# e15 Infectious Complications of Burns and Bites

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The skin is an essential component of the nonspecific immune system, protecting the host from potential pathogens in the environment. Breaches in this protective barrier thus represent a form of immunocompromise that predisposes the patient to infection. Thermal burns may cause massive destruction of the integument as well as derangements in humoral and cellular immunity, permitting the development of infection caused by environmental opportunists and components of the host's skin flora. Bites and scratches from animals and humans allow the inoculation of microorganisms past the skin's protective barrier into deeper, susceptible host tissues.

## BURNS

### EPIDEMIOLOGY

Over the past decade, the estimated incidence of burn injuries in the United States has steadily declined; still, however, >1 million burn injuries are brought to medical attention each year. While many burn injuries are minor and require little or no intervention, 50,000 persons are hospitalized for these injuries, and 20,000 have major burns involving at least 25% of the total body surface area. The majority of burn patients are men. Infants account for ~10% of all reported cases. Scalds, structural fires, and flammable liquids and gases are the major causes of burns, but electrical, chemical, and smoking-related sources are also important. Burns predispose to infection by damaging the protective barrier function of the skin, thus facilitating the entry of pathogenic microorganisms, and by inducing systemic immunosuppression. It is therefore not surprising that multiorgan failure and infectious complications are the major causes of morbidity and death in serious burn injury and that as many as 10,000 patients in the United States die of burn-related infections each year.

### PATHOPHYSIOLOGY

Loss of the cutaneous barrier facilitates entry of the patient's own flora and of organisms from the hospital environment into the burn wound. Initially, the wound is colonized with gram-positive bacteria from the surrounding tissue, but the number of bacteria grows rapidly beneath the burn eschar, reaching ~$8.4 \times 10^3$ cfu/g on day 4 after the burn. The avascularity of the eschar, along with the impairment of local immune responses, favors further bacterial colonization and proliferation. By day 7, the wound is colonized with other microbes, including gram-positive bacteria, gram-negative bacteria, and yeasts derived from the gastrointestinal and upper respiratory flora. Invasive infection—localized and/or systemic—occurs when these bacteria penetrate viable tissue. In addition, a role for biofilms has been recognized in experimental animal models of burn-wound infection. (Biofilms are surface-associated communities of bacteria, often embedded in a matrix, that allow the microbes to persist and to resist the effects of host immunity and antimicrobial agents.)

Streptococci and staphylococci were the predominant causes of burn-wound infection in the preantibiotic era and remain important pathogens at present. With the advent of antimicrobial agents, *Pseudomonas aeruginosa* became a major problem in burn-wound management. Less common anaerobic bacteria are typically found in infections of electrical burns or when open wound dressings are used. As antibiotics more effective against *Pseudomonas* have become available, fungi (particularly *Candida albicans*, *Aspergillus* spp., and the agents of mucormycosis) have emerged as increasingly important pathogens in burn-wound patients. Herpes simplex virus (HSV) infection has also been found in burn wounds, especially those on the face.

The cascade of events that follow a severe burn injury and that lead to multiorgan system failure and death are thought to represent a two-step process: The burn injury itself, with ensuing hypovolemia and tissue hypoxia, is followed by invasive infection arising from large amounts of devitalized tissue. The frequency of infection parallels the extent and severity of the burn injury. Severe burn injuries cause a state of immunosuppression that affects innate and adaptive immune responses. The substantial impact of immunocompromise on infection is due to effects on both the cellular and the humoral arms of the immune system. For example, decreases in the number and activity of circulating helper T cells, increases in suppressor T cells, decreases in production and release of monocytes and macrophages, and diminution in levels of immunoglobulin follow major burns. Neutrophil and complement functions have also been shown to be impaired after burns. The increased levels of multiple cytokines detected in burn patients are compatible with the widely held belief that the inflammatory response becomes dysregulated in these individuals; bacterial cell products play a potent role in inducing proinflammatory mediators that contribute to this uncontrolled systemic inflammatory response. Increased permeability of the gut wall to bacteria and their components (e.g., endotoxin) also contributes to immune dysregulation and sepsis. Thus, the burn patient is predisposed to infection at remote sites (see below) as well as at the sites of burn injury. Another contributor to secondary immunosuppression after burn injuries is the endocrine system; increasing levels of vasopressin, aldosterone, cortisol, glucagon, growth hormone, catecholamines, and other hormones that directly affect lymphocyte proliferation, secretion of proinflammatory cytokines, natural killer cell activity, and suppressive T cells are seen.

