Chapter 19: Fever and Rash

Elaine T. Kaye; Kenneth M. Kaye

INTRODUCTION

The acutely ill patient with fever and rash often presents a diagnostic challenge for physicians, yet the distinctive appearance of an eruption in concert with a clinical syndrome can facilitate a prompt diagnosis and the institution of life-saving therapy or critical infection-control interventions. **Representative images of many of the rashes discussed in this chapter are included in Chap. A1.**

APPROACH TO THE PATIENT WITH FEVER AND RASH

A thorough history of patients with fever and rash includes the following relevant information: immune status, medications taken within the previous month, specific travel history, immunization status, exposure to domestic pets and other animals, history of animal (including arthropod) bites, recent dietary exposures, existence of cardiac abnormalities, presence of prosthetic material, recent exposure to ill individuals, and sexual exposures. The history should also include the site of onset of the rash and its direction and rate of spread.

Physical Examination

A thorough physical examination entails close attention to the rash, with an assessment and precise definition of its salient features. First, it is critical to determine what *type* of lesions make up the eruption. *Macules* are flat lesions defined by an area of changed color (i.e., a blanchable erythema). *Papules* are raised, solid lesions <5 mm in diameter; *plaques* are lesions >5 mm in diameter with a flat, plateau-like surface; and *nodules* are lesions >5 mm in diameter with a more rounded configuration. *Wheals* (urticaria, hives) are papules or plaques that are pale pink and may appear annular (ringlike) as they enlarge; classic (nonvasculitic) wheals are transient, lasting only 24 h in any defined area. *Vesicles* (<5 mm) and *bullae* (>5 mm) are circumscribed, elevated lesions containing fluid. *Pustules* are raised lesions containing purulent exudate; vesicular processes such as varicella or herpes simplex may evolve to pustules. *Nonpalpable purpura* is a flat lesion that is due to bleeding into the skin. If <3 mm in diameter, the purpuric lesions are termed *petechiae*; if >3 mm, they are termed *ecchymoses. Palpable purpura* is a raised lesion that is due to inflammation of the vessel wall (vasculitis) with subsequent hemorrhage. An *ulcer* is a defect in the skin extending at least into the upper layer of the dermis, and an *eschar* (tâche noire) is a necrotic lesion covered with a black crust.

Other pertinent features of rashes include their *configuration* (i.e., annular or target), the *arrangement* of their lesions, and their *distribution* (i.e., central or peripheral).

For further discussion, see Chaps. 56, 58, 122, and 129.

CLASSIFICATION OF RASH

This chapter reviews rashes that reflect systemic disease, but it does not include localized skin eruptions (i.e., cellulitis, impetigo) that may also be associated with fever **(Chap. 129)**. The chapter is not intended to be all-inclusive, but it covers the most important and most common diseases associated with fever and rash. Rashes are classified herein on the basis of lesion morphology and distribution. For practical purposes, this classification system is based on the most typical disease presentations. However, morphology may vary as rashes evolve, and the presentation of diseases with rashes is subject to many variations **(Chap. 58)**. For instance, the classic petechial rash of Rocky Mountain spotted fever **(Chap. 187)** may initially consist of blanchable erythematous macules distributed peripherally; at times, however, the rash associated with this disease may not be predominantly acral, or no rash may develop at all.

Diseases with fever and rash may be classified by type of eruption: centrally distributed maculopapular, peripheral, confluent desquamative

erythematous, vesiculobullous, urticaria-like, nodular, purpuric, ulcerated, or with eschars. Diseases are listed by these categories in **Table 19-1**, and many are highlighted in the text. However, for a more detailed discussion of each disease associated with a rash, the reader is referred to the chapter dealing with that specific disease. **(Reference chapters are cited in the text and listed in Table 19-1.)**

TABLE 19-1

Diseases Associated with Fever and Rash

DISEASE	ETIOLOGY	DESCRIPTION	GROUP AFFECTED/EPIDEMIOLOGIC FACTORS	CLINICAL SYNDROME	CHAPTER
Centrally Distributed Maculopapular Eruptions					
Acute meningococcemia[a]	—	—	—	—	155
Drug reaction with eosinophilia and systemic symptoms (DRESS); also termed drug-induced hypersensitivity syndrome (DIHS)[b]; Chikungunya[c]; COVID-19[c]	—	—	—	—	60
Rubeola (measles, first disease) **(Fig. 19-1, Fig. A1-2, Fig. A1-3)**	Paramyxovirus	Discrete lesions that become confluent as rash spreads from hairline downward, usually sparing palms and soles; lasts ≥3 days; Koplik's spots	Nonimmune individuals	Cough, conjunctivitis, coryza, severe prostration	205
Rubella (German measles, third disease) **(Fig. A1-4)**	Togavirus	Spreads from hairline downward, clearing as it spreads; Forchheimer spots	Nonimmune individuals	Adenopathy, arthritis	206
Erythema infectiosum (fifth disease) **(Fig. A1-1)**	Human parvovirus B19	Bright-red "slapped-cheeks" appearance followed by lacy reticular rash that waxes and wanes over 3 weeks; rarely, papular-purpuric "gloves-and-socks" syndrome on hands and feet	Most common among children 3–12 years old; occurs in winter and spring	Mild fever; arthritis in adults; rash following resolution of fever	197
Exanthem subitum (roseola, sixth	Human herpesvirus 6 or, less commonly, the	Diffuse maculopapular eruption over trunk and	Usually affects children <3 years old	Rash following resolution of fever;	195

