18

Allergic and Immunologic Emergencies

■ I. ANAPHYLAXIS

A. Definition. Anaphylaxis is an immediate, generalized, life-threatening reaction resulting from the release of bioactive substances from mast cells and basophils. Anaphylaxis can occur in more than one time period. The so-called biphasic anaphylaxis is defined as a recurrence of symptoms that develops following the "resolution" of the initial anaphylactic reaction. It can occur in up to 20% of anaphylactic reactions and typically occurs within 8 h after resolution of the initial symptoms. Recurrences up to 72 h later can occur.

B. Etiology. The most common causes of anaphylaxis in medical practice are depicted in Table 18.1.

C. Clinical Manifestations
   1. The onset may vary from individual to individual depending on the sensitivity of the person and the route, quantity, and rate of administration of the allergen.
   2. Early signs and symptoms that require a high index of suspicion may include
      a. Agitation
      b. Dizziness
      c. Headache
      d. Nausea, vomiting
   3. Cutaneous involvement
      a. Generalized pruritus
      b. Flushing
      c. Urticaria
   4. Upper airway obstruction as a consequence of edema of the larynx, swelling of tongue and lips (angioedema). This may result in stridor and suffocation.
   5. Respiratory failure (manifestations range from tachypnea to apnea) that may be related to the factors mentioned above as well as bronchoconstriction of the lower airways manifested by wheezing. These patients may also develop adult respiratory distress syndrome (ARDS).

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Table 18.1. Common Causes of Systemic Anaphylactic Reactions

1. Drugs
   —Antibiotics (i.e., penicillins, cephalosporins, sulfonamides, vancomycin)
   — Local anesthetics (i.e., lidocaine, procaine)
   — Muscle relaxants
   — Others (i.e., insulin, protamine)
2. Foods
   — Nuts and seeds
   — Fish, shellfish
   — Milk, eggs
3. Food additives
   — Aspartame
   — Monosodium glutamate
4. Diagnostics
   — Iodinated radiographic materials
5. Insect and snakes (stings and bites)
6. Exercise
7. Other
   — Latex gloves
   — Heterologous serum (i.e., tetanus antitoxin)

6. Cardiovascular collapse: The pathophysiology is thought to be related to enhanced vascular permeability, peripheral vasodilation, and intravascular volume depletion. A heart rate increase >20 bpm from baseline and a decrease of mean arterial pressure >20 torr (mmHg) are characteristic.
7. Dysrhythmias: Both supraventricular and ventricular rhythm disorders have been described in patients with anaphylaxis.

D. Laboratory Findings
1. Do not wait for laboratory data to institute therapy!
2. Patients with anaphylaxis may present with leukocytosis or leukopenia.
3. Thrombocytopenia may appear in severe cases.
4. Immunoglobulin E (IgE) measurements may not be helpful, because many patients may manifest non-IgE-mediated anaphylaxis.

E. Management
1. ABCs
   Secure the airway, and assist with breathing and circulation as with any other patient presenting with a potentially critical illness.
2. The drug of choice for patients with acute anaphylaxis is epinephrine. The dosage is 0.3–0.5 mL of 1:1000 dilution (0.3–0.5 mg) subcutaneously every 10–20 min or intravenously as described below. Endotracheal administration can be attempted when no other route is available.
3. Antihistamines
   Traditionally, H_1-receptor antihistamines have been used; i.e., diphenhydramine (Benadryl) 25–50 mg intramuscularly (IM), intravenously (IV), or PO q6–8 h. In theory, the combination of H_1- and H_2-receptor antihistamines might

be a better chance of preventing further histamine-mediated reactions than H_1 blockers alone; i.e., cimetidine (Tagamet) 300 mg IV or PO q6 h.

4. Corticosteroids have an uncertain place in the management of acute reaction, since there is a 4–6 h latent period before such agents are pharmacologically effective. The current recommended agents are hydrocortisone (Solu-Cortef) 250 mg IV q6 h or methylprednisolone (Solu-Medrol) 50 mg IV q6 h for 2–4 doses.
5. In cases of severe bronchospasm, the following drugs can be used:
   a. Metaproterenol 0.3 mL (5% solution) in 2.5 mL of saline, inhaled through a nebulizer
   b. Aminophylline loading dose of 6 mg/kg IV over 30 min followed by 0.3–0.9 mg/kg/h
6. In patients with profound hypotension
   a. Adequate IV fluid administration (up to 1 L every 20–30 min as needed).
   b. Epinephrine 1 mL of 1:1000 dilution in 500 mL of D_5W at a rate of 0.5–5 μg (0.25–2.5 mL)/min.
   c. Norepinephrine (Levophed): 4 mg in 1 L of D_5W at a rate of 2–12 μg (0.5–3 mL)/min.
   d. Glucagon may be particularly useful in patients taking beta-adrenergic blockers. The recommended dose is 1 mg in 1 L of D_5W at a rate of 5–15 μg (5–15 mL)/min.

