13 - 134 Infections of the Skin, Muscles, and Soft Tissues

134 Infections of the Skin, Muscles, and Soft Tissues

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Infections of the Skin,

Muscles, and Soft Tissues Skin and soft tissue infections occur in all races, all ethnic groups, and all geographic locations, although some have unique geographic niches. In modern times, the frequency and severity of some skin and soft tissue infections have increased for several reasons. First, microbes are rapidly disseminated throughout the world via efficient air travel, acquiring genes for virulence factors and antibiotic resistance. Second, natural disasters, such as earthquakes, tsunamis, tornadoes, and hur ricanes, appear to be increasing in frequency, and the injuries sustained during these events commonly cause major skin and soft tissue damage that predisposes to infection. Third, trauma and casualties resulting from combat and terrorist activities can markedly damage or destroy tissues and provide both endogenous and exogenous pathogens with ready access to deeper structures. Unfortunately, because the marvels of modern medicine may not be available during human-instigated and natural disasters, primary treatment may be delayed and the likelihood of severe infection and death increased. ANATOMIC RELATIONSHIPS: CLUES TO THE DIAGNOSIS OF SOFT TISSUE INFECTIONS Skin and soft tissue infections have been common human afflictions for centuries. However, between 2000 and 2004, hospital admissions for these infections rose by 27%, a remarkable increase that was attributable largely to the emergence of the USA300 clone of methicillinresistant Staphylococcus aureus (MRSA). This chapter provides an anatomic approach to understanding the types of soft tissue infections and the diverse microbes responsible. Protection against infection of the epidermis depends on the mechanical barrier afforded by the stratum corneum since the epi dermis itself is devoid of blood vessels (Fig. 134-1). Disruption of this layer by burns or bites, abrasions, foreign bodies, primary dermatologic disorders (e.g., herpes simplex, varicella, ecthyma gangrenosum), sur gery, or vascular or pressure ulcers allows penetration of bacteria to the deeper structures. Similarly, the hair follicle can serve as a portal either for components of the normal flora (e.g., Staphylococcus) or for extrinsic bacteria

(e.g., Pseudomonas in hot-tub folliculitis). Intracel lular infection of the squamous epithelium with vesicle formation may arise from cutaneous inoculation, as in infection with herpes simplex virus (HSV) type 1; from the dermal capillary plexus, as in varicella and Crust Bulla Eschar Vesicle Hair follicle Stratum corneum Stratum germinativum Erysipelas Dermal papillae Sebaceous gland Post-capillary venule Cellulitis Subcutaneous fat Necrotizing fasciitis Deep fascia Lymphatic channel Vein Artery Myositis Muscle Bone FIGURE 134-1 Structural components of the skin and soft tissues, superficial infections, and infections of the deeper structures. The rich capillary network beneath the dermal papillae plays a key role in the localization of infection and in the development of the acute inflammatory reaction.

infections due to other viruses associated with viremia; or from cutane ous nerve roots, as in herpes zoster. Bacteria infecting the epidermis, such as Streptococcus pyogenes, may be translocated laterally to deeper structures via lymphatics, an event that results in the rapid superficial spread of erysipelas. Later, engorgement or obstruction of lymphat ics causes flaccid edema of the epidermis, another characteristic of erysipelas.

The rich plexus of capillaries beneath the dermal papillae provides nutrition to the stratum germinativum, and physiologic responses of this plexus produce important clinical signs and symptoms. For exam ple, infective vasculitis of the plexus results in petechiae, Osler nodes, Janeway lesions, and palpable purpura, which, if present, are impor tant clues to the existence of endocarditis (Chap. 133). In addition, metastatic infection within this plexus can result in cutaneous mani festations of disseminated fungal infection (Chap. 222), gonococcal infection (Chap. 161), Salmonella infection (Chap. 171), Pseudomonas infection (i.e., ecthyma gangrenosum; Chap. 170), meningococcemia (Chap. 160), and staphylococcal infection (Chap. 152). The plexus also provides bacteria with access to the circulation, thereby facilitat ing local spread or bacteremia. The postcapillary venules of this plexus are a prominent site of polymorphonuclear leukocyte sequestration, diapedesis, and chemotaxis to the site of cutaneous infection. Amplification of these physiologic mechanisms by excessive levels of cytokines or bacterial toxins causes leukostasis, venous occlusion, and pitting edema. Edema with purple bullae, ecchymosis, and cutaneous anesthesia suggests loss of vascular integrity and necessitates explora tion of the deeper structures for evidence of necrotizing fasciitis or myonecrosis. An early diagnosis requires a high level of suspicion in instances of unexplained fever and of pain and tenderness in the soft tissue, even in the absence of acute cutaneous inflammation. CHAPTER 134 Table 134-1 indicates the chapters in which the infections described below are discussed in greater detail. Many of these infections are illustrated in the chapters cited or in Chap. A1. Infections of the Skin, Muscles, and Soft Tissues INFECTIONS ASSOCIATED WITH VESICLES (Table 134-1) Vesicle formation due to infection is caused by viral proliferation within the epidermis. In varicella and variola, viremia precedes the onset of a diffuse centripetal rash that progresses from macules to vesicles, then to pustules, and finally to scabs over the course of 1–2 weeks. Vesicles of varicella have a “dewdrop” appearance and develop in crops randomly about the trunk, extremities, and face over 3–4 days. Herpes zoster occurs in a single dermatome; the appear ance of vesicles is preceded by pain for several days. Zoster may occur in persons of any age but is most common among immunosuppressed individuals and elderly patients, whereas most cases of varicella occur in young children. Vesicles due to HSV are found on or around the lips (HSV-1) or genitals (HSV-2) but also may appear on the head and neck of young wrestlers (herpes gladiatorum) or on the digits of health care workers (herpetic whitlow). Recurrent herpes labialis (HSV-1) and herpes genitalis