disease) **(Fig. A1-5)**	closely related human herpesvirus 7	neck; resolves within 2 days		similar to Boston exanthem (echovirus 16); febrile seizures may occur	
Primary HIV infection **(Fig. A1-6)**	HIV	Nonspecific diffuse macules and papules most commonly on upper thorax, face, collar region; less commonly, urticarial or vesicular lesions; oral or genital ulcers	Individuals recently infected with HIV	Pharyngitis, adenopathy, arthralgias	**202**
Infectious mononucleosis	Epstein-Barr virus	Diffuse maculopapular eruption (5% of cases; 30–90% if ampicillin is given); urticaria, petechiae in some cases; periorbital edema (50%); palatal petechiae (25%)	Adolescents, young adults	Hepatosplenomegaly, pharyngitis, cervical lymphadenopathy, atypical lymphocytosis, heterophile antibody	**194**
Other viral exanthems	Echoviruses 2, 4, 9, 11, 16, 19, 25; coxsackieviruses A9, B1, B5; etc.	Wide range of skin findings that may mimic rubella or measles	Affect children more commonly than adults	Nonspecific viral syndromes	**204**
Exanthematous drug-induced eruption **(Fig. A1-7)**	Drugs (antibiotics, anticonvulsants, diuretics, etc.)	Intensely pruritic, bright-red macules and papules, symmetric on trunk and extremities; may become confluent	Occurs 2–3 days after exposure in previously sensitized individuals; otherwise, after 2–3 weeks (but can occur anytime, even shortly after drug is discontinued)	Variable findings: fever and eosinophilia	**60**
Epidemic typhus	*Rickettsia prowazekii*	Maculopapular eruption appearing in axillae, spreading to trunk and later to extremities; usually spares face, palms, soles; evolves from blanchable macules to confluent eruption with petechiae; rash evanescent in recrudescent typhus (Brill-Zinsser disease)	Exposure to body lice; occurrence of recrudescent typhus as relapse after 30–50 years	Headache, myalgias; mortality rates 10–40% if untreated; milder clinical presentation in recrudescent form	**187**
Endemic (murine) typhus	*Rickettsia typhi*	Maculopapular eruption, usually sparing palms, soles	Exposure to rat or cat fleas	Headache, myalgias	**187**
Scrub typhus	*Orientia tsutsugamushi*	Diffuse macular rash starting on trunk; eschar at site of mite bite	Endemic in South Pacific, Australia, Asia; transmitted by mites	Headache, myalgias, regional adenopathy; mortality rates up to	**187**

				30% if untreated	
Rickettsial spotted fevers **(Fig. 19-8)**	*Rickettsia conorii* (boutonneuse fever), *Rickettsia australis* (North Queensland tick typhus), *Rickettsia sibirica* (Siberian tick typhus), *Rickettsia africae* (African tick-bite fever), and others	Eschar common at bite site; maculopapular (rarely, vesicular and petechial) eruption on proximal extremities, spreading to trunk and face	Exposure to ticks; *R. conorii* in Mediterranean region, India, Africa; *R. australis* in Australia; *R. sibirica* in Siberia, Mongolia; *R. africae* in Africa, Caribbean	Headache, myalgias, regional adenopathy	**187**
Human monocytotropic ehrlichiosis[d]	*Ehrlichia chaffeensis*	Maculopapular eruption (40% of cases), involves trunk and extremities; may be petechial	Tick-borne; most common in U.S. Southeast, southern Midwest, and mid-Atlantic regions	Headache, myalgias, leukopenia	**187**
Leptospirosis	*Leptospira interrogans* and other *Leptospira* species	Maculopapular eruption; conjunctivitis; scleral hemorrhage in some cases	Exposure to water contaminated with animal urine	Myalgias; aseptic meningitis; *fulminant form*: icterohemorrhagic fever (Weil's disease)	**184**
Lyme disease **(Fig. A1-8)**	*Borrelia burgdorferi* (sole cause in U.S.), *Borrelia afzelii, Borrelia garinii*	Papule expanding to erythematous annular lesion with central clearing (erythema migrans; average diameter, 15 cm), sometimes with concentric rings, sometimes with indurated or vesicular center; multiple secondary erythema migrans lesions in some cases	Bite of *Ixodes* tick vector	Headache, myalgias, chills, photophobia occurring acutely; CNS disease, myocardial disease, arthritis weeks to months later in some cases	**186**
Southern tick-associated rash illness (STARI, Master's disease)	Unknown (possibly *Borrelia lonestari* or other *Borrelia* spirochetes)	Similar to erythema migrans of Lyme disease with several differences, including: multiple secondary lesions less likely; lesions tending to be smaller (average diameter, ~8 cm); central clearing more likely	Bite of tick vector *Amblyomma americanum* (Lone Star tick); often found in regions where Lyme disease is uncommon, including southern United States	Compared with Lyme disease: fewer constitutional symptoms, tick bite more likely to be recalled; other Lyme disease sequelae lacking	**186**
Typhoid fever **(Fig. A1-9)**	*Salmonella typhi*	Transient, blanchable erythematous macules and papules, 2–4 mm, usually on trunk (rose spots)	Ingestion of contaminated food or water (rare in U.S.)	Variable abdominal pain and diarrhea; headache, myalgias, hepatosplenomegaly	**165**
Dengue fever[e] **(Fig. A1-53)**	Dengue virus (4 serotypes; flaviviruses)	Rash in 50% of cases; initially diffuse flushing; midway	Occurs in tropics and subtropics; transmitted by	Headache; musculoskeletal pain	**209**

		through illness, onset of maculopapular rash, which begins on trunk and spreads centrifugally to extremities and face; pruritus, hyperesthesia in some cases; after defervescence, petechiae on extremities may occur	mosquito	("breakbone fever"); leukopenia; occasionally biphasic ("saddleback") fever	
Rat-bite fever (sodoku)	*Spirillum minus*	Eschar at bite site; then blotchy violaceous or red-brown rash involving trunk and extremities	Rat bite; primarily found in Asia; rare in U.S.	Regional adenopathy; recurrent fevers if untreated	141
Relapsing fever	*Borrelia* species	Central rash at end of febrile episode; petechiae in some cases	Exposure to ticks or body lice	Recurrent fever, headache, myalgias, hepatosplenomegaly	185
Erythema marginatum (rheumatic fever)	Group A *Streptococcus*	Erythematous annular papules and plaques occurring as polycyclic lesions in waves over trunk, proximal extremities; evolving and resolving within hours	Patients with rheumatic fever	Pharyngitis preceding polyarthritis, carditis, subcutaneous nodules, chorea	388
Systemic lupus erythematosus (SLE) **(Fig. A1-10, Fig. A1-11, Fig. A1-12)**	Autoimmune disease	Macular and papular erythema, often in sun-exposed areas; discoid lupus lesions (local atrophy, scale, pigmentary changes); periungual telangiectasis; malar rash; vasculitis sometimes causing urticaria, palpable purpura; oral erosions in some cases	Most common in young to middle-aged women; flares precipitated by sun exposure	Arthritis; cardiac, pulmonary, renal, hematologic, and vasculitic disease	359
Still's disease **(Fig. A1-13)**	Autoimmune disease	Transient 2- to 5-mm erythematous papules appearing at height of fever on trunk, proximal extremities; lesions evanescent	Children and young adults	High spiking fever, polyarthritis, splenomegaly; erythrocyte sedimentation rate >100 mm/h	—
African trypanosomiasis **(Fig. A1-47)**	*Trypanosoma brucei rhodesiense/gambiense*	Blotchy or annular erythematous macular and papular rash (trypanid), primarily on trunk; pruritus; chancre at site of tsetse fly	Tsetse fly bite in eastern (*T. brucei rhodesiense*) or western (*T. brucei gambiense*) Africa	Hemolymphatic disease followed by meningoencephalitis; Winterbottom's sign (posterior cervical	227

