory rate, cutaneous color, uvular examination, stridor or wheezing, pulmonary auscultation, peak flow, pulse oxymeter), cardiovascular function (cardiac rate and regularity, arterial blood pressure, skin blotches, dizziness, syncope), and body temperature. The ER physician must focus constant attention on the patency of the upper airway, as well as the patient's hemodynamic state because laryngeal edema and shock are the principal causes of deaths in anaphylaxis. The physician must be alert to possible concomitant laryngeal edema when the following clinical signs appear: hoarseness, foreign body sensation, dysphagia, edema of the uvula, tongue, soft palate or lips, and stridor. Tachycardia, hypotension, agitation, and other signs of cerebral hypoperfusion occur typically in patients in anaphylactic shock. Evidence of severe asthma must also not be overlooked.

Emergency Treatment

ER personnel must be trained to provide rapid management according to widely accepted protocols (Tables 2–4). The presence or appearance of any abnormal cardiovascular or pulmonary signs requires prompt administration of oxygen, establishment of venous access, and frequent monitoring of vital signs—at least every 5 min. The

Table 2
Acute Urticaria: Practical Recommendations^a

Antihistamines

In emergency setting: 5 mg of dexchlorpheniramine by parenteral route (im, iv) (be careful if the patient must drive car)

Then orally during 8 d: loratadine or cetirizine 10 mg daily at morning, and/or hydroxyzine 50 mg daily or dexchlorpheniramine 6 mg LP daily at night

Corticosteroids

Debated prescription

For some authors: in spread forms and/or developing during several days

Seems to improve more quickly the symptomatic and clinical response

In emergency setting: 40–60 mg methylprednisolone iv

Then orally: 20 mg b.i.d. during 4 d of prednisone or prednisolone

Adrenaline

0.10–0.25 mg by sc or sublingual route

The sublingual route is not referenced

Every 6 h

Local treatments to relieve pruritus

Cold or luke-warm showers, cold compresses, cold ambient temperature

Application of 1% menthol in aqueous creme

Reassure ++ and avoid factors that trigger relapses

^aim: intramuscularly; iv: intravenously; sc: subcutaneous.

main goals of treatment at this stage are, first, to maintain airway patency with an endotracheal tube or, if necessary, by cricothyroidotomy and, second, to maintain hemodynamic stability.

Adrenaline, because of its pharmacologic properties—vasoconstriction, bronchodilatation, and inhibition of mast cells degranulation—is the universally recommended treatment for an anaphylactic reaction (19). As secondary drugs, H1 antihistamines and corticosteroids may be useful in some patients.

The corticosteroids have multiple effects: they inhibit leukotriene production, they stabilize mast cell membranes, and they have an antichemotactic effect. They may also enhance the action of β_2 -adrenergic agents. Although corticosteroids have no immediate effect on anaphylaxis, they may be beneficial in preventing or improving prolonged or late-phase responses.

Adrenaline must be used when there is pharyngo-laryngeal obstruction or shock. Some authors estimate that adrenaline is underemployed in the treatment of urticaria or cutaneous angioedema and recommend that it be used even in the most moderate forms of systemic allergic reactions, since it can relieve the signs and symptoms of urticaria more rapidly than antihistamines (20). If there is difficulty in establishing parenteral access, the sublingual route is an option for the administration of adrenaline. In addition, the inhaled route may be