### CLINICAL MANIFESTATIONS

Since clinical indications of wound infection are difficult to interpret, wounds must be monitored carefully for changes that may reflect infection. A margin of erythema frequently surrounds the sites of burns and by itself is not usually indicative of infection. Signs of infection include the conversion of a partial-thickness to a full-thickness burn, color changes (e.g., the appearance of a dark brown or black discoloration of the wound), the new appearance of erythema or violaceous edema in normal tissue at the wound margins, the sudden separation of the eschar from subcutaneous tissues, and the degeneration of the wound with the appearance of a new eschar.

Early surgical excision of devitalized tissue is now widely used, and burn-wound infections can be classified in relation to the excision site as (1) burn-wound impetigo (infection characterized by loss of epithelium from a previously reepithelialized surface, as seen in a partial-thickness burn that is allowed to close by secondary intention, a grafted burn, or a healed skin donor site); (2) burn-related surgical wound infection (purulent infection of excised burn and donor sites that have not yet epithelialized, accompanied by positive cultures); (3) burn-wound cellulitis (extension of infection to surrounding healthy tissue; Fig. e15-1); and (4) invasive infection in unexcised burn wounds (infection that is secondary to a partial- or full-thickness burn wound and is manifested by separation of the eschar or by violaceous, dark brown, or black discoloration of the eschar; Fig. e15-2). The appearance of a green discoloration of the wound or subcutaneous fat (Fig. e15-3) or the development of ecthyma gangrenosum at a remote site points to a diagnosis of invasive *P. aeruginosa* infection.

Changes in body temperature, hypotension, tachycardia, altered mentation, neutropenia or neutrophilia, thrombocytopenia, and renal failure may result from invasive burn wounds and sepsis. However, because profound alterations in homeostasis occur as a consequence of burns per se and because inflammation without infection is a normal component of these injuries, the assessment of these changes is complicated. Alterations in body temperature, for example, are attributable to thermoregulatory dysfunction; tachycardia and hyperventilation accompany the metabolic changes induced by extensive burn injury and are not necessarily indicative of bacterial sepsis.

Given the difficulty of evaluating burn wounds solely on the basis of clinical observation and laboratory data, wound biopsies are necessary for definitive diagnosis of infection. The timing of these biopsies can be guided by clinical changes, but in some centers burn wounds are rou-

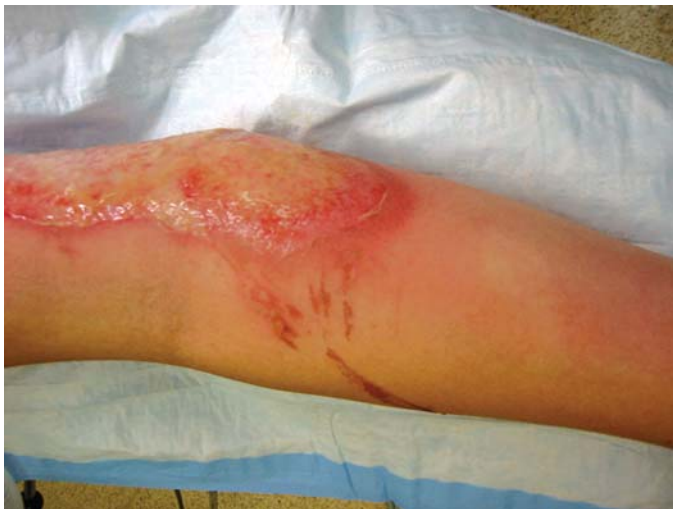

**FIGURE e15-1 Cellulitis complicating a burn wound of the arm** and demonstrating extension of the infection to adjacent healthy tissue. *(Courtesy of Dr. Robert L. Sheridan, Massachusetts General Hospital, Boston; with permission.)*

