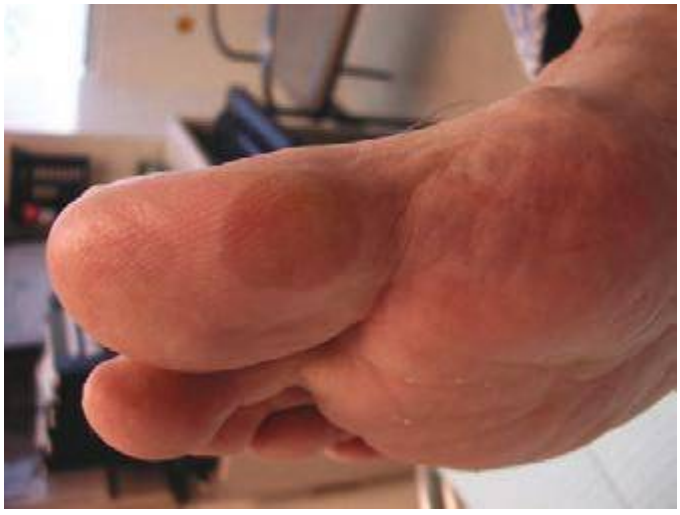

FIGURE 74-5 Sorafenib-associated hand-foot syndrome.

absence of ear, nose, throat, and upper respiratory tract symptoms; and polymorphism of the skin lesions support a drug rather than a viral eruption. Certain medications carry very high rates of morbilliform eruption, including nevirapine and lamotrigine, even in the absence of hypersensitivity reactions. Lamotrigine morbilliform rash is associated with higher starting doses, rapid dose escalation, concomitant use of valproate (which increases lamotrigine levels and half-life) and use in children, especially with seizure disorder.

Maculopapular reactions usually develop within 1 week of initiation of therapy and last less than 2 weeks. Occasionally, these eruptions resolve despite continued use of the responsible drug. Because the eruption may also worsen, the suspect drug should be discontinued unless it is essential; it is important to note that the rash may continue to progress for a few days to up to one week following medication discontinuation. Oral antihistamines and emollients may help relieve pruritus. Short courses of potent topical glucocorticoids can reduce inflammation and symptoms. Systemic glucocorticoid treatment is rarely indicated.

Pruritus Pruritus is associated with almost all drug eruptions and, in some cases, may represent the only symptom of the adverse cutaneous reaction. It is usually alleviated by antihistamines such as hydroxyzine or diphenhydramine. Pruritus stemming from specific medications may require distinct treatment; opiate-related pruritus may require selective opiate antagonists to gain relief. Pruritus is a common complication of antimalarial therapy, occurring in up to 50% of black patients receiving chloroquine, and may be severe enough to lead to discontinuation of treatment. It is much rarer in Caucasians taking chloroquine. Intense pruritus, sometimes accompanied by an eczematous rash, may occur in 20% of patients receiving IFN and ribavirin for hepatitis C; addition of the protease inhibitor telaprevir may increase this occurrence to 50% of treated patients.

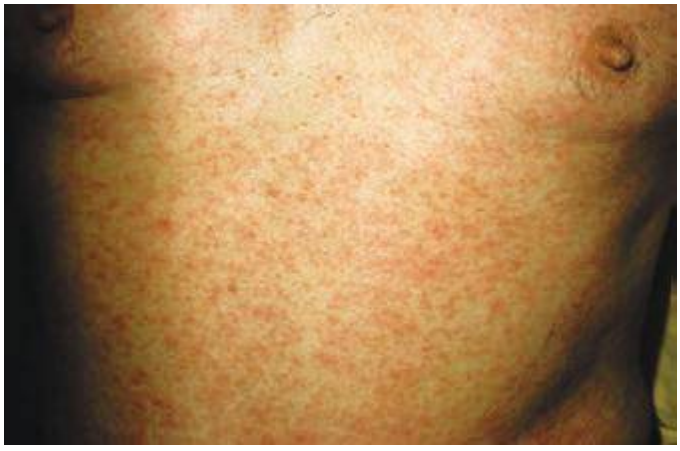

FIGURE 74-6 Morbilliform drug eruption.