(HSV-2) commonly follow primary infection. Coxsackievirus A16 characteristically causes vesicles on the hands, feet, and mouth of children. Orf is caused by a DNA virus related to small pox virus and infects the fingers of individuals who work around goats and sheep. Molluscum contagiosum virus induces flaccid vesicles on the skin of healthy and immunocompromised individuals. Although variola (smallpox) in nature was eradicated as of 1977, postmillennial terrorist events have renewed interest in this devastating infection (Chap. S4). Viremia beginning after an incubation period of 12 days is followed by a diffuse maculopapular rash, with rapid evolution to vesicles, pustules, and then scabs. Secondary cases can occur among close contacts. Rickettsialpox begins after mite-bite inoculation of Rickettsia akari into the skin. A papule with a central vesicle evolves to form a 1- to 2.5-cm painless crusted black eschar with an erythematous halo and proximal adenopathy. While more common in the northeastern United States and Ukraine in 1940–1950, rickettsialpox has recently been described in Ohio, Arizona, and Utah. Blistering dactylitis is a painful, vesicular, localized S. aureus or group A streptococcal infec tion of the pulps of the distal digits of the hands.

PART 5 Infectious Diseases TABLE 134-1 Skin and Soft Tissue Infections LESION, CLINICAL SYNDROME INFECTIOUS AGENT(S) SEE ALSO CHAP(S). Vesicles Smallpox Variola virus S4 Chickenpox Varicella-zoster virus

Shingles (herpes zoster) Varicella-zoster virus

Cold sores, herpetic whitlow, herpes gladiatorum Herpes simplex virus

Hand-foot-and-mouth disease Coxsackievirus A16

Orf Parapoxvirus

Molluscum contagiosum Molluscum contagiosum poxvirus

Rickettsialpox Rickettsia akari

Blistering distal dactylitis Staphylococcus aureus or Streptococcus pyogenes 152, 153 Bullae Staphylococcal scalded-skin syndrome S. aureus

Necrotizing fasciitis S. pyogenes, Clostridium spp., mixed aerobes and anaerobes 153, 159, 182 Gas gangrene Clostridium spp.

Halophilic Vibrio Vibrio vulnificus

Crusted lesions Bullous impetigo/ecthyma S. aureus

Impetigo contagiosa S. pyogenes

Ringworm Superficial dermatophyte fungi

Sporotrichosis Sporothrix schenckii

Histoplasmosis Histoplasma capsulatum

Coccidioidomycosis Coccidioides immitis

Blastomycosis Blastomyces dermatitidis

Cutaneous leishmaniasis Leishmania spp.

Cutaneous tuberculosis Mycobacterium tuberculosis

Nocardiosis Nocardia asteroides

Folliculitis Furunculosis S. aureus

Hot-tub folliculitis Pseudomonas aeruginosa

Swimmer’s itch Schistosoma spp.

Acne vulgaris Propionibacterium acnes

Papular and nodular lesions Fish-tank or swimming-pool granuloma Mycobacterium marinum

Creeping eruption (cutaneous larva migrans) Ancylostoma braziliense

Dracunculiasis Dracunculus medinensis

Cercarial dermatitis Schistosoma mansoni

Verruca vulgaris Human papillomaviruses 1, 2, 4

Condylomata acuminata (anogenital warts) Human papillomaviruses 6, 11, 16, 18

Onchocerciasis nodule Onchocerca volvulus

Cutaneous myiasis Dermatobia hominis

Verruca peruana Bartonella bacilliformis

Cat-scratch disease Bartonella henselae

Lepromatous leprosy Mycobacterium leprae

Secondary syphilis (papulosquamous and nodular lesions, condylomata lata) Treponema pallidum

Tertiary syphilis (nodular gummatous lesions) T. pallidum

Ulcers with or without eschars Anthrax Bacillus anthracis S4 Ulceroglandular tularemia Francisella tularensis 175, S4 Bubonic plague Yersinia pestis 176, S4 Buruli ulcer Mycobacterium

ulcerans

Leprosy M. leprae

Cutaneous tuberculosis M. tuberculosis

Chancroid Haemophilus ducreyi

Primary syphilis T. pallidum

Erysipelas S. pyogenes

Cellulitis Staphylococcus spp., Streptococcus spp., various other bacteria Various Necrotizing fasciitis Streptococcal gangrene S. pyogenes

Fournier gangrene Mixed aerobic and anaerobic bacteria

Staphylococcal necrotizing fasciitis Methicillin-resistant S. aureus

Myositis and myonecrosis Pyomyositis S. aureus

Streptococcal necrotizing myositis S. pyogenes

Gas gangrene Clostridium spp.