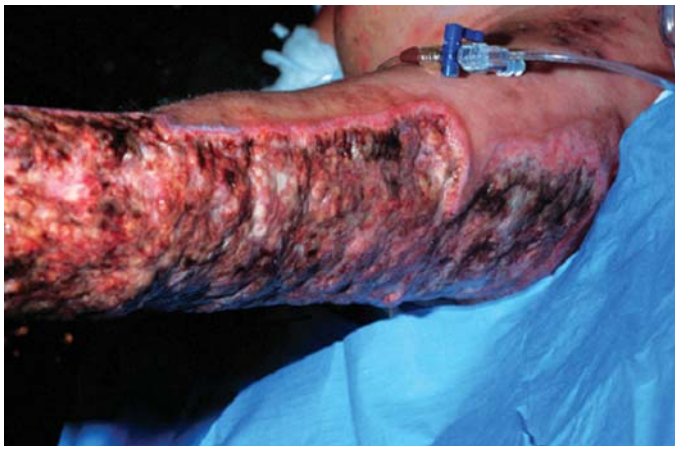

**FIGURE e15-2 A severe upper-extremity burn infected with *Pseudomonas aeruginosa*.** The wound requires additional debridement. Note the dark brown to black discoloration of the eschar. *(Courtesy of Dr. Robert L. Sheridan, Massachusetts General Hospital, Boston; with permission.)*

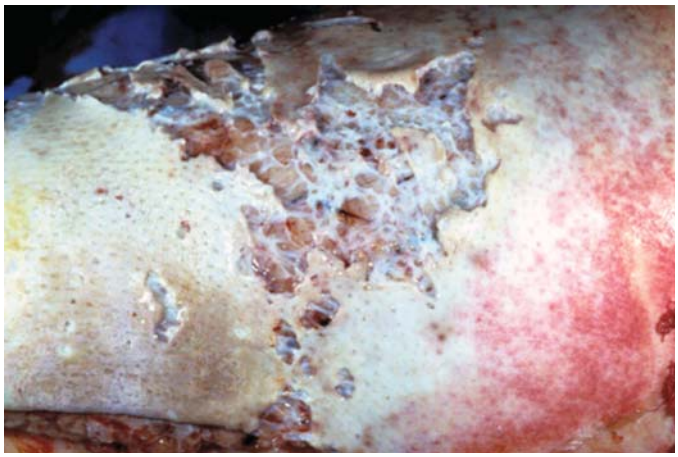

**FIGURE e15-3 A burn wound infected with *Pseudomonas aeruginosa*, with liquefaction of tissue.** Note the green discoloration at the wound margins, which is suggestive of *Pseudomonas* infection. *(Courtesy of Dr. Robert L. Sheridan, Massachusetts General Hospital, Boston; with permission.)*

tinely biopsied at regular intervals. The biopsy specimen is examined for histologic evidence of bacterial invasion, and quantitative microbiologic cultures are performed. The presence of $>10^5$ viable bacteria per gram of tissue is highly suggestive of invasive infection and of a dramatically increased risk of sepsis. Histopathologic evidence of invasion of viable tissue by microorganisms is a more definitive indicator of infection. A blood culture positive for the same organism seen in large quantities in biopsied tissue is a reliable indicator of burn sepsis. Surface cultures may provide some indication of the microorganisms present in the hospital environment but are not indicative of the etiology of infection. This noninvasive technique might be of use in determining the flora present in excised burn areas or in areas where the skin is too thin for biopsy (e.g., over the ears, eyes, or digits).

In addition to infection of the burn wound itself, a number of other infections due to the immunosuppression caused by extensive burns and the manipulations necessary for clinical care put burn patients at risk. Pneumonia, now the most common infectious complication among hospitalized burn patients, is most often nosocomially acquired via the respiratory route; among the risk factors associated with secondary pneumonia are inhalation injury, intubation, full-thickness chest wall burns, immobility, and uncontrolled wound sepsis with hematogenous spread. Septic pulmonary emboli may also occur. Suppurative thrombophlebitis may complicate the vascular catheterization necessary for fluid and nutritional support in burns. Endocarditis, urinary tract infection, bacterial chondritis (particularly in patients with burned ears), and intraabdominal infection also complicate serious burn injury.