		bite may precede rash by several weeks		lymphadenopathy) *(T. brucei gambiense)*	
Arcanobacterial pharyngitis	*Arcanobacterium (Corynebacterium) haemolyticum*	Diffuse, erythematous, maculopapular eruption involving trunk and proximal extremities; may desquamate	Children and young adults	Exudative pharyngitis, lymphadenopathy	150
West Nile virus infection	West Nile virus	Maculopapular eruption involving the trunk, extremities, and head or neck; rash in 20–50% of cases	Mosquito bite; rarely, blood transfusion or transplanted organ	Headache, weakness, malaise, myalgia, neuroinvasive disease (encephalitis, meningitis, flaccid paralysis)	209
Zika virus infection (Fig. A1-51)	Zika virus	Pruritic macular and papular erythema; rash may begin on trunk and descend to lower body; conjunctival injection; palatal petechiae may occur	Mosquito bite; sexual transmission or blood transfusion less common	Arthralgia (especially of small joints), myalgia, lymphadenopathy, headache, low-grade fever; illness in pregnancy may cause severe birth defects, including microcephaly; neurologic complications, including Guillain-Barré, may occur	209
Peripheral Eruptions					
Chronic meningococcemia, disseminated gonococcal infection,[a] human parvovirus B19 infection,[f] MIRM[g]	—	—	—	—	155, 156, 197
Rocky Mountain spotted fever (Fig. 19-2, Fig. A1-16)	*Rickettsia rickettsii*	Rash beginning on wrists and ankles and spreading centripetally; appears on palms and soles later in disease; lesion evolution from blanchable macules to petechiae	Tick vector; widespread but more common in southeastern and southwest-central U.S.	Headache, myalgias, abdominal pain; mortality rates up to 40% if untreated	187
Secondary syphilis (Figs. A1-18, Fig.	*Treponema pallidum*	Coincident primary chancre in 10% of cases; copper-	Sexually transmitted	Fever, constitutional symptoms	182

A1-19, Fig. A1-20, Fig. A1-21)		colored, scaly papular eruption, diffuse but prominent on palms and soles; rash never vesicular in adults; condyloma latum, mucous patches, and alopecia in some cases			
Chikungunya fever (Fig. A1-54)	Chikungunya virus	Maculopapular eruption; typically occurs on trunk, but also occurs on extremities and face	*Aedes aegypti* and *A. albopictus* mosquito bites; tropical and subtropical regions	Severe polyarticular, migratory arthralgias, especially involving small joints (e.g., hands, wrists, ankles)	209
Hand-foot-and-mouth disease (Fig. A1-22)	Coxsackievirus A16 and enterovirus 71 most common causes; coxsackievirus A6 associated with atypical syndrome	Tender vesicles, erosions in mouth; 0.25-cm papules on hands and feet with rim of erythema evolving into tender vesicles; shedding of nails (onychomadesis) can occur 1–2 months after acute illness; coxsackievirus A6 lesions may also be maculopapular, petechial, purpuric, or erosive; atypical form often extends to perioral area, extremities, trunk, buttocks, genitals, and areas affected by eczema (eczema coxsackium)	Summer and fall; primarily children <10 years old; multiple family members; coxsackievirus A6 infection also occurs in young adults	Transient fever; enterovirus 71 can be associated with brain stem encephalitis, flaccid paralysis resembling polio, or aseptic meningitis	204
Erythema multiforme (EM) (Fig. A1-24)	Infection, drugs, idiopathic causes	Target lesions (central erythema surrounded by area of clearing and another rim of erythema) up to 2 cm; symmetric on knees, elbows, palms, soles; spreads centripetally; papular, sometimes vesicular; when extensive and involving mucous membranes, termed *EM major*	Herpes simplex virus or *Mycoplasma pneumoniae* infection; drug intake (i.e., sulfa, phenytoin, penicillin)	50% of patients <20 years old; fever more common in most severe form, EM major, which can be confused with Stevens-Johnson syndrome (but EM major lacks prominent skin sloughing)	—h
Rat-bite fever (Haverhill fever)	*Streptobacillus moniliformis*	Maculopapular eruption over palms, soles, and extremities; tends to be more severe at joints; eruption sometimes becoming generalized; may be purpuric; may desquamate	Rat bite, ingestion of contaminated food	Myalgias; arthritis (50%); fever recurrence in some cases	141

Bacterial endocarditis **(Fig. A1-23)**	*Streptococcus*, *Staphylococcus*, etc.	*Subacute course* (e.g., viridans streptococci): Osler's nodes (tender pink nodules on finger or toe pads); petechiae on skin and mucosa; splinter hemorrhages. *Acute course* (e.g., *Staphylococcus aureus*): Janeway lesions (painless erythematous or hemorrhagic macules, usually on palms and soles)	Abnormal heart valve (e.g., viridans streptococci), intravenous drug use	New or changing heart murmur	**128**
COVID-19 **(Fig. A1-57)**	SARS-CoV-2	*Mild or asymptomatic COVID-19:* Pernio (macules, papules, or plaques that are tender, erythematous/violaceous; acral, feet more common than hands); *Moderate/severe COVID-19:* vesicles, urticaria, maculopapular erythema; often pruritic; occur on trunk, extremities; *Severe COVID-19:* Retiform purpura (net-like, purple patches/plaques often with necrosis); lesions often asymptomatic; occur on extremities, buttocks; *Multisystem inflammatory syndrome in children (MIS-C):* findings *similar to Kawasaki disease*	Infection with SARS-CoV-2; MIS-C in older children/adolescents	Ranging from asymptomatic to mild/ moderate with loss of taste/smell, pharyngitis, cough, fever, to severe with dyspnea, ARDS; complications include thrombosis, especially with retiform purpura; lesions may be delayed compared to other COVID-19 symptoms; MIS-C occurs ~2-6 weeks following acute (often asymptomatic) infection	
Confluent Desquamative Erythemas					
Scarlet fever (second disease) **(Fig. A1-25)**	Group A *Streptococcus* (pyrogenic exotoxins A, B, C)	Diffuse blanchable erythema beginning on face and spreading to trunk and extremities; circumoral pallor; "sandpaper" texture to skin; accentuation of linear erythema in skin folds (Pastia's lines); enanthem of white evolving into red "strawberry" tongue; desquamation in second week	Most common among children 2–10 years old; usually follows group A streptococcal pharyngitis	Fever, pharyngitis, headache	**148**