Nonclostridial (crepitant) myositis Mixed aerobic and anaerobic bacteria

Synergistic nonclostridial anaerobic myonecrosis Mixed aerobic and anaerobic bacteria

The recent spike in mpox (formerly monkeypox virus; MPXV) (Chap. 201) cases has raised concerns due to its clinical resemblance to smallpox in terms of symptom onset, timing of rash occurrence, and rash distribution. MPXV infection is generally less severe than smallpox in terms of complication rate and levels of scarification. The case fatality rate (1–10%) is also less than that of smallpox. Though largely endemic in West and Central Africa, cases have recently emerged in at least 10 other African countries. In addition, cases have been reported in Israel, the United Kingdom, and in six midwestern states of the United States. Most non-African cases are associated with tourism to endemic African countries or with exposure to small mam mals imported from such areas. However, human-to-human disease transmission was clearly documented in a British health care worker who attended a patient that had acquired the infection during a trip to Nigeria. Most patients are in lower age groups (<40 years) due to a lack cross-protective immunity, having been born after discontinuation of the smallpox eradication campaign in the 1980s. This finding height ens the concern for potential global disease spread. INFECTIONS ASSOCIATED WITH BULLAE (Table 134-1) Staphylococcal scalded-skin syndrome (SSSS) in neonates is caused by a toxin (exfoliatin) from phage group II S. aureus. SSSS must be distinguished from toxic epidermal necrolysis (TEN), which occurs primarily in adults, is drug-induced, and is associated with a higher mortality rate. Punch biopsy with frozen section is useful in making this distinction since the cleavage plane is the stratum corneum in SSSS and the stratum germinativum in TEN (Fig. 134-1). Treatment with

intravenous immune globulin plus corticosteroids may reduce recovery time and improve prognosis in patients with TEN. Necrotizing fasciitis and gas gangrene also induce bulla formation (see “Necrotizing Fasciitis,” below). Halophilic Vibrio infection can be as aggressive and fulminant as necrotizing fasciitis; a helpful clue in its diagnosis is a his tory of exposure to waters of the Gulf of Mexico or the Atlantic seaboard or (in a patient with cirrhosis) the ingestion of raw seafood. The etio logic organism (Vibrio vulnificus) is highly susceptible to tetracycline. INFECTIONS ASSOCIATED WITH

CRUSTED LESIONS (Table 134-1) Impetigo contagiosa is caused by S. pyogenes, and bul lous impetigo is due to S. aureus. Both skin lesions may have an early bullous stage but then appear as thick crusts with a golden-brown color. Epidemics of impetigo caused by MRSA have been reported. Streptococcal lesions are most common among children 2–5 years of age, and epidemics may occur in settings of poor hygiene, par ticularly among children in lower socioeconomic settings in tropical climates. It is important to recognize impetigo contagiosa because of its relationship to poststreptococcal glomerulonephritis. Rheumatic fever is not a complication of skin infection caused by S. pyogenes. Superficial dermatophyte infection (ringworm) can occur on any skin surface, and skin scrapings with KOH staining are diagnostic. Primary infections with dimorphic fungi such as Blastomyces dermatitidis and Sporothrix schenckii can initially present as crusted skin lesions resem bling ringworm. Disseminated infection with Coccidioides immitis can also involve the skin, and biopsy and culture should be performed on crusted lesions when the patient is from an endemic area. Crusted nodular lesions caused by Mycobacterium chelonae have been described in HIV-seropositive patients. FOLLICULITIS (Table 134-1) Hair follicles serve as portals for a number of bacteria, although S. aureus is the most common cause of localized folliculitis. Sebaceous glands empty into hair follicles and ducts and, if these portals are blocked, form sebaceous cysts that may resemble staphy lococcal abscesses or may become secondarily infected. Inflammation of sweat glands (hidradenitis suppurativa) also can mimic infection of hair follicles, particularly in the axillae, but new treatments with potent anti-inflammatory agents hold promise. Chronic folliculitis is uncom mon except in acne vulgaris, where constituents of the normal flora (e.g., Propionibacterium acnes) may play a role.

Diffuse folliculitis occurs in two settings. Hot-tub folliculitis is caused by Pseudomonas aeruginosa in waters that are insufficiently chlorinated and maintained at temperatures of 37–40°C. Infection is usually selflimited, although bacteremia and shock have been reported. Swimmer’s itch occurs when a skin surface is exposed to water infested with fresh water avian schistosomes. Warm water temperatures and alkaline pH are suitable for mollusks that serve as intermediate hosts between birds and humans. Free-swimming schistosomal cercariae readily penetrate human hair follicles or pores but quickly die and elicit a brisk allergic reaction, causing intense itching and erythema.