Table 3
Angioedema—Asthmatic Manifestations: Practical Purposes^a

In the absence of edema of uvela and/or bronchospasm
Corticosteroids
In emergency setting: 40–80 mg of methylprednisolone intravenously
Then orally: 60 mg of prednisone or prednisolone immediately, then 20 mg t.i.d. during 3 d and 20 mg daily during 3 d
H1 antihistamines
In emergency setting: 5 mg of dexchlorpheniramine by parenteral route (im, iv)
Then orally during 8 d (cf. Table 2)
Watch over the patient in emergency room: during 2–3 h
In case of edema of uvela and/or dyspnea
In case of respiratory difficulty
Oxygen with mask or nasal canula, with high flow > 6–8 L/min
Sit the patient down
Establish promptly and systematically an iv access
Close monitoring of respiratory and cardiac functions
Adrenaline
0.25–0.50 mg by im or sc route
1 mg in 5 mL of saline inhaled through nebulizer
Corticosteroids
In emergency setting: 40–80 mg of methylprednisolone iv
Carry on 40–80 mg t.i.d. of methylprednisolone iv
Then orally (cf. Table 2)
Inhaled β_2 -agonist in case of bronchospasm
Salbutamol (for nebulizer): 5 mg (1 mL) in 4 mL saline inhaled through nebulizer
H1 antihistamines
In emergency setting: 5 mg of dexchlorpheniramine by parenteral route (im, iv)
Then orally during 8 d (cf. Table 2)
Hospitalization for at least 12 h

^aim: intramuscularly; iv: intravenously; sc: subcutaneous.

useful in case of laryngeal dyspnea or bronchospasm, but it must be administered carefully if adrenaline has also been given parenterally because excessively high plasma concentrations may be reached quickly (21). Excessive levels of adrenaline can precipitate arterial hypertension, myocardial ischemia, and cardiac arrhythmias. Such effects are more frequent in older adults with underlying cardiovascular disease. Other vasoconstrictors (metaraminol, dopamine) are effective and may be less arrhythmogenic than adrenaline. However, they have no effect on bronchospasm, and their value in the treatment of anaphylaxis has not been established (22). Methylene blue has been used to reverse anaphylactic shock that is refractory to adrenaline (23). In addition to adrenaline, nebulized or iv β_2 -agonists can be given

Table 4
Anaphylactic Shock: Practical Purposes

Immediate procedures

- Discontinuation of further administration or absorption of the suspected antigenic agent
- Elevate legs or Trendelenberg's position, except if respiratory difficulties are the dominant feature, when it may be better to sit the patient down
- Maintain the airways patency, oxygen with mask or nasal canula and high flow > 6–8 L/min
 - Intubation, cricothyrotomy if airways patency is compromised
- Establish promptly and systematically an iv access
- Close monitoring of respiratory and cardiac functions
- Adrenaline: life-threatening anaphylaxis requires immediate administration
 - +++ im or sc: 0.25–0.5 mg time to prepare adrenaline iv or in less serious cases, repeat every 5–10 min, if needed
 - iv 10 µg/kg, but in current practice
 - Dilute 1 mg with 10 mL normal saline
 - Injection at a rate of 0.5–1 mL every minute to obtain a sufficient blood pressure
- Then continuous infusion if needed: 0.1–0.5 µg/kg/min
- For patients treated with β blocking agents
 - Use adrenaline with 2 to 5 times higher posologies
 - If bradycardia: atropine 0.5–1 mg iv; isoproterenol 2–20 µg/min
 - In refractory cases: glucagon 1–5 mg iv
 - Use caution in case of ischemic heart disease or in patient older than 50 yr
- Volume expansion
 - Ringer's lactate, saline, hydroxyethylamidon
 - 500–1000 mL in 15 min if persistent hypotension after adrenaline

Second-line drugs

- Corticosteroids
 - In emergency setting: 40–80 mg of methylprednisolone iv
 - Carry on 40–80 mg t.i.d. of methylprednisolone iv
 - Then orally (cf. Table 2)
- H1 antihistamines
 - In emergency setting: 5 mg of dexchlorpheniramine by parenteral route (im, iv)
 - Then orally (cf. Table 2)

Hospitalization for at least 12 h because of the possible risk of relapses

when there is airway obstruction owing to bronchospasm. Patients receiving β-adrenergic blocking agents may be refractory to adrenaline and fluid replacement, but they may respond to glucagon, which increases cyclic AMP by an action independent of β-receptors (24). However, because of its vasodilatation effect, glucagon may increase the hypotension, and it often causes nausea and vomiting. Atropine or isoproterenol can be given when there is bradycardia.