Kawasaki disease **(Fig. A1-29)**	Idiopathic	Rash similar to scarlet fever (scarlatiniform) or EM; fissuring of lips, strawberry tongue; conjunctivitis; edema of hands, feet; desquamation later in disease	Children <8 years old	Cervical adenopathy, pharyngitis, coronary artery vasculitis	**58, 363**
Streptococcal toxic shock syndrome	Group A *Streptococcus* (associated with pyrogenic exotoxin A and/or B or certain M types)	When present, rash often scarlatiniform	May occur in setting of severe group A streptococcal infections (e.g., necrotizing fasciitis, bacteremia, pneumonia)	Multiorgan failure, hypotension; mortality rate 30%	**148**
Staphylococcal toxic shock syndrome	*S. aureus* (toxic shock syndrome toxin 1, enterotoxins B and others)	Diffuse erythema involving palms; pronounced erythema of mucosal surfaces; conjunctivitis; desquamation 7–10 days into illness	Colonization with toxin-producing *S. aureus*	Fever >39°C (>102°F), hypotension, multiorgan dysfunction	**147**
Staphylococcal scalded-skin syndrome **(Fig. 19-3, Fig. A1-28)**	*S. aureus*, phage group II	Diffuse tender erythema, often with bullae and desquamation; Nikolsky's sign	Colonization with toxin-producing *S. aureus*; occurs in children <10 years old (termed *Ritter's disease* in neonates) or adults with renal dysfunction	Irritability; nasal or conjunctival secretions	**147**
Exfoliative erythroderma syndrome **(Fig. A1-27)**	Underlying psoriasis, eczema, drug eruption, mycosis fungoides	Diffuse erythema (often scaling) interspersed with lesions of underlying condition	Usually occurs in adults over age 50; more common among men	Fever, chills (i.e., difficulty with thermoregulation); lymphadenopathy	**58, 60**
DRESS (drug-induced hypersensitivity syndrome [DIHS]) **(Fig. A1-48)**	Aromatic anticonvulsants; other drugs, including sulfonamides, minocycline	Maculopapular eruption (mimicking exanthematous drug rash), sometimes progressing to exfoliative erythroderma; profound edema, especially facial; pustules may occur	Individuals genetically unable to detoxify arene oxides (anticonvulsant metabolites), patients with slow *N*-acetylating capacity (sulfonamides)	Lymphadenopathy, multiorgan failure (especially hepatic), eosinophilia, atypical lymphocytes; mimics sepsis	**60**
Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) **(Fig. A1-26)**	Drugs (80% of cases; often allopurinol, anticonvulsants, antibiotics), infection, idiopathic factors	Erythematous and purpuric macules, sometimes targetoid, or diffuse erythema progressing to bullae, with sloughing and necrosis of entire epidermis; Nikolsky's sign; involves mucosal surfaces; TEN (>30% epidermal necrosis) is maximal form; SJS involves <10% of epidermis; SJS/TEN	Uncommon among children; more common among patients with HIV infection, systemic lupus erythematosus, certain HLA types, or slow acetylators	Dehydration, sepsis sometimes resulting from lack of normal skin integrity; mortality rates up to 30%	**60**

		overlap involves 10–30% of epidermis			
Vesiculobullous or Pustular Eruptions					
Hand-foot-and-mouth syndrome[c]; staphylococcal scalded-skin syndrome[b]; TEN[b]; DRESS[b]; COVID-19[c]	—	—	—	—	—[h]
Varicella (chickenpox) **(Fig. 19-4, Fig. A1-30)**	Varicella-zoster virus (VZV)	Macules (2–3 mm) evolving into papules, then vesicles (sometimes umbilicated), on an erythematous base ("dewdrops on a rose petal"); pustules then forming and crusting; lesions appearing in crops; may involve scalp, mouth; intensely pruritic	Usually affects children; 10% of adults susceptible; most common in late winter and spring; incidence down by 90% in U.S. as a result of varicella vaccination	Malaise; generally mild disease in healthy children; more severe disease with complications in adults and immunocompromised children	**193**
Pseudomonas "hot-tub" folliculitis **(Fig. A1-55)**	*Pseudomonas aeruginosa*	Pruritic erythematous follicular, papular, vesicular, or pustular lesions that may involve axillae, buttocks, abdomen, and especially areas occluded by bathing suits; can manifest as tender isolated nodules on palmar or plantar surfaces (the latter designated "*Pseudomonas* hot-foot syndrome")	Bathers in hot tubs or swimming pools; occurs in outbreaks	Earache, sore eyes and/or throat; fever may be absent; generally self-limited	**164**
Variola (smallpox) **(Fig. A1-50)**	Variola major virus	Red macules on tongue and palate evolving to papules and vesicles; skin macules evolving to papules, then vesicles, then pustules over 1 week, with subsequent lesion crusting; lesions initially appearing on face and spreading centrifugally from trunk to extremities; differs from varicella in that (1) skin lesions in any given area are at same stage of development and (2) there is a prominent distribution of	Nonimmune individuals exposed to smallpox	Prodrome of fever, headache, backache, myalgias; vomiting in 50% of cases	**S3**

		lesions on face and extremities (including palms, soles)			
Primary herpes simplex virus (HSV) infection	HSV	Erythema rapidly followed by hallmark painful *grouped vesicles* that may evolve into pustules that ulcerate, especially on mucosal surfaces; lesions at site of inoculation: commonly gingivostomatitis for HSV-1 and genital lesions for HSV-2; recurrent disease milder (e.g., herpes labialis does not involve oral mucosa)	Primary infection most common among children and young adults for HSV-1 and among sexually active young adults for HSV-2; no fever in recurrent infection	Regional lymphadenopathy	192
Disseminated herpesvirus infection **(Fig. A1-31)**	VZV or HSV	Generalized vesicles that can evolve to pustules and ulcerations; individual lesions similar for VZV and HSV. *Zoster cutaneous dissemination*: >25 lesions extending outside involved dermatome. *HSV*: extensive, progressive mucocutaneous lesions that may occur in absence of dissemination, sometimes disseminate in eczematous skin (eczema herpeticum); HSV visceral dissemination may occur with only localized mucocutaneous disease; in disseminated neonatal disease, skin lesions diagnostically helpful when present, but rash absent in a substantial minority of cases	Patients with immunosuppression, eczema; neonates	Visceral organ involvement (e.g., liver, lungs) in some cases; neonatal disease particularly severe	138, 192, 193
Rickettsialpox **(Fig. A1-33)**	*Rickettsia akari*	Eschar found at site of mite bite; generalized rash involving face, trunk, extremities; may involve palms and soles; <100 papules and plaques (2–10 mm); centers of papules develop vesicles or pustules	Seen in urban settings; transmitted by mouse mites	Headache, myalgias, regional adenopathy; mild disease	187
Acute generalized	Drugs (mostly	Tiny, sterile, nonfollicular	Appears 2–21 days after start	Acute fever, pruritus,	60