PAPULAR AND NODULAR LESIONS (Table 134-1) Raised lesions of the skin occur in many different forms. Mycobacterium marinum infections of the skin may present as cel lulitis or as raised erythematous nodules. Similar lesions caused by Mycobacterium abscessus and M. chelonae have been described among patients undergoing cosmetic laser surgery and tattooing, respectively. Erythematous papules are early manifestations of cat-scratch disease (with lesions developing at the primary site of inoculation of Bartonella henselae) and bacillary angiomatosis (also caused by B. henselae). Raised serpiginous or linear eruptions are characteristic of cutaneous larva migrans, which is caused by burrowing larvae of dog or cat hook worms (Ancylostoma braziliense) and which

humans acquire through contact with soil that has been contaminated with dog or cat feces. Similar burrowing raised lesions are present in dracunculiasis caused by migration of the adult female nematode Dracunculus medinensis. Nodules caused by Onchocerca volvulus measure 1–10 cm in diameter and occur mostly in persons bitten by Simulium flies in Africa. The nodules contain the adult worm encased in fibrous tissue. Migration of microfilariae into the eyes may result in blindness. Verruga peruana is caused by Bartonella bacilliformis, which is transmitted to humans by the sandfly Phlebotomus. This condition can take the form of single gigantic lesions (several centimeters in diameter) or multiple small lesions (several millimeters in diameter). Numerous subcutaneous nodules may also be present in cysticercosis caused by larvae of Taenia solium. Multiple erythematous papules develop in schistosomiasis; each represents a cercarial invasion site. Skin nodules as well as thick ened subcutaneous tissue are prominent features of lepromatous lep rosy. Large nodules or gummas are features of tertiary syphilis, whereas flat papulosquamous lesions are characteristic of secondary syphilis. Human papillomavirus may cause singular warts (verruca vulgaris) or multiple warts in the anogenital area (condylomata acuminata). The latter are major problems in HIV-infected individuals and others with defects in cell-mediated immunity. CHAPTER 134 Infections of the Skin, Muscles, and Soft Tissues ULCERS WITH OR WITHOUT ESCHARS (Table 134-1) Cutaneous anthrax begins as a pruritic papule, which develops within days into an ulcer with surrounding vesicles and edema and then into an enlarging ulcer with a black eschar. Cutaneous anthrax may cause chronic nonhealing ulcers with an overlying dirtygray membrane, although lesions may also mimic psoriasis, eczema, or impetigo. Ulceroglandular tularemia may have associated ulcerated skin lesions with painful regional adenopathy. Although buboes are the major cutaneous manifestation of plague, ulcers with eschars, papules, or pustules also are present in 25% of cases. Mycobacterium ulcerans typically causes chronic skin ulcers on the extremities of individuals living in the tropics. Mycobacterium leprae may be associated with cutaneous ulcerations in patients with lepro matous leprosy related to Lucio’s phenomenon, in which immunemediated destruction of tissue bearing high concentrations of M. leprae bacilli occurs, usually several months after initiation of effective therapy. Mycobacterium tuberculosis also may cause ulcerations, pap ules, or erythematous macular lesions of the skin in both immunocom petent and immunocompromised patients. Decubitus ulcers are due to tissue hypoxemia secondary to pressureinduced vascular insufficiency and may become secondarily infected with components of the skin and gastrointestinal flora, including anaerobes. Ulcerative lesions on the anterior shins may be due to pyo derma gangrenosum, which must be distinguished from similar lesions

of infectious etiology by histologic evaluation of biopsy sites. Ulcerated lesions on the genitals may be either painful (chancroid) or painless (primary syphilis).

ERYSIPELAS (Table 134-1) Erysipelas is due to S. pyogenes and is characterized by an abrupt onset of fiery-red swelling of the face or extremities. The distinctive features of erysipelas are well-defined indurated margins, particularly along the nasolabial fold; rapid progression; and intense pain. Flaccid bullae may develop during the second or third day of illness, but extension to deeper soft tissues is rare. Treatment with peni cillin is effective; swelling may progress despite appropriate treatment, although fever, pain, and the intense red color diminish. Desquama tion of the involved skin occurs 5–10 days into the illness. Infants and elderly adults are most commonly afflicted, and the severity of systemic toxicity varies. CELLULITIS (Table 134-1) Cellulitis is an acute inflammatory condition of the skin that is characterized by localized pain, erythema, swelling, and