## BURN-WOUND INFECTIONS

The ultimate goal of burn-wound management is closure and healing of the wound. Early surgical excision of burned tissue, with extensive debridement of necrotic tissue and grafting of skin or skin substitutes, greatly decreases mortality rates associated with severe burns. In addition, the four widely used topical antimicrobial agents—silver sulfadiazine cream, mafenide acetate cream, silver nitrate cream, and nanocrystalline silver dressings—dramatically decrease the bacterial burden of burn wounds and reduce the incidence of burn-wound infection; these agents are routinely applied to partial- and full-thickness burns. The bactericidal properties of silver are related to its effect on respiratory enzymes on bacterial cell walls; its interaction with structural proteins causes keratinocyte and fibroblast toxicity that can delay wound healing if silver-based compounds are used indiscriminately. All four agents are broadly active against many bacteria and some fungi and are useful before bacterial colonization is established. Silver sulfadiazine is often used initially, but its value can be limited by bacterial resistance, poor wound penetration, or toxicity (leukopenia). Mafenide acetate has broader activity against gram-negative bacteria. The cream penetrates eschars and thus can prevent or treat infection beneath them; its use without dressings allows regular examination of the wound area. The foremost disadvantages of mafenide acetate are that it can inhibit carbonic anhydrase, resulting in metabolic acidosis, and that it elicits hypersensitivity reactions in up to 7% of patients. This agent is most often used when gram-negative bacteria invade the burn wound and when treatment with silver sulfadiazine fails. The activity of mafenide acetate against gram-positive bacteria is limited. Nanocrystalline silver dressings provide broader antimicrobial coverage than any other available topical preparation, exhibiting activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), moderate ability to penetrate eschars, and limited toxicity. In addition, this approach provides controlled and prolonged release of nanocrystalline silver into the wound, limiting the number of dressing changes and therefore reducing the risk of nosocomial infections as well as the cost of treatment. Mupirocin, a topical antimicrobial agent used to eradicate nasal colonization with MRSA, is increasingly being used in burn units where MRSA is prevalent. The efficacy of mupirocin in reducing burn-wound bacterial counts and preventing systemic infections is comparable to that of silver sulfadiazine.

In recent years, rates of fungal infection have increased in burn patients. When superficial fungal infection occurs, nystatin may be mixed with silver sulfadiazine or mafenide acetate as topical therapy. A small study found

that nystatin powder (6 million units/g) was effective for treatment of superficial and deep burn-wound infections caused by *Aspergillus* or *Fusarium* spp. In addition to these products, moisture-retention ointments with antimicrobial properties can promote rapid autolysis, debridement, and moist healing of partial-thickness wounds.

When invasive wound infection is diagnosed, topical therapy should be changed to mafenide acetate. Subeschar clysis (the direct instillation of an antibiotic, often piperacillin, into wound tissues under the eschar) is a useful adjunct to surgical and systemic antimicrobial therapy. Systemic treatment with antibiotics active against the pathogens present in the wound should be instituted. In the absence of culture data, treatment should be broad in spectrum, covering organisms commonly encountered in that particular burn unit. Such coverage is usually achieved with an antibiotic active against gram-positive pathogens (e.g., oxacillin, 2 g IV every 4 h) and with a drug active against *P. aeruginosa* and other gram-negative rods (e.g., mezlocillin, 3 g IV every 4 h; and gentamicin, 5 mg/kg IV per day). In penicillin-allergic patients, vancomycin (1 g IV every 12 h) may be substituted for oxacillin (and is efficacious against MRSA), and ciprofloxacin (400 mg IV every 12 h) may be substituted for mezlocillin. Patients with burn wounds frequently have alterations in metabolism and renal clearance mechanisms that mandate the monitoring of serum antibiotic levels; the levels achieved with standard doses are often subtherapeutic.

Treatment of infections caused by emerging resistant pathogens remains a challenge in the care of burn patients. MRSA, resistant enterococci, multidrug-resistant gram-negative rods, and Enterobacteriaceae producing extended-spectrum β-lactamases have been associated with burn-wound infections and identified in burn-unit outbreaks. Strict infection-control practices (including microbiologic surveillance in burn units) and appropriate antimicrobial therapy remain important measures in reducing rates of infection due to resistant organisms.

