TABLE 24-1 DISEASES ASSOCIATED WITH FEVER AND RASH (*CONTINUED*)

Disease	Etiology	Description	Group Affected/ Epidemiologic Factors	Clinical Syndrome	Chapter
Eruptions with Ulcers and/or Eschars (*Continued*)					
Tularemia	*Francisella tularensis*	Ulceroglandular form: erythematous, tender papule evolves into necrotic, tender ulcer with raised borders; in 35% of cases, eruptions (maculopapular, vesiculopapular, acneiform, or urticarial; erythema nodosum; or EM) may occur	Exposure to ticks, biting flies, infected animals	Fever, headache, lymphadenopathy	195
Anthrax	*Bacillus anthracis*	Pruritic papule enlarging and evolving into a 1- by 3-cm painless ulcer surrounded by vesicles and then developing a central eschar with edema; residual scar	Exposure to infected animals or animal products, other exposure to anthrax spores	Lymphadenopathy, headache	261e

[a]See "Purpuric Eruptions." [b]See "Confluent Desquamative Erythemas." [c]In human granulocytotropic ehrlichiosis or anaplasmosis (caused by *Anaplasma phagocytophila;* most common in the upper midwestern and northeastern United States), rash is rare. [d]See "Viral hemorrhagic fever" under "Purpuric Eruptions" for dengue hemorrhagic fever/dengue shock syndrome. [e]See "Centrally Distributed Maculopapular Eruptions." [f]See etiology-specific chapters. [g]See "Peripheral Eruptions." [h]See "Vesiculobullous or Pustular Eruptions."

Abbreviations: CNS, central nervous system; DIC, disseminated intravascular coagulation; G-CSF, granulocyte colony-stimulating factor; HLA, human leukocyte antigen.

seen in urban environments where rodents proliferate. Outside the United States, other rickettsial diseases cause a spotted-fever syndrome and should be considered in residents of or travelers to endemic areas. Similarly, *typhoid fever*, a nonrickettsial disease caused by *Salmonella typhi* (Chap. 190), is usually acquired during travel outside the United States. *Dengue fever*, caused by a mosquito-transmitted flavivirus, occurs in tropical and subtropical regions of the world (Chap. 233).

Some centrally distributed maculopapular eruptions have distinctive features. Erythema migrans, the rash of *Lyme disease* (Chap. 210), typically manifests as single or multiple annular plaques. Untreated erythema migrans lesions usually fade within a month but may persist for more than a year. *Southern tick-associated rash illness* (STARI) (Chap. 210) has an erythema migrans–like rash but is less severe than Lyme disease and often occurs in regions where Lyme is not endemic. *Erythema marginatum*, the rash of *acute rheumatic fever* (Chap. 381), has a distinctive pattern of enlarging and shifting transient annular lesions.

Collagen vascular diseases may cause fever and rash. Patients with *systemic lupus erythematosus* (Chap. 378) typically develop a sharply defined, erythematous eruption in a butterfly distribution on the cheeks (malar rash) as well as many other skin manifestations. *Still's disease* (Chap. 398) presents as an evanescent, salmon-colored rash on the trunk and proximal extremities that coincides with fever spikes.

PERIPHERAL ERUPTIONS

These rashes are alike in that they are most prominent peripherally or begin in peripheral (acral) areas before spreading centripetally. Early diagnosis and therapy are critical in *Rocky Mountain spotted fever* (Chap. 211) because of its grave prognosis if untreated. Lesions evolve from macular to petechial, start on the wrists and ankles, spread centripetally, and appear on the palms and soles only later in the disease. The rash of *secondary syphilis* (Chap. 206), which may be generalized but is prominent on the palms and soles, should be considered in the differential diagnosis of pityriasis rosea, especially in sexually active patients. *Chikungunya fever* (Chap. 233), which is transmitted by mosquito bite in Africa and the Indian Ocean region, is associated with a maculopapular eruption and severe polyarticular small-joint arthralgias. *Hand-foot-and-mouth disease* (Chap. 228), most commonly caused by coxsackievirus A16, is distinguished by tender vesicles distributed peripherally and in the mouth; outbreaks commonly occur within families. The classic target lesions of *erythema multiforme* appear symmetrically on the elbows, knees, palms, soles, and face. In severe cases, these lesions spread diffusely and involve mucosal surfaces. Lesions may develop on the hands and feet in *endocarditis* (Chap. 155).