heat. It may be caused by indigenous flora colonizing the skin and append ages (e.g., S. aureus and S. pyogenes) or by a wide variety of exogenous bacteria. Because the exogenous bacteria involved in cellulitis occupy unique niches in nature, a thorough history (including epidemiologic data) offers important clues to etiology. When there is drainage, an open wound, or an obvious portal of entry, Gram stain and culture provide a definitive diagnosis. In the absence of these findings, the bacterial etiology of cellulitis is difficult to establish, and in some cases, staphylococcal and streptococcal cellulitis may have similar features. Even with needle aspiration of the leading edge or a punch biopsy of the cellulitis tissue itself, cultures are positive in only 20% of cases. This observation suggests that relatively low numbers of bacteria may cause cellulitis and that the expanding area of erythema within the skin may be a direct effect of extracellular toxins or of the soluble mediators of inflammation elicited by the host. PART 5 Infectious Diseases Bacteria may gain access to the epidermis through cracks in the skin, abrasions, cuts, burns, insect bites, surgical incisions, and IV catheters. Cellulitis caused by S. aureus spreads from a central local ized infection, such as an abscess, folliculitis, or an infected foreign body (e.g., a splinter, a prosthetic device, an IV catheter). MRSA is rapidly replacing methicillin-sensitive S. aureus (MSSA) as a cause of cellulitis in both inpatient and outpatient settings. Cellulitis caused by MSSA or MRSA is usually associated with a focal infection, such as a furuncle, a carbuncle, a surgical wound, or an abscess; the U.S. Food and Drug Administration preferentially refers to these types of infec tion as purulent cellulitis. In contrast, cellulitis due to S. pyogenes is a more rapidly spreading, diffuse process that is frequently associated with lymphangitis and fever and should be referred to as nonpurulent cellulitis. Recurrent streptococcal cellulitis of the lower extremities may be caused by organisms of group A, C, or G in association with chronic venous stasis or with saphenous venectomy for coronary artery bypass surgery. Streptococci also cause recurrent cellulitis among patients with chronic lymphedema resulting from elephantiasis, lymph node dissection, or congenital disorders. Recurrent staphylococcal cutane ous infections are more common among individuals who have Job syndrome, the autosomal dominant hyper-IgE recurrent infection syndrome, and among nasal carriers of staphylococci. Cellulitis caused by Streptococcus agalactiae (group B Streptococcus) occurs primarily in elderly patients and those with diabetes mellitus or peripheral vascular disease. Haemophilus influenzae typically causes periorbital cellulitis in children in association with sinusitis, otitis media, or epiglottitis. It is unclear whether this form of cellulitis will (like meningitis) become less common as a result of the impressive efficacy of the H. influenzae type b vaccine. Many other bacteria also cause cellulitis. It is fortunate that these organisms occur in such characteristic settings that a good history pro vides useful clues to the diagnosis. Cellulitis associated with cat bites and, to a lesser degree, with dog bites is commonly caused by Pasteu rella multocida, although in the latter case Staphylococcus intermedius

and Capnocytophaga canimorsus also must be considered. Sites of cellulitis and abscesses associated with dog bites and human bites also contain a variety of anaerobic organisms, including Fusobacterium, Bacteroides, aerobic and anaerobic streptococci, and Eikenella cor rodens. Pasteurella is notoriously resistant to dicloxacillin and nafcillin but is sensitive to other β-lactam antimicrobial agents as well as to quinolones, tetracycline, and erythromycin. Amoxicillin-clavulanate, ampicillin-sulbactam, and cefoxitin are good choices for the treatment of animal or human bite infections. Aeromonas hydrophila causes aggressive cellulitis and occasionally necrotizing fasciitis in tissues surrounding lacerations sustained in freshwater (lakes, rivers, and streams). This organism remains sensitive to aminoglycosides, fluo roquinolones, chloramphenicol, trimethoprim-sulfamethoxazole, and third-generation cephalosporins; it is resistant to ampicillin,

however. P. aeruginosa causes three types of soft tissue infection: ecthyma gan grenosum in neutropenic patients, hot-tub folliculitis, and cellulitis fol lowing penetrating injury. Most commonly, P. aeruginosa is introduced into the deep tissues following a significant penetrating injury, such as occurs when a person steps on a nail. Treatment includes surgical inspection and drainage, particularly if the injury also involves bone or joint capsule. Choices for empirical treatment (while antimicrobial susceptibility data are awaited) include an aminoglycoside, a thirdgeneration cephalosporin (ceftazidime, cefoperazone), a semisynthetic penicillin (ticarcillin or piperacillin), or a fluoroquinolone (Chap. 170). Gram-negative bacillary cellulitis, including that due to P. aerugi nosa, is most common among hospitalized, immunocompromised hosts. Cultures and sensitivity tests are critically important in this set ting because of multidrug resistance (Chap. 170). The gram-positive aerobic rod Erysipelothrix rhusiopathiae is most often associated with fish and domestic swine and causes cellulitis primarily in bone renderers and fishmongers. E. rhusiopathiae remains susceptible to most β-lactam antibiotics (including penicillin), eryth romycin, clindamycin, tetracycline, and cephalosporins but is resistant to sulfonamides, chloramphenicol, and vancomycin. Its resistance to vancomycin, which is unusual among gram-positive bacteria, is of potential clinical significance since this agent is sometimes used in empirical therapy for skin infection. Fish food containing the water flea Daphnia is sometimes contaminated with M. marinum, which can cause cellulitis or granulomas on skin surfaces exposed to the water in aquariums or injured in swimming pools (Chap. 185). Ethambutol and either clarithromycin or azithromycin are the best therapies.
NECROTIZING FASCIITIS (Table 134-1) Necrotizing fasciitis, formerly called streptococcal gan grene, may be associated with group A Streptococcus or mixed aerobic– anaerobic bacteria or may occur as a component of gas gangrene caused by Clostridium perfringens. Strains of MRSA that produce the Panton-Valentine leukocidin (PVL) toxin have been reported to cause necrotizing fasciitis. Early diagnosis may be difficult when pain or unexplained fever is the only presenting manifestation. Swelling then develops and is followed by brawny edema and tenderness. With pro gression, dark-red induration of the epidermis appears, along with bul lae filled with blue or purple fluid. Later the skin becomes friable and takes on a bluish, maroon, or black color. By this stage, thrombosis of blood vessels in the dermal papillae (Fig. 134-1) is extensive. Extension of infection to the level of the deep fascia causes this tissue to take on a brownish-gray appearance. Rapid spread occurs along fascial planes, through venous channels and lymphatics. Patients in the later stages are toxic and frequently manifest shock and multiorgan failure. Necrotizing fasciitis caused by mixed aerobic–anaerobic bacteria begins with a breach in the integrity of a mucous membrane barrier, such as the mucosa of the gastrointestinal or genitourinary tract. The portal can be a malignancy, a diverticulum, a hemorrhoid, an anal fis sure, or a urethral tear. Other predisposing factors include peripheral vascular disease, diabetes mellitus, surgery, and penetrating injury to the abdomen. Leakage into the perineal area results in a syndrome called Fournier gangrene, characterized by massive swelling of the scrotum and penis with extension into the perineum or the abdominal wall and the legs.

