

with red papillae); petechiae of the palate; a facial flush with circumoral pallor; linear petechiae in the antecubital fossae; and desquamation of the involved skin, palms, and soles 5–20 days after onset of the eruption. A similar desquamation of the palms and soles is seen in toxic shock syndrome (TSS), in Kawasaki disease, and after severe febrile illnesses. Certain strains of staphylococci also produce an erythrogenic toxin that leads to the same clinical findings as in streptococcal scarlet fever, except that the anti-streptolysin O or -DNase B titers are not elevated.

In *toxic shock syndrome*, staphylococcal (phage group I) infections produce an exotoxin (TSST-1) that causes the fever and rash as well as enterotoxins. Initially, the majority of cases were reported in menstruating women who were using tampons. However, other sites of infection, including wounds and nasal packing, can lead to TSS. The diagnosis of TSS is based on clinical criteria (Chap. 172), and three of these involve mucocutaneous sites (diffuse erythema of the skin, desquamation of the palms and soles 1–2 weeks after onset of illness, and involvement of the mucous membranes). The latter is characterized as hyperemia of the vagina, oropharynx, or conjunctivae. Similar systemic findings have been described in *streptococcal toxic shock syndrome* (Chap. 173), and although an exanthem is seen less often than in TSS due to a staphylococcal infection, the underlying infection is often in the soft tissue (e.g., cellulitis).

The cutaneous eruption in *Kawasaki disease* (Chap. 385) is polymorphous, but the two most common forms are morbilliform and scarlatiniform. Additional mucocutaneous findings include bilateral conjunctival injection; erythema and edema of the hands and feet followed by desquamation; and diffuse erythema of the oropharynx, red strawberry tongue, and dry fissured lips. This clinical picture can resemble TSS and scarlet fever, but clues to the diagnosis of Kawasaki disease are cervical lymphadenopathy, cheilitis, and thrombocytosis. The most serious associated systemic finding in this disease is coronary aneurysms secondary to arteritis. Scarlatiniform eruptions are also seen in the early phase of SSSS (see “Vesicles/Bullae,” above), in young adults with *Arcanobacterium haemolyticum* infection, and as reactions to drugs.

URTICARIA

(Table 72-14) *Urticaria* (hives) are transient lesions that are composed of a central wheal surrounded by an erythematous halo or flare. Individual lesions are round, oval, or figurate and are often pruritic. Acute and chronic urticaria have a wide variety of allergic etiologies and reflect edema in the dermis. Urticarial lesions can also be seen in patients with mastocytosis (urticaria pigmentosa), hypo- or hyperthyroidism, and systemic-onset juvenile idiopathic arthritis (Still's disease). In both juvenile- and adult-onset Still's disease, the lesions

coincide with the fever spike, are transient, and are due to dermal infiltrates of neutrophils.

The common *physical urticarias* include dermatographism, solar urticaria, cold urticaria, and cholinergic urticaria. Patients with *dermatographism* exhibit linear wheals following minor pressure or scratching of the skin. It is a common disorder, affecting ~5% of the population. *Solar urticaria* characteristically occurs within minutes of sun exposure and is a skin sign of one systemic disease—erythropoietic protoporphyria. In addition to the urticaria, these patients have subtle pitted scarring of the nose and hands. *Cold urticaria* is precipitated by exposure to the cold, and therefore exposed areas are usually affected. In occasional patients, the disease is associated with abnormal circulating proteins—more commonly cryoglobulins and less commonly cryofibrinogens. Additional systemic symptoms include wheezing and syncope, thus explaining the need for these patients to avoid swimming in cold water. Autosomal dominantly inherited cold urticaria is associated with dysfunction of cryopyrin. *Cholinergic urticaria* is precipitated by heat, exercise, or emotion and is characterized by small wheals with relatively large flares. It is occasionally associated with wheezing.

Whereas urticarias are the result of dermal edema, subcutaneous edema leads to the clinical picture of *angioedema*. Sites of involvement include the eyelids, lips, tongue, larynx, and gastrointestinal tract as well as the subcutaneous tissue. Angioedema occurs alone or in combination with urticaria, including urticarial vasculitis and the physical urticarias. Both acquired and hereditary (autosomal dominant) forms of angioedema occur (Chap. 376), and in the latter, urticaria is rarely, if ever, seen.

Urticarial vasculitis is an immune complex disease that may be confused with simple urticaria. In contrast to simple urticaria, individual lesions tend to last longer than 24 h and usually develop central petechiae that can be observed even after the urticarial phase has resolved. The patient may also complain of burning rather than pruritus. On biopsy, there is a leukocytoclastic vasculitis of the small dermal blood vessels. Although many cases of urticarial vasculitis are idiopathic in origin, it can be a reflection of an underlying systemic illness such as lupus erythematosus, Sjögren's syndrome, or hereditary complement deficiency. There is a spectrum of urticarial vasculitis that ranges from purely cutaneous to multisystem involvement. The most common systemic signs and symptoms are arthralgias and/or arthritis, nephritis, and crampy abdominal pain, with asthma and chronic obstructive lung disease seen less often. Hypocomplementemia occurs in one- to two-thirds of patients, even in the idiopathic cases. Urticarial vasculitis can also be seen in patients with *hepatitis B* and *hepatitis C* infections, *serum sickness*, and *serum sickness-like illnesses* (e.g., due to cefaclor, minocycline).

PAPULONODULAR SKIN LESIONS

(Table 72-15) In the *papulonodular diseases*, the lesions are elevated above the surface of the skin and may coalesce to form larger plaques. The location, consistency, and color of the lesions are the keys to their diagnosis; this section is organized on the basis of color.

WHITE LESIONS

In *calcinosis cutis*, there are firm white to white-yellow papules with an irregular surface. When the contents are expressed, a chalky white material is seen. *Dystrophic calcification* is seen at sites of previous inflammation or damage to the skin. It develops in acne scars as well as on the distal extremities of patients with systemic sclerosis and in the subcutaneous tissue and intermuscular fascial planes in DM. The latter is more extensive and is more commonly seen in children. An elevated calcium phosphate product, most commonly due to secondary hyperparathyroidism in the setting of renal failure, can lead to nodules of *metastatic calcinosis cutis*, which tend to be subcutaneous and periarticular. These patients can also develop calcification of muscular arteries and subsequent ischemic necrosis (calciphylaxis). *Osteoma cutis*, in the form of small papules, most commonly occurs on the face

TABLE 72-14 CAUSES OF URTICARIA AND ANGIOEDEMA

- I. Primary cutaneous disorders
 - A. Acute and chronic urticaria^a
 - B. Physical urticaria
 1. Dermatographism
 2. Solar urticaria^b
 3. Cold urticaria^b
 4. Cholinergic urticaria^b
 - C. Angioedema (hereditary and acquired)^{b,c}
- II. Systemic diseases
 - A. Urticarial vasculitis
 - B. Hepatitis B or C infection
 - C. Serum sickness
 - D. Angioedema (hereditary and acquired)

^aA small minority develop anaphylaxis. ^bAlso systemic. ^cAcquired angioedema can be idiopathic, associated with a lymphoproliferative disorder, or due to a drug, e.g., angiotensin-converting enzyme (ACE) inhibitors.