exanthematous pustulosis **(Fig. A1-49)**	anticonvulsants or antimicrobials); also viral	pustules on erythematous, edematous skin; begins on face and in body folds, then becomes generalized	of drug therapy, depending on whether patient has been sensitized	leukocytosis	
Disseminated *Vibrio vulnificus* infection	*V. vulnificus*	Erythematous lesions evolving into hemorrhagic bullae and then into necrotic ulcers	Patients with cirrhosis, diabetes, renal failure; exposure by ingestion of contaminated saltwater, seafood	Hypotension; mortality rate 50%	**168**
Ecthyma gangrenosum **(Fig. A1-34)**	*P. aeruginosa*, other gram-negative rods, fungi	Indurated plaque evolving into hemorrhagic bulla or pustule that sloughs, resulting in eschar formation; erythematous halo; most common in axillary, groin, perianal regions	Usually affects neutropenic patients; occurs in up to 28% of individuals with *Pseudomonas* bacteremia	Clinical signs of sepsis	**164**
Mycoplasma-induced rash and mucositis (MIRM)	*Mycoplasma pneumoniae*	Severe mucositis of at least two sites (e.g., oropharynx, ocular, genital) with nearly universal hemorrhagic crusting of lips; sparse, vesiculobullous, or atypical targetoid rash over <10% of body; lesions typically on extremities but can be truncal; rash sometimes absent (MIRM sine rash)	More common in males; usually children (mean age 11–12 years old)	Evidence *of M. pneumoniae* infection (typically pneumonia); good prognosis; distinct from SJS/TEN; rarely *Chlamydophila pneumoniae* can cause similar syndrome	
Urticaria-Like Eruptions					
COVID-19[c]					
Urticarial vasculitis **(Fig. 19-5, Fig. A1-35)**	Serum sickness, often due to infection (including acute hepatitis B, enteroviral, parasitic), drugs; connective tissue disease	Erythematous, edematous "urticaria-like" plaques, pruritic or burning; unlike urticaria: typical lesion duration >24 h (up to 5 days) and lack of complete lesion blanching with compression due to hemorrhage	Patients with serum sickness (including acute hepatitis B), connective tissue disease	Fever variable; arthralgias/arthritis	**363**[h]
Nodular Eruptions					
Disseminated infection **(Fig. 19-6, Fig. A1-36, Fig. A1-37, Fig. A1-38)**	Fungal infections (e.g., candidiasis, histoplasmosis, cryptococcosis,	Subcutaneous nodules (up to 3 cm); fluctuance, draining common with mycobacteria; necrotic nodules (extremities,	Immunocompromised hosts (e.g., bone marrow transplant recipients, patients undergoing chemotherapy,	Features vary with organism	—[h]

	sporotrichosis, coccidioidomycosis); mycobacteria	periorbital or nasal regions) common with *Aspergillus*, *Mucor*	HIV-infected patients)		
Erythema nodosum (septal panniculitis) **(Fig. A1-39)**	Infections (e.g., streptococcal, fungal, mycobacterial, yersinial); drugs (e.g., sulfas, penicillins, oral contraceptives); sarcoidosis; idiopathic causes	Large, violaceous, nonulcerative, subcutaneous nodules; exquisitely tender; usually on lower legs but also on upper extremities	More common among females 15–30 years old	Arthralgias (50%); features vary with associated condition	—[h]
Sweet syndrome (acute febrile neutrophilic dermatosis) **(Fig. A1-40)**	*Yersinia* infection; upper respiratory infection; inflammatory bowel disease; pregnancy; malignancy (usually hematologic); drugs (G-CSF)	Tender red or blue edematous nodules giving impression of vesiculation; usually on face, neck, upper extremities; when on lower extremities, may mimic erythema nodosum	More common among women and among persons 30–60 years old; 20% of cases associated with malignancy (men and women equally affected in this group)	Headache, arthralgias, leukocytosis	**58**
Bacillary angiomatosis	*Bartonella henselae*, *B. quintana*	Many forms, including erythematous, smooth vascular nodules; friable, exophytic lesions; erythematous plaques (may be dry, scaly); subcutaneous nodules (may be erythematous)	Immunosuppressed individuals, especially those with advanced HIV infection	Peliosis of liver and spleen in some cases; lesions sometimes involving multiple organs; bacteremia	**172**
Purpuric Eruptions					
Rocky Mountain spotted fever, rat-bite fever, endocarditis[c]; epidemic typhus[f]; dengue fever[e,f]; human parvovirus B19 infection[f]; COVID-19[c]	—	—	—	—	—[h]
Acute meningococcemia	*Neisseria meningitidis*	Initially pink maculopapular lesions evolving into petechiae; petechiae rapidly becoming numerous, sometimes enlarging and becoming vesicular; trunk, extremities most commonly	Most common among children, individuals with asplenia or terminal complement component deficiency (C5–C8)	Hypotension, meningitis (sometimes preceded by upper respiratory infection)	**155**