In general, prophylactic systemic antibiotics have no role in the management of burn wounds and can in fact lead to colonization with resistant microorganisms. In some studies, antibiotic prophylaxis has been associated with increased secondary infections of the upper and lower respiratory tract and the urinary tract as well as with prolonged hospitalization. An exception involves cases requiring burn-wound manipulation. Since procedures such as debridement, excision, or grafting frequently result in bacteremia, prophylactic systemic antibiotics are administered at the time of wound manipulation; the specific agents used should be chosen on the basis of data obtained by wound culture or data on the hospital's resident flora.

The use of oral antibiotics for selective digestive decontamination (SDD) to decrease bacterial colonization and the risk of burn-wound infection is controversial and has not been widely adopted. In a randomized, double-blind, placebo-controlled trial in patients with burns involving >20% of the total body surface area, SDD was associated with reduced mortality rates in the burn intensive care unit and in the hospital and also with a reduced incidence of pneumonia. The effects of SDD on the normal anaerobic bowel flora must be taken into consideration before this approach is used.

All burn-injury patients should undergo tetanus booster immunization if they have completed primary immunization but have not received a booster dose in the past 5 years. Patients without prior immunization should receive tetanus immune globulin and undergo primary immunization.

## BITES AND SCRATCHES

Each year in the United States, millions of animal-bite wounds are sustained. The vast majority are inflicted by pet dogs and cats, which number >100 million; the annual incidence of dog and cat bites has been reported as 300 bites per 100,000 population. Other bite wounds are a consequence of encounters with animals in the wild or in occupational settings. While many of these wounds require minimal or no therapy, a significant number result in infection, which may be life-threatening. The microbiology of bite-wound infections in general reflects the oropharyngeal flora of the biting animal, although organisms from the soil, the skin of the animal and victim, and the animal's feces may also be involved.

### DOG BITES

In the United States, dogs bite >4.7 million people each year and are responsible for 80% of all animal-bite wounds, an estimated 15–20% of which become infected. Each year, 800,000 Americans seek medical attention for dog bites; of those injured, 386,000 require treatment in an emergency department, with >1000 emergency department visits each day and about a dozen deaths per year. Most dog bites are provoked and are inflicted by the victim's pet or by a dog known to the victim. These bites frequently occur during efforts to break up a dogfight. Children are more likely than adults to sustain canine bites, with the highest incidence of 6 bites per 1000 population among boys 5–9 years old. Victims are more often male than female, and bites most often involve an upper extremity. Among children <4 years old, two-thirds of all these injuries involve the head or neck. Infection typically manifests 8–24 h after the bite as pain at the site of injury with cellulitis accompanied by purulent, sometimes foul-smelling discharge. Septic arthritis and osteomyelitis may develop if a canine tooth penetrates synovium or bone. Systemic manifestations (e.g., fever, lymphadenopathy, and lymphangitis) may also occur. The microbiology of dog-bite wound infections is usually mixed and includes β-hemolytic streptococci, *Pasteurella* spp., *Staphylococcus* spp., *Eikenella corrodens*, and *Capnocytophaga canimorsus* (formerly designated DF-2). Many wounds also include anaerobic bacteria such as *Actinomyces*, *Fusobacterium*, *Prevotella*, and *Porphyromonas* spp.

While most infections resulting from dog-bite injuries are localized to the area of injury, many of the microorganisms involved are capable of causing systemic infection, including bacteremia, meningitis, brain abscess, endocarditis, and chorioamnionitis. These infections are particularly likely in hosts with edema or compromised lymphatic drainage in the involved extremity (e.g., after a bite on the arm in a woman who has undergone radical or modified radical mastectomy) and in patients who are immunocompromised by medication or disease (e.g., glucocorticoid use, systemic lupus erythematosus, acute leukemia, or hepatic cirrhosis). In addition, dog bites and scratches may result in systemic illnesses such as rabies (Chap. 188) and tetanus (Chap. 133).

Infection with *C. canimorsus* following dog-bite wounds may result in fulminant sepsis, disseminated intravascular coagulation, and renal failure, particularly in hosts who have impaired hepatic function, who have undergone splenectomy, or who are immunosuppressed. This organism is a thin gram-negative rod that is difficult to culture on most solid media but grows in a variety of liquid media. The bacteria are occasionally seen within polymorphonuclear leukocytes on Wright-stained smears of peripheral blood from septic patients. Tularemia (Chap. 151) has also been reported to follow dog bites.