H1 antihistamines competitively inhibit the action of histamine on vascular tissues and on smooth muscle, but after the onset of the

reaction, they do not inhibit release mediators. The use of the classic H1 antihistamines is limited by their undesirable side effects, including daytime sedation (accentuated by alcohol) and anticholinergic effects. On the other hand, their anxiolytic and sedative properties may be sometimes used with profit. The new generation of H1 antagonists does not possess these effects. In general, the administration of antihistamines is not recommended during pregnancy, although no serious adverse effects have been reported in pregnant women.

Acute urticaria usually responds to antihistamines, but corticosteroids may be required when the condition is refractory to antihistamines. Combined H1 and H2 antihistamine therapy is not a current practice, although a synergetic and favorable action has been described in patients with acute urticaria, cold urticaria, or dermatographism (25). Corticosteroids are regularly used to treat severe urticaria, angioedema, and serum sickness. The combined use of a corticosteroid and an antihistamine for 4 d led to a better response than either drug alone in patients with acute urticaria (26). No clinical study has evaluated the ability of corticosteroids to inhibit or diminish a late-phase reaction in anaphylaxis.

It is absolutely necessary to observe patients with anaphylaxis in the ER for several hours after the patient is first seen, and the staff must be convinced of the usefulness of this supervision, even if the patient's signs are within normal limits. When the patient has recovered, he/she should be instructed in measures to minimize subsequent allergen exposure. Before being discharged, many patients should be provided with drugs for the medical treatment of anaphylaxis (e.g., a self-administered adrenaline syringe). Consultation with an allergist is imperative.

The Etiologic Inquiry

An etiologic inquiry is essential, and it should begin while the patient is still in the ER. In some cases, it will take a lot of time and effort, and its realization in the ER is often difficult. It must be initiated in this setting, with the aim of prevention through avoidance in the future of the allergen that caused the reaction. Emergency department physicians should be aware of the possible etiologic agents in order to orient their case history, and they should have made a preliminary inquiry before sending the patient to an allergist. The following describes the principal causes of systemic allergic reactions that are encountered in the emergency department.

Allergic Drug Reactions

Allergic drug reactions may be classified into the four types of hypersensitivity according to Gell and Coombs' classification. For a given drug, several mechanisms can be involved. In IgE-mediated

reactions, sensitization to the drug may be induced by the drug itself if it is antigenic (e.g., drugs that are proteins) or in the case of low-mol-wt drugs or their metabolite products (known as haptens), which become immunogenic by combining with serum proteins. The metabolic products of most anaphylaxis-inducing drugs are unknown or poorly defined except in a few cases such as the β -lactam antibiotics.

A study carried out by investigators at the University of Helsinki implicated penicillins and nonsteroidal anti-inflammatory drugs (NSAIDs) as the drugs responsible for acute urticaria in 33 and 37%, respectively, of all cases (27). The β -lactam antibiotics are a major cause of anaphylactic reactions (28). Severe reactions to penicillins occur with a frequency of 1–5/10,000 patient courses of treatment, and the mortality rate is 1 death/50,000–100,000 courses of penicillin therapy. It has been also estimated that 75% of all fatal cases of anaphylaxis in the United States were caused by penicillin (29). Some degree of cross-reactivity does exist between penicillins and cephalosporins, ranging from 5 to 16% with first-generation cephalosporins. This risk has also been documented with newer cephalosporins and the carbapenems, but it appears to be weak with the monobactams.