Necrotizing fasciitis caused by S. pyogenes has increased in frequency and severity since 1985. There are two distinct clinical presentations: patients without, versus those with, a defined portal of bacterial entry. Infections in the first category often begin deep at the site of a nonpen etrating, relatively minor trauma, such as a bruise or a muscle strain. Seeding of the site via transient bacteremia is likely, although most patients deny antecedent streptococcal infection. Affected patients present with only severe pain and fever and are frequently misdiag nosed (e.g., thrombophlebitis), given pain-relieving drugs, and sent home. Later in the course, the classic signs

of necrotizing fasciitis, such as purple (violaceous) bullae, skin sloughing, and progressive toxicity, develop. Mortality in this setting is high, and survivors often undergo repeated surgeries including amputations. In infections of the second type, S. pyogenes may reach the deep fascia from a site of cutaneous infection or penetrating trauma. These patients have early signs of superficial skin infection with progression to necrotizing fasciitis. In either setting, toxicity is severe, and renal impairment may precede the development of shock. In 20–40% of cases, myositis occurs con comitantly, and, as in gas gangrene (see below), serum creatine phos phokinase levels may be markedly elevated. Necrotizing fasciitis due to mixed aerobic–anaerobic bacteria may be associated with gas in deep tissue, but gas usually is not present when the cause is S. pyogenes or MRSA. Prompt surgical exploration down to the deep fascia and mus cle is essential. Necrotic tissue must be surgically removed, and Gram staining and culture of excised tissue are useful in establishing whether group A streptococci, mixed aerobic–anaerobic bacteria, MRSA, or Clostridium species are present (see “Treatment,” below). MYOSITIS AND MYONECROSIS (Table 134-1) Muscle involvement can occur with viral infection (e.g., influenza, dengue, or coxsackievirus B infection) or parasitic invasion (e.g., trichinellosis, cysticercosis, or toxoplasmosis). Although myalgia develops in most of these infections, severe muscle pain is the hall mark of pleurodynia (coxsackievirus B), trichinellosis, and bacterial infection. Acute rhabdomyolysis predictably occurs with clostridial and streptococcal myositis but may also be associated with influenza virus, echovirus, coxsackievirus, Epstein-Barr virus, and Legionella infections. Pyomyositis is usually due to S. aureus, is common in tropical areas, and generally has no known portal of entry. Cases of pyomyositis caused by MRSA producing the PVL toxin have been described among children in the United States. Muscle infection begins at the exact site of blunt trauma or muscle strain. Infection remains localized, and shock does not develop unless organisms produce toxic shock syndrome toxin 1 or certain enterotoxins and the patient lacks antibodies to the toxin produced by the infecting organisms. In contrast, S. pyogenes may induce primary myositis (referred to as streptococcal necrotizing

myositis) in association with severe systemic toxicity. Myonecrosis occurs concomitantly with necrotizing fasciitis in ~50% of cases. Both are part of the streptococcal toxic shock syndrome. Gas gangrene usually follows severe penetrating injuries that result in interruption of the blood supply and introduction of soil into wounds. Such cases of traumatic gangrene are usually caused by the clostridial species C. perfringens, C. septicum, and C. histolyticum. Rarely, latent or recurrent gangrene can occur years after penetrating trauma; dormant spores that reside at the site of previous injury are most likely responsible. Spontaneous nontraumatic gangrene among patients with neutropenia, gastrointestinal malignancy, diverticulosis, or recent radiation therapy to the abdomen is caused by several clos tridial species, of which C. septicum is the most commonly involved. The tolerance of this anaerobe to oxygen probably explains why it can initiate infection spontaneously in normal tissue anywhere in the body. Gas gangrene of the uterus, especially that due to Clostridium

sordellii, historically occurred as a consequence of illegal or selfinduced abortion and nowadays also follows spontaneous abortion, vaginal delivery, and Caesarean section. C. sordellii has also been impli cated in medically induced abortion. Postpartum C. sordellii infections in young, previously healthy women present with little or no fever, lack of a purulent discharge, refractory hypotension, extensive peripheral