		involved; may appear on face, hands, feet; may include purpura fulminans (see below) reflecting DIC			
Purpura fulminans **(Fig. 19-7, Fig. A1-41)**	Severe DIC	Large ecchymoses with sharply irregular shapes evolving into hemorrhagic bullae and then into black necrotic lesions	Individuals with sepsis (e.g., involving *N. meningitidis*), malignancy, or massive trauma; asplenic patients at high risk for sepsis	Hypotension	**155, 304**
Chronic meningococcemia **(Fig. A1-42)**	*N. meningitidis*	Variety of recurrent eruptions, including pink maculopapular; nodular (usually on lower extremities); petechial (sometimes developing vesicular centers); purpuric areas with pale blue-gray centers	Individuals with complement deficiencies	Fevers, sometimes intermittent; arthritis, myalgias, headache	**155**
Disseminated gonococcal infection **(Fig. A1-43)**	*Neisseria gonorrhoeae*	Papules (1–5 mm) evolving over 1–2 days into hemorrhagic pustules with gray necrotic centers; hemorrhagic bullae occurring rarely; lesions (usually <40) distributed peripherally near joints (more commonly on upper extremities)	Sexually active individuals (more often females), some with complement deficiency	Low-grade fever, tenosynovitis, arthritis	**156**
Enteroviral petechial rash	Usually echovirus 9 or coxsackievirus A9	Disseminated petechial lesions (may also be maculopapular, vesicular, or urticarial)	Often occurs in outbreaks	Pharyngitis, headache; aseptic meningitis with echovirus 9	**204**
Viral hemorrhagic fever	Arenaviruses, bunyaviruses, filoviruses (including Ebola), flaviviruses (including dengue)	Petechial rash	Residence in or travel to endemic areas, other virus exposure	Triad of fever, shock, hemorrhage from mucosa or gastrointestinal tract	**209, 210**
Thrombotic thrombocytopenic purpura/hemolytic-uremic syndrome	Idiopathic, bloody diarrhea caused by Shiga toxin–generating bacteria (e.g., *Escherichia coli* O157:H7), deficiency in ADAMTS13 (cleaves von Willebrand factor),	Petechiae	Individuals with *E. coli* O157:H7 gastroenteritis (especially children), cancer chemotherapy, HIV infection, autoimmune diseases, pregnant/postpartum women, those with ADAMTS13 deficiency	Fever (not always present), microangiopathic hemolytic anemia, thrombocytopenia, renal dysfunction, neurologic dysfunction;	**58, 100, 115, 161, 166**

	drugs (e.g., quinine, chemotherapy, immunosuppression)			coagulation studies normal	
Cutaneous small-vessel vasculitis (leukocytoclastic vasculitis) **(Fig. A1-44)**	Infections (including group A streptococcal infection, hepatitis B or C), drugs, idiopathic factors	Palpable purpuric lesions appearing in crops on legs or other dependent areas; may become vesicular or ulcerative	Occurs in a wide spectrum of diseases, including connective tissue disease, cryoglobulinemia, malignancy, Henoch-Schönlein purpura (HSP); more common among children	Fever (not always present), malaise, arthralgias, myalgias; systemic vasculitis in some cases; renal, joint, and gastrointestinal involvement common in HSP	**58**
Eruptions with Ulcers and/or Eschars					
Scrub typhus, rickettsial spotted fevers, rat-bite fever, African trypanosomiasis[f]; rickettsialpox, ecthyma gangrenosum[g]	—	—	—	—	—[h]
Tularemia **(Fig. A1-45, Fig. A1-46)**	*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	**170**
Anthrax **(Fig. A1-52)**	*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	**S3**

[a] See "Purpuric Eruptions."

[b] See "Confluent Desquamative Erythemas."

[c] See "Peripheral Eruptions."

[d] Rash is rare in human granulocytotropic ehrlichiosis or anaplasmosis (caused by *Anaplasma phagocytophilum*; most common in the upper midwestern and

northeastern United States).

[e]See “Viral hemorrhagic fever” under “Purpuric Eruptions” for dengue hemorrhagic fever/dengue shock syndrome.

[f]See “Centrally Distributed Maculopapular Eruptions.”

[g]See “Vesiculobullous or Pustular Eruptions.”

[h]See etiology-specific chapters.

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

CENTRALLY DISTRIBUTED MACULOPAPULAR ERUPTIONS

Centrally distributed rashes, in which lesions are primarily truncal, are the most common type of eruption. The rash of *rubeola* (measles) starts at the hairline 2–3 days into the illness and moves down the body, typically sparing the palms and soles **(Fig. 19-1; see also Fig. A1-3) (Chap. 205)**. It begins as discrete erythematous lesions, which become confluent as the rash spreads. Koplik’s spots (1- to 2-mm white or bluish lesions with an erythematous halo on the buccal mucosa) **(Fig. A1-2)** are pathognomonic for measles and are generally seen during the first 2 days of symptoms. They should not be confused with Fordyce’s spots (ectopic sebaceous glands), which have no erythematous halos and are found in the mouth of healthy individuals. Koplik’s spots may briefly overlap with the measles exanthem.

FIGURE 19-1

Centrally distributed, maculopapular eruption on the trunk in a patient with measles. *(From EJ Mayeaux Jr et al: Measles, in Usatine RP et al [eds]: Color Atlas and Synopsis of Family Medicine, 3rd ed. New York, McGraw-Hill, 2019, p. 797, Figure 132-2. Reproduced with permission from Richard P. Usatine, MD.)*

Source: Joseph Loscalzo, Anthony Fauci, Dennis Kasper, Stephen Hauser, Dan Longo, J. Larry Jameson: Harrison's Principles of Internal Medicine, 21e

Rubella (German measles) **(Fig. A1-4)** also spreads from the hairline downward; unlike that of measles, however, the rash of rubella tends to clear from originally affected areas as it migrates, and it may be pruritic **(Chap. 206)**. Forchheimer spots (palatal petechiae) may develop but are nonspecific because they also develop in *infectious mononucleosis* **(Chap. 194)**, *scarlet fever* **(Chap. 148)**, and *Zika virus infection* **(Chap. 209)** **(Fig. A1-51D)**. Postauricular and suboccipital adenopathy and arthritis are common among adults with rubella. Exposure of pregnant women to ill individuals should be avoided, as rubella causes severe congenital abnormalities. Numerous strains of *enteroviruses* **(Chap. 204)**, primarily echoviruses and coxsackieviruses, cause nonspecific syndromes of fever and eruptions that may mimic rubella or measles. Patients with *infectious mononucleosis* caused by Epstein-Barr virus **(Chap. 194)** or with *primary HIV infection* **(Fig. A1-6; see also Chapter 202)** may exhibit pharyngitis, lymphadenopathy, and a nonspecific maculopapular exanthem.

The rash of *erythema infectiosum* (fifth disease), which is caused by human parvovirus B19, primarily affects children 3–12 years old; it develops after fever has resolved as a bright blanchable erythema on the cheeks ("slapped cheeks") **(Fig. A1-1A)** with perioral pallor **(Chap. 197)**. A more diffuse rash (often pruritic) appears the next day on the trunk and extremities and then rapidly develops into a lacy reticular eruption **(Fig. A1-1B)** that may wax and wane (especially with temperature change) over 3 weeks. Adults with fifth disease often have arthritis, and fetal hydrops can develop in association with this condition in pregnant women.

Exanthem subitum (roseola) is caused by human herpesvirus 6, or less commonly by the closely related human herpesvirus 7, and is most common among children <3 years of age **(Chap. 195)**. As in erythema infectiosum, the rash usually appears after fever has subsided. It consists of 2- to 3-mm rose-pink macules and papules that coalesce only rarely, occur initially on the trunk **(Fig. A1-5)** and sometimes on the extremities (sparing the face), and fade within 2 days.