F. Preventive measures for patients at high risk of anaphylaxis are depicted in Table 18.2.

Table 18.2. Preventive Measures for Patients at High Risk for Anaphylaxis

1. Avoid exposure
2. Slow administration of suspected agents under medical supervision in adequate facility (i.e., ICU)
3. Optimal management of underlying disorders
4. Short- and long-term desensitization (i.e., penicillin, aspirin)

■ II. STEVENS-JOHNSON SYNDROME (ERYTHEMA MULTIFORME)

A. Definition. Erythema multiforme (EM) is an erythematous maculopapular cutaneous eruption of variable form. When EM grades into a more serious clinical state, the term Stevens-Johnson syndrome (SJS) is used.

B. Etiology. Common causes of EM and SJS are depicted in Table 18.3.

C. Clinical Manifestations
1. Prodromal symptoms may include
   a. Malaise, headache
   b. Pharyngitis, rhinorrhea
   c. Diarrhea
   d. Arthralgias

Table 18.3. Causes of Erythema Multiforme/Stevens-Johnson Syndrome

1. Infections
   - — Viral (i.e., herpes simplex, measles, hepatitis B)
   - — Bacterial (i.e., streptococcus, pseudomonas)
   - — Mycobacterial (i.e., tuberculosis)
   - — Spirochetes (i.e., syphilis)
   - — Fungal (i.e., histoplasmosis)
2. Drugs
   - — Analgesics (i.e., aspirin, nonsteroidal anti-inflammatory drugs)
   - — Antibiotics (i.e., sulfonamides, penicillins, tetracycline)
   - — Anticonvulsants (i.e., ethosuximide)
   - — Antihypertensives (i.e., minoxidil)
   - — Glucocorticoids
   - — H_2-blockers (i.e., cimetidine)
3. Immunizations
   - — Horse serum
   - — Polio vaccine
   - — Pertussis vaccine
4. Neoplasms (i.e., lymphomas)
5. Connective tissue disorders (i.e., lupus erythematosus)
6. Physical agents
   - — Radiation therapy
   - — Sunlight
7. Others
   - — Inflammatory bowel disease
   - — Sarcoidosis

2. The earliest lesions in EM are often red, edematous papules surrounded by blanching. They enlarge to form small plaques with concentric alterations in color and morphology.
3. The so-called Target lesions are areas of central epidermal necrosis with or without bullae formation.
4. Patients admitted to the ICU with SJS usually present with extensive tissue necrosis and severe fluid depletion.

D. Laboratory Findings
1. Usually nondiagnostic.
2. Skin biopsy reveals a perivascular lymphocytic infiltrate in the upper dermis, subepidermal bullae formation, and endothelial cell swelling.

E. Management
1. Immediately discontinue suspected drugs or agents as well as all *nonessential* drugs.
2. The usefulness of systemic corticosteroids in this setting is controversial. In the absence of controlled clinical trials, some authors recommend beginning therapy with prednisone 1 mg/kg/d (or IV equivalent).

3. Fluid replacement as indicated by severity of the disease.
4. Evaluate for infection and treat appropriately.
5. Obtain consultation depending on the degree and sites of involvement (i.e., ophthalmology, plastic surgery).
6. Transfer the patient to a burn unit.
7. Intravenous gammaglobulin has been utilized with conflictive results.
8. Plasmapheresis has been used in some patients with success.

■ III. ANGIONEUROTIC LARYNGEAL EDEMA

A. Definition. Angioneurotic laryngeal edema (ALE) is characterized by nonpruritic local swelling involving the face, larynx, and skin of the extremities.

B. Etiology
1. Allergic
Related to foods (i.e., fish), drugs (i.e., angiotensin-converting enzyme [ACE] inhibitors), inhaled substances, insect stings (i.e., bees).
2. Hereditary
Caused by a deficiency in C_1-esterase inhibitor. Autosomal dominant. Precipitating events may include trauma and emotional stress.

C. Clinical Manifestations
1. Swelling of face, larynx, and skin of extremities.
2. Depending on the progression, stridor may be a prominent feature with ensuing respiratory distress.
3. Abdominal pain, nausea, and vomiting.

D. Laboratory Findings. Nondiagnostic except in cases of hereditary ALE.

E. Management
1. ABCs
Secure the airway, and assist with breathing and circulation as with any other patient presenting with a potentially critical illness.
2. Avoid precipitating allergens.
3. If ALE is thought to be allergic in origin, administer parenteral epinephrine and antihistamines (as noted in "Anaphylaxis," above).
4. Intubation is only rarely required for patients with allergic ALE, while in patients with hereditary ALE, the treatment of the acute episode may require urgent intubation or tracheostomy.