### CAT BITES

Although less common than dog bites, cat bites and scratches result in infection in more than half of all cases. Because the narrow, sharp feline incisors penetrate deeply into tissue, cat bites are more likely than dog bites to cause septic arthritis and osteomyelitis; the development of these conditions is particularly likely when punctures are located over or near a joint, especially in the hand. Women sustain cat bites more frequently than do men. These bites most often involve the hands and arms. Both bites and scratches from cats are prone to infection from organisms in the cat's oropharynx. *Pasteurella multocida*, a normal component of the feline oral flora, is a small gram-negative coccobacillus implicated in the majority of cat-bite wound infections. Like that of dog-bite wound infections, however, the microflora of cat-bite wound infections is usually mixed. Other microorganisms causing infection after cat bites are similar to those causing dog-bite wound infections.

The same risk factors for systemic infection following dog-bite wounds apply to cat-bite wounds. *Pasteurella* infections tend to advance rapidly, often within hours, causing severe inflammation accompanied by purulent drainage; *Pasteurella* may also be spread by respiratory droplets from animals, resulting in pneumonia or bacteremia. Like dog-bite wounds, cat-bite wounds may result in the transmission of rabies or in the development of tetanus. Infection with *Bartonella henselae* causes cat-scratch disease (Chap. 153) and is an important late consequence of cat bites and scratches. Tularemia (Chap. 151) has also been reported to follow cat bites.

## OTHER ANIMAL BITES

Infections have been attributed to bites from many animal species. Often these bites are sustained as a consequence of occupational exposure (farmers, laboratory workers, veterinarians) or recreational exposure (hunters and trappers, wilderness campers, owners of exotic pets). Generally, the microflora of bite wounds reflects the oral flora of the biting animal. Most members of the cat family, including feral cats, harbor *P. multocida*. Bite wounds from aquatic animals such as alligators or piranhas may contain *Aeromonas hydrophila*. Venomous snakebites (Chap. 391) result in severe inflammatory responses and tissue necrosis—conditions that render these injuries prone to infection. The snake's oral flora includes many species of aerobes and anaerobes, such as *P. aeruginosa*, *Proteus* spp., *Staphylococcus epidermidis*, *Bacteroides fragilis*, and *Clostridium* spp. Bites from nonhuman primates are highly susceptible to infection with pathogens similar to those isolated from human bites (see below). Bites from Old World monkeys (*Macaca*) may also result in the transmission of B virus (*Herpesvirus simiae*, cercopithecine herpesvirus), a cause of serious infection of the human central nervous system. Bites of seals, walruses, and polar bears may cause a chronic suppurative infection known as *seal finger*, which is probably due to one or more species of *Mycoplasma* colonizing these animals.

Small rodents, including rats, mice, and gerbils, as well as animals that prey on rodents may transmit *Streptobacillus moniliformis* (a microaerophilic, pleomorphic gram-negative rod) or *Spirillum minor* (a spirochete), which cause a clinical illness known as *rat-bite fever*. The vast majority of cases in the United States are streptobacillary, whereas *Spirillum* infection occurs mainly in Asia.

In the United States, the risk of rodent bites is usually greatest among laboratory workers or inhabitants of rodent-infested dwellings (particularly children). Rat-bite fever is distinguished from acute bite-wound infection by its typical manifestation after the initial wound has healed. Streptobacillary disease follows an incubation period of 3–10 days. Fever, chills, myalgias, headache, and severe migratory arthralgias are usually followed by a maculopapular rash, which characteristically involves the palms and soles and may become confluent or purpuric. Complications include endocarditis, myocarditis, meningitis, pneumonia, and abscesses in many organs. *Haverhill fever* is an *S. moniliformis* infection acquired from contaminated milk or drinking water and has similar manifestations. Streptobacillary rat-bite fever was frequently fatal in the preantibiotic era. The differential diagnosis includes Rocky Mountain spotted fever, Lyme disease, leptospirosis, and secondary syphilis. The diagnosis is made by direct observation of the causative organisms in tissue or blood, by culture of the organisms on enriched media, or by serologic testing with specific agglutinins.