Although drug reactions have many manifestations, including urticaria, exanthematous *drug-induced eruptions* **(Chap. 60)** **(Fig. A1-7)** are most common and are often difficult to distinguish from viral exanthems. Eruptions elicited by drugs are usually more intensely erythematous and pruritic than viral exanthems, but this distinction is not reliable. A history of new medications and an absence of prostration may help to distinguish a drug-related rash from an eruption of another etiology. Rashes may persist for up to 2 weeks after administration of the offending agent is discontinued. Certain populations are more prone than others to drug rashes. Of HIV-infected patients, 50–60% develop a rash in response to sulfa drugs; 30–90% of

patients with mononucleosis due to Epstein-Barr virus develop a rash when given ampicillin.

Rickettsial illnesses **(Chap. 187)** should be considered in the evaluation of individuals with centrally distributed maculopapular eruptions. The usual setting for *epidemic typhus* is a site of war or natural disaster in which people are exposed to body lice. Endemic typhus or *leptospirosis* (the latter caused by a spirochete) **(Chap. 184)** may be 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. 165)** **(Fig. A1-9)**, is usually acquired during travel outside the United States. *Dengue fever* **(Fig. A1-53)**, caused by a mosquito-transmitted flavivirus, occurs in tropical and subtropical regions of the world **(Chap. 209)**.

Some centrally distributed maculopapular eruptions have distinctive features. Erythema migrans **(Fig. A1-8)**, the rash of *Lyme disease* **(Chap. 186)**, typically manifests as single or multiple annular lesions. Untreated erythema migrans lesions usually fade within a month but may persist for more than a year. *Southern tick-associated rash illness* (STARI) **(Chap. 186)** 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. 359)**, 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. 356)** typically develop a sharply defined, erythematous eruption in a butterfly distribution on the cheeks (malar rash) **(Fig. A1-10)** as well as many other skin manifestations **(Figs. A1-11, A1-12)**. *Still's disease* presents as an evanescent, salmon-colored rash on the trunk and proximal extremities that coincides with fever spikes **(Fig. A1-13)**.

Hemophagocytic lymphohistiocytosis may be familial or triggered by infection, autoimmunity, or neoplasia. Cutaneous manifestations are protean and can present as an erythematous maculopapular eruption, pyoderma gangrenosum, purpura, panniculitis, or Stevens Johnson syndrome.

Zika virus is a mosquito-transmitted flavivirus that is associated with severe birth defects **(Chap. 209)**. Zika is widespread among tropical and subtropical regions of the world. The eruption of Zika virus infection **(Fig. A1-51A, A1-51B)** is typically pruritic and often accompanied by conjunctival injection **(Fig. A1-51C)**.

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. 187)** because of its grave prognosis if untreated. Lesions **(Fig. 19-2; see also Fig. A1-16)** 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. 182)**, which may be generalized **(Fig. A1-18)** but is prominent on the palms and soles **(Fig. A1-19)**, should be considered in the differential diagnosis of pityriasis rosea, especially in sexually active patients. *Chikungunya fever* **(Chap. 209)**, which is transmitted by mosquito bite in tropical and subtropical regions, is associated with a maculopapular eruption **(Fig. A1-54)** and severe polyarticular small-joint arthralgias. *Hand-foot-and-mouth disease* **(Chap. 204)**, most commonly caused by coxsackievirus A16 or enterovirus 71, is distinguished by tender vesicles distributed on the hands and feet and in the mouth **(Fig. A1-22)**; coxsackievirus A6 causes an atypical syndrome with more extensive lesions. The classic target lesions of *erythema multiforme* **(Fig. A1-24)** 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* **(Fig. A1-23)** **(Chap. 128)**. Pernio, tender violaceous lesions that are acral **(Fig. A1-57)**, occur most commonly on the feet, in asymptomatic or mild COVID-19. Vesicles, urticaria, or maculopapular eruptions, often pruritic, may occur on the trunk and extremities in moderate or severe disease, while retiform purpura occurs on the extremities and buttocks in severe COVID-19.

FIGURE 19-2

Peripheral eruption on the wrist and palm exhibiting erythematous macules in the process of evolving into petechial lesions in a patient with Rocky Mountain spotted fever. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 562, Figure 25-50; with permission.)*

Source: Joseph Loscalzo, Anthony Fauci, Dennis Kasper, Stephen Hauser, Dan Longo, J. Larry Jameson: Harrison's Principles of Internal Medicine, 21e

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. 148) (Fig. A1-25)** usually follows pharyngitis; patients have a facial flush, a "strawberry" tongue, and accentuated petechiae in body folds (Pastia's lines). *Kawasaki disease* **(Fig. A1-29) (Chaps. 58 and 363)** presents in the pediatric population as fissuring of the lips, a strawberry tongue, conjunctivitis, adenopathy, and sometimes cardiac abnormalities. *Streptococcal toxic shock syndrome* **(Chap. 148)** manifests with hypotension, multiorgan failure, and, often, a severe group A streptococcal infection (e.g., necrotizing fasciitis). *Staphylococcal toxic shock syndrome* **(Chap. 147)** 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* **(Fig. A1-28) (Chap. 147)** 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) **(Fig. 19-3)**. 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. 60)**, a maximal variant of *Stevens-Johnson syndrome*, involves sloughing of the entire epidermis **(Fig. A1-26)**, resulting in severe disease. *Exfoliative erythroderma syndrome* **(Chaps. 58 and 60)** is a serious reaction associated with systemic toxicity that is often due to eczema, psoriasis **(Fig. A1-27)**, a drug reaction, or mycosis fungoides. *Drug rash with eosinophilia and systemic symptoms (DRESS)*, often due to antiepileptic and antibiotic agents **(Chap. 60)**, initially appears similar to an exanthematous drug reaction **(Fig. A1-48)** but may progress to exfoliative erythroderma; it is accompanied by multiorgan failure and has an associated mortality rate of ~10%.

