anaphylactic reactions, and skin testing may be performed after the patient has recovered to elicit a local wheal and flare in response to the putative antigen. Elevations of tryptase levels in serum implicate mast cell activation in a systemic reaction and are particularly informative for anaphylaxis with episodes of hypotension during general anesthesia or when there has been a fatal outcome. However, because of the short half-life of tryptase, elevated levels are best detected within 4 h of a systemic reaction. Moreover, anaphylactic reactions to foods characteristically are not associated with elevations in serum tryptase.

TREATMENT ANAPHYLAXIS

Early recognition of an anaphylactic reaction is mandatory, since death can occur within minutes to hours after the first symptoms. Mild symptoms such as pruritus and urticaria can be controlled by administration of 0.3–0.5 mL of 1:1000 (1 mg/mL) epinephrine SC or IM, with repeated doses as required at 5- to 20-min intervals for a severe reaction. The failure to use epinephrine within the first 20 min of symptoms is a risk factor for poor outcome in studies of anaphylaxis to food. If the antigenic material was injected into an extremity, the rate of absorption may be reduced by prompt application of a tourniquet proximal to the reaction site, administration of 0.2 mL of 1:1000 epinephrine into the site, and removal without compression of an insect stinger, if present. An IV infusion should be initiated to provide a route for administration of 2.5 mL epinephrine, diluted 1:10,000, at 5- to 10-min intervals, volume expanders such as normal saline, and vasopressor agents such as dopamine if intractable hypotension occurs. Replacement of intravascular volume due to postcapillary venular leakage may require several liters of saline. Epinephrine provides both α- and β-adrenergic effects, resulting in vasoconstriction, bronchial smooth-muscle relaxation, and attenuation of enhanced venular permeability. Oxygen alone via a nasal catheter or with nebulized albuterol may be helpful, but either endotracheal intubation or a tracheostomy is mandatory for oxygen delivery if progressive hypoxia develops. Ancillary agents such as the antihistamine diphenhydramine, 50–100 mg IM or IV, and aminophylline, 0.25–0.5 g IV, are appropriate for urticaria-angioedema and bronchospasm, respectively. Intravenous glucocorticoids, 0.5–1 mg/kg of methylprednisolone, are not effective for the acute event but may alleviate later recurrence of bronchospasm, hypotension, or urticaria.

PREVENTION

Prevention of anaphylaxis must take into account the sensitivity of the individual, the dose and character of the diagnostic or therapeutic agent, and the effect of the route of administration on the rate of absorption. Beta blockers are relatively contraindicated in persons at risk for anaphylactic reactions, especially those sensitive to Hymenoptera venom or those undergoing immunotherapy for respiratory system allergy. If there is a definite history of a past anaphylactic reaction to a medication, it is advisable to select a structurally unrelated agent. A knowledge of cross-reactivity among agents is critical since, for example, cephalosporins have a cross-reactive ring structure with the penicillins. When skin testing, a prick or scratch skin test should precede an intradermal test, since the latter has a higher risk of causing anaphylaxis. These tests should be performed before the administration of certain materials that are likely to elicit anaphylactic reactions, such as allergenic extracts. Skin testing for antibiotics or chemotherapeutic agents should be performed only on patients with a positive clinical history consistent with an IgE-mediated reaction and in imminent need of the antibiotic in question; skin testing is of no value for non-IgE-mediated eruptions. With regard to penicillin, two-thirds of patients with a positive reaction history and positive skin tests to benzylpenicilloyl-polylysine (BPL) and/or the minor determinant mixture (MDM) of benzylpenicillin products experience allergic reactions with treatment, and these reactions are almost uniformly of the anaphylactic type in those patients with minor determinant reactivity. Even patients without a history of previous clinical reactions have a 2–6% incidence of positive skin tests to the two test materials, and about 3 per 1000 with a negative history experience anaphylaxis with therapy, with a mortality of about 1 per 100,000.

If an agent carrying a risk of eliciting an anaphylactic response is required because a non-cross-reactive alternative is not available, desensitization can be performed with most antibiotics and other classes of therapeutic agents by the IV, SC, or PO route. Typically, graded quantities of the drug are given by the selected route starting below the threshold dose for an adverse reaction and then doubling each dose until a therapeutic dosage is achieved. Due to the risk of systemic anaphylaxis during the course of desensitization, such a procedure should be performed under the supervision of a specialist and in a setting in which resuscitation equipment is at hand and an IV line is in place. Once a desensitized state is achieved, it is critical to continue administration of the therapeutic agent at regular intervals throughout the treatment period to prevent the reestablishment of a significant pool of sensitized cells.

A different form of protection involves the development of blocking antibody of the IgG class, which protects against Hymenoptera venom–induced anaphylaxis by interacting with antigen so that less reaches the sensitized tissue mast cells. The maximal risk for systemic anaphylactic reactions in persons with Hymenoptera sensitivity occurs in association with a currently positive skin test. Although there is little cross-reactivity between honey bee and yellow jacket venoms, there is a high degree of cross-reactivity between yellow jacket venom and the rest of the vespid venoms (yellow or white-faced hornets and wasps). Prevention involves modification of outdoor activities to exclude bare feet, wearing perfumed toiletries, eating in areas attractive to insects, clipping hedges or grass, and hauling away trash or fallen fruit. As with each anaphylactic sensitivity, the individual should wear an informational bracelet and have immediate access to an unexpired autoinjectable epinephrine kit. Venom immunotherapy for 5 years can induce a state of resistance to sting reactions that is independent of serum levels of specific IgG or IgE. For children under the age of 10 with a systemic reaction limited to skin, the likelihood of progression to more serious respiratory or vascular manifestations is low, and thus immunotherapy is not recommended.

URTICARIA AND ANGIOEDEMA

DEFINITION

Urticaria and angioedema may appear separately or together as cutaneous manifestations of localized nonpitting edema; a similar process may occur at mucosal surfaces of the upper respiratory or gastrointestinal tract. *Urticaria* involves only the superficial portion of the dermis, presenting as well-circumscribed wheals with erythematous raised serpiginous borders and blanched centers that may coalesce to become giant wheals. *Angioedema* is a well-demarcated localized edema involving the deeper layers of the skin, including the subcutaneous tissue, and can also involve the bowel wall. Recurrent episodes of urticaria and/or angioedema of less than 6 weeks' duration are considered acute, whereas attacks persisting beyond this period are designated chronic.

PREDISPOSING FACTORS AND ETIOLOGY

Urticaria and angioedema probably occur more frequently than reported because of the evanescent, self-limited nature of such eruptions, which seldom require medical attention when limited to the skin. Although persons in any age group may experience acute or chronic urticaria and/or angioedema, these lesions increase in frequency after adolescence, with the highest incidence occurring in persons in the third decade of life; indeed, one survey of college students indicated that 15–20% had experienced a pruritic wheal reaction.

The classification of urticaria-angioedema presented in Table 376-1 focuses on the different mechanisms for eliciting clinical disease and can be useful for differential diagnosis; nonetheless, most cases of chronic urticaria are idiopathic. Urticaria and/or angioedema occurring during the appropriate season in patients with seasonal respiratory allergy or as a result of exposure to animals or molds is attributed to inhalation or physical contact with pollens, animal dander, and mold spores, respectively. However, urticaria and angioedema secondary to inhalation are relatively uncommon compared to urticaria and