The true prevalence of anaphylactic reactions to NSAIDs, including aspirin, is not known. In one report, of 51,797 patients exposed to NSAIDs, 102 instances of urticaria, 11 of angioedema, and 35 of shock were reported to have occurred (30). Aspirin- and NSAID-sensitive syndromes are characterized by the acute flare-up of symptoms occurring after ingestion of the drug by patients with chronic respiratory (rhinosinusitis, nasal polyps, asthma) or cutaneous (urticaria, angioedema) conditions. In some patients, the hallmark of this syndrome is the appearance of a facial or generalized flush, nasal and ocular congestion and watering, and an acute, often severe, bronchospasm beginning within 20 min to 3 h after ingestion of the responsible drug. In other patients, there is an exacerbation of pre-existing cutaneous signs. In patients who do not have this syndrome, this class of drugs can nevertheless cause adverse reactions, ranging from urticaria and angioedema to a severe generalized reaction. These reactions, which are not IgE-mediated, but linked to increased production of leukotrienes through inhibition of the cyclooxygenase pathway, are usually limited to a particular drug in this category. In contrast, patients with the aspirin- and NSAID-sensitivity syndrome may react to related drugs.

IgE-mediated reactions owing to opiates, drugs that are commonly used in the ER for their analgesic property, occur infrequently. Morphine and codeine, but not fentanyl and sufentanyl, are able to produce anaphylactoid reactions owing to direct mast cell activation. Acetaminophen allergy is also exceptional (31). Angioedema, sometimes limited to the face, is an increasingly recognized adverse reaction

caused by angiotensin-converting enzyme inhibitors. The cumulative incidence of these adverse reactions is 0.1–0.2% of patients treated. This risk is particularly important during the first week of treatment, 60% of cases appearing during this period (32), but it can be observed later, even after several years of continuous treatment. These reactions are thought to be owing to inhibition of kinin metabolism, with an excess accumulation of bradykinin.

Local anesthetics are commonly administered to injured patients in the ER, but IgE-mediated allergy accounts for <1% of the adverse reactions to these agents (33). Most of these adverse reactions appear to result from vasovagal manifestations or toxic reactions owing to these product or to other drugs that have been given concomitantly (e.g., adrenaline, antibiotics, and so forth). Among other drugs sometimes used in the emergency departments, *N*-acetylcysteine, a paracetamol poisoning antidote, can induce allergic manifestations (34). Allergic reactions to the thrombolytic agent streptokinase have been reported, and various thrombolytic agents can cause angioneurotic edema (35). For example, in fibrinolytic therapy, the plasmin that results from the degradation of plasminogen can activate the complement cascade, which can lead to an anaphylactoid reaction manifest as angioneurotic edema. This class of drugs has also been reported to cause bronchospasm and serum sickness. Radiographic contrast agents, which are discussed in another chapter in this volume, are a major cause of adverse systemic reactions, acting in most cases by activating the complement cascade; true allergy IgE-mediated to these agents is exceptional. The use of iso-osmolar products has decreased risks of accidents (36).

Immediate hypersensitivity reactions to latex can occur in the ER during such procedures as vaginal examination or surgery on contact with latex gloves or other medical devices. Healthcare personnel are known to be at risks for such reactions. The prevalence of latex sensitivity has been reported to be from 2 to 17%, and it is especially high in those who use and change powdered latex gloves frequently (37).

Stings and Bites

Hymenoptera stings are a frequent seasonal pathology seen in the ER. Bees and, in Europe, especially wasps account for a majority of the allergic accidents, whereas stinging ants are not a real problem in Europe. Individuals allergic to apidae stings are not allergic to vespidae stings, but there is a venom crossreactivity into the species. Anaphylaxis from bites or stings of other insects (bugs, horseflies) is extremely rare. In North Africa, scorpion bites are relatively frequent and can result in anaphylaxis. Insect stings are usually benign, but may elicit an intensely painful local reaction, which disappears in

several hours. In contrast, in sensitized individuals, the clinical features are variable, ranging from an exaggerated local reaction to anaphylactic shock. Most symptoms begin within minutes after the sting, although there have been rare reports of reactions developing only several hours later. It is estimated that the number of deaths owing to hymenoptera stings each year is 50–150 in the United States, 10 in Germany and in France, and 6 in Great Britain. This is almost certainly an underestimate because venom anaphylaxis is not always recognized as a cause of sudden death.