FIGURE 134-2 CT showing edema and inflammation of the left chest wall in a patient with necrotizing fasciitis and myonecrosis caused by group A Streptococcus. edema and effusions, hemoconcentration, and a markedly elevated white blood cell count. The infection is often fatal, with death ensuing rapidly. C. sordellii and C. novyi have also been associated with cutane ous injection of black tar heroin; mortality rates are lower among these individuals, probably because their injection-site infections are readily apparent and diagnosis is therefore prompt. Synergistic nonclostridial anaerobic myonecrosis, also known as necrotizing cutaneous myositis and synergistic necrotizing cellulitis, is a variant of necrotizing fasciitis caused by mixed aerobic and anaerobic bacteria with the exclusion of clostridial organisms (see “Necrotizing Fasciitis,” above). CHAPTER 134 DIAGNOSIS This chapter emphasizes the physical appearance and location of lesions within the soft tissues as important diagnostic clues. Other crucial considerations in narrowing the differential diagnosis are the temporal progression of the lesions as well as the patient’s travel history, animal exposure or bite history, age, underlying disease status, and lifestyle. However, even the astute clinician may find it challenging to diagnose all infections of the soft tissues by history and inspection alone. Soft tissue radiography, computed tomography (CT) (Fig. 134-2), and magnetic resonance imaging (MRI) may be useful in determining the depth of infection and should be performed when the patient has rapidly progressing lesions or evidence of a sys temic inflammatory response syndrome. These tests are particularly valuable for defining a localized abscess or detecting gas in tissue. Unfortunately, they may reveal only soft tissue swelling and thus are not specific for fulminant infections such as necrotizing fasciitis or myonecrosis caused by group A Streptococcus (Fig. 134-2), where gas is not found in lesions. Infections of the Skin, Muscles, and Soft Tissues Aspiration of the leading edge or punch biopsy with frozen section may be helpful if the results of imaging tests are positive, but negative results occur in ~80% of cases. There is some evidence that aspiration alone may be superior to injection and aspiration with normal saline. Frozen sections are especially useful in distinguishing SSSS from TEN and are quite valuable in cases of necrotizing fasciitis. Open surgical inspection, with debridement as indicated, is the best way to determine the extent and severity of infection and to obtain material for Gram staining and culture. Such an aggressive approach is important and may be lifesaving if undertaken early in the course of fulminant infec tions when there is evidence of systemic toxicity. TREATMENT Infections of the Skin, Muscles, and Soft Tissues A full description of the treatment of all the clinical entities described herein is beyond the scope of this chapter. As a guide to the clinician in selecting appropriate treatment, the antimicrobial agents useful in the most common and the most fulminant cutane ous infections are listed in Table 134-2. Newer antibiotics approved

TABLE 134-2 Treatment of Common Infections of the Skin DIAGNOSIS/CONDITION PRIMARY TREATMENT ALTERNATIVE TREATMENT SEE ALSO CHAP(S). Animal bite (prophylaxis or early infection)a Amoxicillin–clavulanate (875/125 mg

PO bid) Animal bitea (established infection) Ampicillin–sulbactam (1.5–3 g IV q6h) Clindamycin (600–900 mg IV q8h) plus Ciprofloxacin (400 mg IV q12h) or cefoxitin (2 g IV q6h) Bacillary angiomatosis Erythromycin (500 mg PO qid) Doxycycline (100 mg PO bid)

Herpes simplex (primary genital) Acyclovir (400 mg PO tid for 10 days) Famciclovir (250 mg PO tid for 5–10 days) or valacyclovir

(1000 mg PO bid for 10 days) Herpes zoster (immunocompetent host >50 years of age) Acyclovir (800 mg PO 5 times daily for 7–10 days) Cellulitis (staphylococcal or streptococcalb,c) Nafcillin or oxacillin (2 g IV q4–6h) Cefazolin (1–2 g q8h) or ampicillin/sulbactam (1.5–3 g IV q6h) or erythromycin (0.5–1 g IV q6h) or clindamycin (600–900 mg IV q8h) MRSA skin infectiond Vancomycin (1 g IV q12h) Linezolid (600 mg IV q12h)