CONFLUENT DESQUAMATIVE ERYTHEMAS

These eruptions consist of diffuse erythema frequently followed by desquamation. The eruptions caused by group A *Streptococcus* or *Staphylococcus aureus* are toxin-mediated. *Scarlet fever* (Chap. 173) usually follows pharyngitis; patients have a facial flush, a "strawberry" tongue, and accentuated petechiae in body folds (Pastia's lines). *Kawasaki disease* (Chaps. 72 and 385) presents in the pediatric population as fissuring of the lips, a strawberry tongue, conjunctivitis, adenopathy, and sometimes cardiac abnormalities. *Streptococcal toxic shock syndrome* (Chap. 173) manifests with hypotension, multiorgan failure, and, often, a severe group A streptococcal infection (e.g., necrotizing fasciitis). *Staphylococcal toxic shock syndrome* (Chap. 172) also presents with hypotension and multiorgan failure, but usually only *S. aureus* colonization—not a severe *S. aureus* infection—is documented. *Staphylococcal scalded-skin syndrome* (Chap. 172) is seen primarily in children and in immunocompromised adults. Generalized erythema is often evident during the prodrome of fever and malaise; profound tenderness of the skin is distinctive. In the exfoliative stage, the skin can be induced to form bullae with light lateral pressure (Nikolsky's sign). In a mild form, a scarlatiniform eruption mimics scarlet fever, but the patient does not exhibit a strawberry tongue or circumoral pallor. In contrast to the staphylococcal scalded-skin syndrome, in which the cleavage plane is superficial in the epidermis, *toxic epidermal necrolysis* (Chap. 74), a maximal variant of *Stevens-Johnson syndrome*, involves sloughing of the entire epidermis, resulting in severe disease. *Exfoliative erythroderma syndrome* (Chaps. 72 and 74) is a serious reaction associated with systemic toxicity that is often due to eczema, psoriasis, a drug reaction, or mycosis fungoides. *Drug rash with eosinophilia and systemic symptoms (DRESS)*, often due to antiepileptic and antibiotic agents (Chap. 74), initially appears similar to an exanthematous drug reaction but may progress to exfoliative erythroderma; it is accompanied by multi-organ failure and has an associated mortality rate of ~10%.

VESICULOBULLOUS OR PUSTULAR ERUPTIONS

Varicella (Chap. 217) is highly contagious, often occurring in winter or spring. At any point in time, within a given region of the body, varicella lesions are in different stages of development. In immunocompromised hosts, varicella vesicles may lack the characteristic erythematous base or may appear hemorrhagic. Lesions of *Pseudomonas "hot-tub" folliculitis* (Chap. 189) are also pruritic and may appear similar to those of varicella. However, hot-tub folliculitis generally occurs in outbreaks after bathing in hot tubs or swimming pools, and lesions occur in regions occluded by bathing suits. Lesions of *variola (smallpox)* (Chap. 261e) also appear similar to those of varicella but are all at the same stage of development in a given region of the body. Variola lesions are most prominent on the face and extremities, while varicella lesions are most prominent on the trunk. *Herpes simplex virus infection* (Chap. 216) is characterized by hallmark grouped vesicles on an erythematous base. Primary herpes infection is accompanied by fever and toxicity, while recurrent disease is milder. *Rickettsialpox* (Chap. 211) is often documented in urban settings and is characterized