Hymenoptera venoms contain distinct major allergens: phospholipase A2 and mellitin in bee venom, antigen 5 in wasp venom, and hyaluronidase in both. Venom also contains many nonallergic amines, such as histamine and kinins. These substances participate in the local nonallergic reactions.

Food Allergy

Recent reports suggest that severe anaphylactic reactions to foods are an increasing problem. Food allergy should be considered when a patient presents with oropharyngeal or digestive manifestations of an allergic nature as well as when there are symptoms and signs of a systemic allergic reaction. Asthma can also occur, but it is rarely a predominant feature of food allergy. The estimated prevalence of IgE-mediated food allergies is reported to be about 1–2% in adults (38) and from 5 to 7% in children (39).

A wide variety of foods and their derivative products can trigger anaphylaxis, but relatively few of them are responsible for the majority of anaphylactic reactions. Their frequency obviously varies with food consumption and diversification. Peanuts are the most common cause of food-related anaphylaxis in the United States. In countries where consumption of fish is important, e.g., Scandinavia and Japan, fish hypersensitivity is more frequent. In Italy, wheat flour is an important food allergen. In French children from 5 mo to 14 yr of age, egg, peanut, fish, and milk account for 75% of food allergies. The number of foods to which adults are allergic is large, but they tend to be sensitized more often to fruits and vegetables than children (40). Common allergenic foods in adults are fruits and vegetables belonging to the *Rosaceae* and *Umbelliferae* families, eggs, crustacea, fish, and wheat flour. Certain “exotic” fruits (e.g., avocado, kiwi, and banana) and condiments and spices are among the more recently recognized allergenic foods owing to their crossreactivity with natural rubber latex (41). Some foods when consumed in great quantity can produce distressing, but otherwise harmless manifestations by inducing the release of histamine. The role of additives and colorings in causing anaphylaxis is controversial. They may, however, elicit an acute flare-up

of urticaria and, more rarely, gastrointestinal symptoms with or without exacerbation of urticaria, asthma, or rhinitis.

Aeroallergens

Patients allergic to common aeroallergens often come to the ER for treatment. Most of them are airborne and present in the atmospheric or domestic environment. Pollens are the major cause of seasonal respiratory allergies: February and March for tree pollens, April to September for weed pollens, and mid-May to mid-July for grass pollens, with important variations according to the region. Allergy to house dust mites is the major cause of perennial allergic manifestations. These insects are ubiquitous in most homes in temperate and tropical climates. Respiratory symptoms related to this allergy are often aggravated during of household activities, in older housing, and in the summer months during the mites' reproductive period. Cockroaches have recently been implicated as an important source of allergen, especially in inner-city households. The skin, saliva, and urine of domestic animals are sources of powerful household allergens. Mold spores appear to be a less important cause of respiratory allergy.

Occupational Allergens

Some of these allergens belong to groups described above, e.g., laboratory animals in the pharmaceutical industry and biomedical research personnel, natural rubber latex in healthcare personnel, and pollens in florists. The inhalation of inorganic and organic substances (e.g., the isocyanates used in the production of paints and plastics and wood dusts in woodworkers) may provoke attacks of asthma. Food allergies can also result from exposure to foods in the workplace. Urticaria and contact dermatitis occur in persons manipulating foods (e.g., cooks). Baker's asthma, caused by inhalation of wheat flour, is a well-known occupational disease. Workers strongly sensitized to foods should avoid places where this food is prepared. Allergic reactions to airborne food allergens have been reported in people who work with peanuts, fish, or crustaceans (42).

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