Miller Anaphylactic Reactions

• Anaphylaxis, Anaphylactoid Responses, and Allergic Disorders Other Than Those Related to Lung Diseases and Asthma

Anaphylactic and Anaphylactoid Reactions

Anaphylaxis is a severe life-threatening allergic reaction. *Allergic* applies to immunologically mediated reactions, as opposed to those caused by pharmacologic idiosyncrasy, by direct toxicity or drug overdosage, or by drug interaction. 466, 470, 471 Anaphylaxis is the typical immediate hypersensitivity reaction (type 1). Such reactions are produced by the immunoglobulin E (IgE)-mediated release of pharmacologically active substances. These mediators in turn produce specific end-organ responses in the skin (urticaria), the respiratory system (bronchospasm and upper airway edema), and the cardiovascular system (vasodilation, changes in inotropy, and increased capillary permeability). Vasodilation occurs at the level of the capillary and postcapillary venule, leading to erythema, edema, and smooth muscle contraction. This clinical syndrome is called *anaphylaxis.* By contrast, *anaphylactoid reaction* denotes an identical or very similar clinical response that is not mediated by IgE or (usually) an antigen-antibody process. 472

In anaphylactic reactions, an injected substance can serve as the allergen itself. Low–molecular-weight agents are believed to act as haptens that form immunologic conjugates with host proteins. The offending substance, whether hapten or not, may be the parent compound, a nonenzymatically generated product, or a metabolic product formed in the patient‘s body. When an allergen binds immunospecific IgE antibodies on the surface of mast cells and basophils, histamine and eosinophilic chemotactic factors of anaphylaxis are released from the storage granules in a calcium- and energy-dependent process. 470 Other chemical mediators are rapidly synthesized and subsequently released in response to cellular activation. These mediators include slow-reacting substance of anaphylaxis, which is a combination of three leukotrienes; other leukotrienes 473 ; kinins; plateletactivating factors; adenosine; chemotactic factors; heparin tryptase; chymase; and prostaglandins, including the potent bronchoconstrictor prostaglandin D2, eosinophil growth and -activating factors, mast-cell growth factors, and proinflammatory and other factors that contribute to the IgE isotype switch.

The end-organ effects of the mediators produce the clinical syndrome of anaphylaxis. Usually a first wave of symptoms, including vasodilation and a feeling of impending doom, is quickly followed by the second wave as the cascade of mediators amplifies the reactions. In a sensitized patient, the onset of the signs and symptoms caused by these mediators is usually immediate but may be delayed 2 to 15 minutes or, in rare instances, as long as 2.5 hours after the parenteral injection of antigen. 473, 474 After oral administration, manifestations may occur at unpredictable times.

Mast-cell proliferation, together with severe progressive inflammation, contributes to the worsening of symptoms that occurs even after there is no longer an allergen load. Both activated mast cells and the antigen present in cells and lymphocytes start to make cytokines. These proinflammatory cytokines recruit more inflammatory cells, which promotes tissue edema and mediates a second wave of mast-cell degranulation. This second wave can promote recurrence of severe symptoms 6 to 8 hours later and necessitates, some believe, at least 8 hours of continued ICU-like observation.

In addition, there are multiple effector processes by which biologically active mediators can be generated to produce an anaphylactoid reaction. Activation of the blood coagulation and fibrinolytic systems, of the kinin-generating sequence, or of the complement cascade can produce the same inflammatory substances that result in an anaphylactic reaction. The two mechanisms known to activate the complement system are called classic and alternate. The classic pathway can be initiated through IgG or IgM (transfusion reactions) or plasmin. The alternate pathway can be activated by lipopolysaccharides (endotoxin), drugs (Althesin 472), radiographic contrast media, 475 membranes (nylon tricot membranes for bubble oxygenators 476), cellophane membranes of dialyzers, 477 vascular graft material, 478 latex or latex-containing products, 479 and perfluorocarbon artificial blood. In addition, histamine can be liberated independent of immunologic reactions. 480 Mast cells and basophils release histamine in response to chemicals or drugs. Most narcotics can release histamine, 480 producing an anaphylactoid reaction, as can radiographic contrast media, 475 *d*-tubocurarine, 481 and thiopental. What makes some patients susceptible to histamine release in response to drugs is unknown, but hereditary and environmental factors may play a role.

Intravenous contrast material is probably the most frequently used agent causing anaphylactoid reactions. Because diagnostic (skin and other) tests are helpful only in IgE-mediated reactions, pretesting is not useful in contrast reactions. Pretreatment with diphenhydramine, cimetidine (or ranitidine), and corticosteroids has been reported to be useful in preventing or ameliorating anaphylactoid reactions to intravenous contrast material 475, 482 and perhaps to narcotics and chymopapain. 483, 484 Unfortunately, very large doses of steroids (1 g of methylprednisolone intravenously) may be necessary to obtain a beneficial effect. 485 The efficacy of large-dose steroid therapy has not been confirmed. Other common substances associated with anaphylactic or anaphylactoid reactions that might merit preoperative therapy include antibiotics, volume expanders, and blood products 470, 486, 487 (Table 25–41). The anesthesiologist should be prepared preoperatively to treat an anaphylactic or anaphylactoid response.

In some cases, a patient with a history of anaphylactic or anaphylactoid reaction must receive a substance suspected of producing such a reaction (e.g., iodinated contrast material). Also, some patients have a higher-than-average likelihood of having a reaction, warranting well-planned pretreatment and therapy for possible anaphylactic and anaphylactoid reactions. 470

Minimizing the Risks Preoperatively

Although virtually all evidence on these subjects is merely anecdotal, enough consistent thought recurs through the literature to justify proposing an optimal approach to these problems. First, predisposing factors should be sought; the patient with a history of atopy or allergic rhinitis should be suspected as being at risk. Because anaphylactic and anaphylactoid reactions to contrast media occur five to ten times more frequently in patients with a previously suspected reaction, consideration should be given to administration of both H1 - and H2 -receptor antagonists for 16 to 24 hours before exposing these patients to a suspected allergen. The H1 -receptor antagonist appears to require this much time to act on the receptor. Volume status should be optimized, 470 and perhaps large doses of steroids (2 g of hydrocortisone) should also be administered before exposing patients to agents associated with a high incidence of anaphylactic or anaphylactoid reactions. 485, 486, 488 Older patients and patients taking ?-adrenergic–blocking drugs present special problems; they are at higher risk of having complications from both pretreatment (especially vigorous hydration) and therapy for anaphylactic reactions and are less responsive to treatment regimens. 489 One approach is to avoid drugs likely to trigger anaphylactic or anaphylactoid reactions or to alter the treatment protocol for this group. Drawing blood for later analysis, especially of tryptase, can be useful in clarifying the diagnosis. 490