Necrotizing fasciitis

(group A streptococcalb) Clindamycin (600–900 mg IV q6–8h) plus penicillin G (4 million units IV q4h) Necrotizing fasciitis (mixed aerobes and anaerobes) Ampicillin (2 g IV q4h) plus clindamycin (600–900 mg IV q6–8h) plus ciprofloxacin (400 mg IV q6–8h) Gas gangrene Clindamycin (600–900 mg IV q6–8h) plus penicillin G (4 million units IV q4–6h) aPasteurella multocida, a species commonly associated with both dog and cat bites, is resistant to cephalexin, dicloxacillin, clindamycin, and erythromycin. Eikenella corrodens, a bacterium commonly associated with human bites, is resistant to clindamycin, penicillinase-resistant penicillins, and metronidazole but is sensitive to trimethoprim-sulfamethoxazole and fluoroquinolones. bThe frequency of erythromycin resistance in group A Streptococcus is currently ~5% in the United States but has reached 70–100% in some other countries. Most, but not all, erythromycin-resistant group A streptococci are susceptible to clindamycin; clindamycin-resistant group A streptococci are susceptible to linezolid and to tedizolid. Approximately 90% of Staphylococcus aureus strains are sensitive to clindamycin, but resistance—both intrinsic and inducible—is increasing. cSevere hospital-acquired S. aureus infections or community-acquired S. aureus infections that are not responding to the β-lactam antibiotics recommended in this table may be caused by methicillin-resistant strains, requiring vancomycin, daptomycin, or linezolid or tedizolid. dSome strains of methicillin-resistant S. aureus (MRSA) remain sensitive to tetracycline and trimethoprim-sulfamethoxazole. Daptomycin (4 mg/kg IV q24h) or tigecycline (100-mg loading dose followed by 50 mg IV q12h) is an alternative treatment for MRSA. PART 5 Infectious Diseases by the U.S. Food and Drug Administration for uncomplicated skin and soft tissue infections including ceftaroline, dalbavancin, orita vancin, tedizolid, delafloxacin, and omadacycline. Furuncles, carbuncles, and abscesses caused by MRSA and MSSA are common, and their treatment depends upon the size of the lesion. Furuncles <2.5 cm in diameter are usually treated with moist heat. Those that are larger (4.5 cm of erythema and indura tion) require surgical drainage, and the occurrence of these larger lesions when associated with fever, chills, or leukocytosis requires both drainage and antibiotic treatment. Previous studies in children demonstrated that surgical drainage of abscesses (mean diameter, 3.8 cm) was as effective when used alone as when combined with trimethoprim-sulfamethoxazole treatment. However, the rate of recurrence of new lesions was lower in the group undergoing both drainage and antibiotic treatment. A more recent study in patients with predominantly MRSA localized abscesses suggested that a 7- to 10-day course of treatment with trimethoprim-sulfamethoxazole or clindamycin was associated with higher cure rates and fewer recurrences. Early and aggressive surgical exploration is essential in cases of suspected necrotizing fasciitis, myositis, or gangrene to (1) visu alize the deep structures, (2) remove necrotic tissue, (3) reduce compartment pressure, and (4) obtain suitable material for Gram staining and for aerobic and anaerobic cultures and antimicrobial sensitivity testing. Appropriate empirical antibiotic treatment for mixed aerobic–anaerobic infections is reviewed in Chap. 159. Group A streptococcal and clostridial infection of the fascia and/or muscle carries a mortality rate of 20–50% with penicillin treatment. In experimental models of streptococcal and clostridial necrotiz ing fasciitis/myositis, clindamycin has

exhibited markedly superior efficacy, but no comparative clinical trials have been performed. A retrospective study of children with invasive group A streptococ cal infection demonstrated higher survival rates with clindamycin treatment than with β-lactam antibiotic therapy. Current guide lines recommend treatment with clindamycin (or linezolid) plus a β-lactam antibiotic. The emergence of macrolide resistance among

Doxycycline (100 mg PO bid)

Famciclovir (500 mg PO tid for 7–10 days) or valacyclovir

(1000 mg PO tid for 7 days)

152, 153 Clindamycin (600–900 mg IV q6–8h) plus a cephalosporin (first- or second-generation)

Vancomycin (1 g IV q6h) plus metronidazole (500 mg IV q6h) plus ciprofloxacin (400 mg IV q6–8h)

Clindamycin (600–900 mg IV q6–8h) plus cefoxitin (2 g IV q6h)

group A streptococci has, however, created therapeutic dilemmas for patients allergic to penicillin and for those with life-threatening infections, such as necrotizing fasciitis/myonecrosis and strep tococcal toxic shock syndrome, where clindamycin has been the treatment of choice. In such instances, linezolid or tedizolid could be used. The use of intravenous immune globulin (IVIg) in patients with invasive group A streptococcal infections has been controversial, and early reports failed to demonstrate efficacy or were terminated early due to low enrollment. More recent prospective studies and one five-study meta-analysis demonstrated that administration of IVIg (often in combination with clindamycin) significantly reduced 30- and 90-day mortality. The combination of clindamycin and IVIg may help reduce production and activities of circulating tox ins produced by group A Streptococcus. IVIg could be given early, and more than one dose should be used because different batches of IVIg have variable neutralizing activity against streptococcal exotoxins. Hyperbaric oxygen (HBO) treatment has been suggested to be useful in gas gangrene due to clostridial species. However, no definitive comparative trials of HBO have been done for the treat ment for invasive group A streptococcal infections, although some reports state that such treatment reduces mortality and the need for further debridements. The use of HBO should not delay, or be used in preference to, surgical debridement when the latter is indicated; such delays significantly contribute to mortality. Antibiotic treat ment should be continued until all signs of systemic toxicity have resolved, all devitalized tissue has been removed, and granulation tissue has developed (Chaps. 153, 159, and 182). In summary, infections of the skin and soft tissues are diverse in presentation and severity and offer a great challenge to the clinician. This chapter provides an approach to diagnosis and understand ing of the pathophysiologic mechanisms involved in these infec tions. More in-depth information is found in chapters on specific infections.

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