Urticaria/Angioedema/Anaphylaxis Urticaria, the second most frequent type of cutaneous reaction to drugs, is characterized by pruritic, red wheals of varying size rarely lasting more than 24 h. It has been observed in association with nearly all drugs, most frequently ACE inhibitors, aspirin, NSAIDs, penicillin, and blood products. However, medications account for no more than 10–20% of acute urticaria cases. Deep edema within dermal and subcutaneous tissues is known as angioedema and may involve respiratory and gastrointestinal mucous membranes as well. Urticaria and angioedema may be part of a life-threatening anaphylactic reaction.

Drug-induced urticaria may be caused by three mechanisms: an IgE-dependent mechanism, circulating immune complexes (serum sickness), and nonimmunologic activation of effector pathways. IgE-dependent urticarial reactions usually occur within 36 h of drug exposure but can occur within minutes. Immune complex–induced urticaria associated with serum sickness–like reactions usually occurs 6–12 days after first exposure. In this syndrome, the urticarial eruption (typically polycyclic plaques) may be accompanied by fever, hematuria, arthralgias, hepatic dysfunction, and neurologic symptoms. Certain drugs, such as NSAIDs, ACE inhibitors, angiotensin II antagonists, radiographic dye, and opiates, may induce urticarial reactions, angioedema, and anaphylaxis in the absence of drug-specific antibody through direct mast-cell degranulation.

Radiocontrast agents are a common cause of urticaria and, in rare cases, can cause anaphylaxis. High-osmolality radiocontrast media were about five times more likely to induce urticaria (1%) or anaphylaxis than were newer low-osmolality media. About one-third of those with mild reactions to previous exposure react on reexposure. Pretreatment with prednisone and diphenhydramine reduces reaction rates. Persons with a reaction to a high-osmolality contrast media may be given low-osmolality media if later contrast studies are required.

The treatment of urticaria or angioedema depends on the severity of the reaction. In severe cases with respiratory or cardiovascular compromise, epinephrine is the mainstay of therapy, but its effect is reduced in patients using beta blockers. Treatment with intravenous systemic glucocorticoids is helpful. For patients with urticaria without symptoms of angioedema or anaphylaxis, drug withdrawal and oral antihistamines are usually sufficient. Future drug avoidance is recommended; rechallenge, especially in individuals with severe reactions, should only occur in an intensive care setting.

Anaphylactoid Reactions Vancomycin is associated with red man syndrome, a histamine-related anaphylactoid reaction characterized by flushing, diffuse maculopapular eruption, and hypotension. In rare cases, cardiac arrest may be associated with rapid IV infusion of the medication.

Irritant/Allergic Contact Dermatitis Patients using topical medications may develop an irritant or allergic contact dermatitis to the medication itself or to a preservative or other component of the formulation. Reactions to chlorhexidine, neomycin sulfate, and polymyxin B are common. Allergic contact dermatitis to topical glucocorticoids may also occur and is paradoxically partially masked by the anti-inflammatory nature of the medication itself; typically this allergy is selective for one of the four classes of glucocorticoid types, as subdivided by allergenic properties. Patch testing can be useful to determine whether a patient is steroid allergic. Desoximetasone is rarely allergenic.

Fixed Drug Eruptions These less common reactions are characterized by one or more sharply demarcated, dull red to brown lesions, sometimes with central bulla (Fig. 74-7). Hyperpigmentation often results after resolution of the acute inflammation. With rechallenge, the lesion recurs in the same (e.g., fixed) location. Lesions often involve the lips, hands, legs, face, genitalia, and oral mucosa and cause a burning sensation. Most patients have multiple lesions. Fixed drug eruptions have been associated with pseudoephedrine (frequently a nonpigmented reaction), phenolphthalein (in laxatives), sulfonamides, tetracyclines, NSAIDs, and barbiturates.