FIGURE 19-3

Confluent desquamative erythema in a patient with Staphylococcal scalded-skin syndrome. Nikolsky sign evident as shearing of epidermis due to gentle, lateral pressure. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 554, Figure 25-42; with permission.)*

VESICULOBULLOUS OR PUSTULAR ERUPTIONS

Varicella **(Chap. 193)** is highly contagious, often occurring in winter or spring, and is characterized by pruritic lesions that, within a given region of the body, are in different stages of development at any point in time **(Fig. 19-4; see also Fig. A1-30)**. In immunocompromised hosts, varicella vesicles may lack the characteristic erythematous base or may appear hemorrhagic. Lesions of *Pseudomonas "hot-tub" folliculitis* **(Chap. 164)** are also pruritic and may appear similar to those of varicella **(Fig. A1-55)**. 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. S3)** also appear similar to those of varicella but are all at the same stage of development in a given region of the body **(Figs. A1-50B, A1-50C)**. Variola lesions are most prominent on the face **(Fig. A1-50A)** and extremities, while varicella lesions are most prominent on the trunk. *Herpes simplex virus infection* **(Chap. 192)** 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. 187)** is often documented in urban settings and is characterized by vesicles followed by pustules **(Figs. A1-33B, A1-33C)**. It can be distinguished from varicella by an eschar at the site of the mouse-mite bite **(Fig. A1-33A)** and the papule/plaque base of each vesicle. *Acute generalized exanthematous pustulosis* **(Fig. A1-49)** should be considered in individuals who are acutely febrile and are taking new medications, especially anticonvulsant or antimicrobial agents **(Chap. 60)**. Disseminated *Vibrio vulnificus* infection **(Chap. 168)** or *ecthyma gangrenosum* due to *Pseudomonas aeruginosa* **(Fig. A1-34) (Chap. 164)** should be considered in immunosuppressed individuals with sepsis and hemorrhagic bullae. In children, *Mycoplasma pneumoniae*–induced rash and mucositis (MIRM) **(Fig. A1-56)** is characterized by a sparse, often vesiculobullous eruption with prominent oral, ocular, or urogenital mucositis.

FIGURE 19-4

Vesicular and pustular lesions on the chest in a patient with varicella. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 695, Figure 27-48; with permission.)*

Source: Joseph Loscalzo, Anthony Fauci, Dennis Kasper, Stephen Hauser, Dan Longo, J. Larry Jameson: Harrison's Principles of Internal Medicine, 21e

URTICARIA-LIKE ERUPTIONS

Individuals with classic urticaria ("hives") **(Fig. 19-5; see also Fig. A1-35)** usually have a hypersensitivity reaction without associated fever. In the presence of fever, urticaria-like eruptions are most often due to *urticarial vasculitis* **(Chap. 363)**. Unlike individual lesions of classic urticaria, which last up to 24 h, these lesions may last 3–5 days. Etiologies include serum sickness (often induced by drugs such as penicillins, sulfas, salicylates, or barbiturates), connective-tissue disease (e.g., systemic lupus erythematosus or Sjögren's syndrome), and infection (e.g., with hepatitis B virus, enteroviruses, or parasites). Malignancy, especially lymphoma, may be associated with fever and chronic urticaria **(Chap. 58)**.

FIGURE 19-5

Urticarial eruption. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 299, Figure 14-2; with permission.)*

NODULAR ERUPTIONS

In immunocompromised hosts, nodular lesions often represent disseminated infection. Patients with disseminated *candidiasis* **(Fig. A1-37)** (often due to *Candida tropicalis*) may have a triad of fever, myalgias, and eruptive nodules **(Chap. 216)**. Disseminated *cryptococcosis* lesions **(Fig. 19-6; see also Fig. A1-36) (Chap. 215)** may resemble molluscum contagiosum **(Chap. 196)**. Necrosis of nodules should raise the suspicion of *aspergillosis* **(Fig. A1-38) (Chap. 217)** or *mucormycosis* **(Chap. 218)**. *Erythema nodosum* presents with exquisitely tender nodules on the lower extremities **(Fig. A1-39)**. *Sweet syndrome* **(Chap. 58)** should be considered in individuals with multiple nodules and plaques, often so edematous **(Fig. A1-40)** that they give the appearance of vesicles or bullae. Sweet syndrome may occur in individuals with infection, inflammatory bowel disease, or malignancy and can also be induced by drugs.

FIGURE 19-6

Nodular eruption on the face due to disseminated Cryptococcus in a patient with HIV infection. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 641, Figure 26-57. Used with permission from Loïc Vallant, MD.)*

PURPURIC ERUPTIONS

Acute meningococcemia **(Chap. 155)** classically presents in children as a petechial eruption, but initial lesions may appear as blanchable macules or urticaria. Rocky Mountain spotted fever should be considered in the differential diagnosis of acute meningococcemia. *Echovirus 9 infection* **(Chap. 204)** may mimic acute meningococcemia; patients should be treated as if they have bacterial sepsis because prompt differentiation of these conditions may be impossible. Large ecchymotic areas of *purpura fulminans* **(Fig. 19-7; see also Fig. A1-41) (Chaps. 155 and 304)** reflect severe underlying disseminated intravascular coagulation, which may be due to infectious or noninfectious causes. The lesions of *chronic meningococcemia* **(Fig. A1-42) (Chap. 155)** may have a variety of morphologies, including petechial. Purpuric nodules may develop on the legs and resemble erythema nodosum but lack its exquisite tenderness. Lesions of *disseminated gonococcemia* **(Chap. 156)** are distinctive, sparse, countable hemorrhagic pustules **(Fig. A1-43)**, usually located near joints. The lesions of chronic meningococcemia and those of gonococcemia may be indistinguishable in terms of appearance and distribution. *Viral hemorrhagic fever* **(Chaps. 209 and 210)** should be considered in patients with an appropriate travel history and a petechial rash. *Thrombotic thrombocytopenic purpura* **(Chaps. 58, 100, and 115)** and *hemolytic-uremic syndrome* **(Chaps. 115, 161, and 166)** are closely related and are noninfectious causes of fever and petechiae. *Cutaneous small-vessel vasculitis* (*leukocytoclastic vasculitis*) typically manifests as palpable purpura **(Fig. A1-44)** and has a wide variety of causes **(Chap. 58)**.

FIGURE 19-7

Purpura fulminans in a patient with acute meningococcemia. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 568, Figure 25-59; with permission.)*

ERUPTIONS WITH ULCERS OR ESCHARS

The presence of an ulcer or eschar **(Fig. 19-8)** in the setting of a more widespread eruption can provide an important diagnostic clue. For example, an eschar may suggest the diagnosis of *scrub typhus* or *rickettsialpox* **(Fig. A1-33A) (Chap. 187)** in the appropriate setting. In other illnesses (e.g., anthrax) **(Fig. A1-52) (Chap. S3)**, an ulcer or eschar may be the only skin manifestation.

FIGURE 19-8

Eschar with surrounding erythema at the site of a tick bite in a patient with African tick-bite fever. *(From K Wolff et al [eds]: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 8th ed. New York, McGraw-Hill, 2017, p. 561, Figure 25-49; with permission.)*

FURTHER READING

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