*Spirillum* infection (referred to in Japan as *sodoku*) causes pain and purple swelling at the site of the initial bite, with associated lymphangitis and regional lymphadenopathy, after an incubation period of 1–4 weeks. The systemic illness includes fever, chills, and headache. The original lesion may eventually progress to an eschar. The infection is diagnosed by direct visualization of the spirochetes in blood or tissue or by animal inoculation.

Finally, NO-1 (CDC nonoxidizer group 1) is a recently identified bacterium associated with dog- and cat-bite wounds. Infections in which NO-1 has been isolated have tended to manifest locally (i.e., as abscess and cellulitis). These infections have occurred in healthy persons with no underlying illness and in some instances have progressed from localized to systemic illnesses. The phenotypic characteristics of NO-1 are similar to those of asaccharolytic *Acinetobacter* species; i.e., NO-1 is oxidase-, indole-, and urease-negative. To date, all strains identified have been shown to be susceptible to aminoglycosides, β-lactam antibiotics, tetracyclines, quinolones, and sulfonamides.

### HUMAN BITES

Human bites may be self-inflicted; may be sustained by medical personnel caring for patients; or may take place during fights, domestic abuse, or sexual activity. Human-bite wounds become infected more frequently (~10–15% of the time) than do bites inflicted by other animals. These infections reflect the diverse oral microflora of humans, which includes multiple species of aerobic and anaerobic bacteria. Common aerobic isolates include viridans streptococci, *Staphylococcus aureus*, *E. corrodens* (which is particularly common in clenched-fist injury; see below), and *Haemophilus influenzae*. Anaerobic species, including *Fusobacterium nucleatum* and *Prevotella*, *Porphyromonas*, and *Peptostreptococcus* spp., are isolated from 50% of human-bite wound infections; many of these isolates produce β-lactamases. The oral flora of hospitalized and debilitated patients often includes Enterobacteriaceae in addition to the usual organisms. Hepatitis B, hepatitis C, HSV infection, syphilis, tuberculosis, actinomycosis, and tetanus have been reported to be transmitted by human bites; it is biologically possible to transmit HIV through human bites, although this event is quite unlikely.

Human bites are categorized as "occlusional" injuries, which are inflicted by actual biting, and "clenched-fist" injuries, which are sustained when the fist of one individual strikes the teeth of another, causing traumatic laceration of the hand. For several reasons, clenched-fist injuries, which are more common than occlusional injuries, result in particularly serious infections. The deep spaces of the hand, including the bones, joints, and tendons, are frequently inoculated with organisms in the course of such injuries. The clenched position of the fist during injury, followed by extension of the hand, may further promote the introduction of bacteria as contaminated tendons retract beneath the skin's surface. Moreover, medical attention is often sought only after frank infection develops.

### APPROACH TO THE PATIENT: Animal or Human Bites

A careful history should be elicited, including the type of biting animal, the type of attack (provoked or unprovoked), and the amount of time elapsed since injury. Local and regional authorities should be contacted to determine whether an individual species could be rabid and/or to locate and observe the biting animal when rabies prophylaxis may be indicated (Chap. 188). Suspicious human-bite wounds should provoke careful questioning regarding domestic or child abuse. Details on antibiotic allergies, immunosuppression, splenectomy, liver disease, mastectomy, and immunization history should be obtained. The wound should be inspected carefully for evidence of infection, including redness, exudate, and foul odor. The type of wound (puncture, laceration, or scratch); the depth of penetration; and the possible involvement of joints, tendons, nerves, and bones should be assessed. It is often useful to include a diagram or photograph of the wound in the medical record. In addition, a general physical examination should be conducted and should include an assessment of vital signs as well as an evaluation for evidence of lymphangitis, lymphadenopathy, dermatologic lesions, and functional limitations. Injuries to the hand warrant consultation with a hand surgeon for the assessment of tendon, nerve, and muscular damage. Radiographs should be obtained when the bone may have been penetrated or a tooth fragment may be present. Culture and Gram's staining of all infected wounds are essential; anaerobic cultures should be undertaken if abscesses, devitalized tissue, or foul-smelling exudate is present. A small-tipped swab may be used to culture deep punctures or small lacerations. It is also reasonable to culture samples from uninfected wounds due to bites inflicted by animals other than dogs and cats, since the microorganisms causing disease are less predictable in these cases. The white blood cell count should be determined and blood cultured if systemic infection is suspected.

### Rx BITE-WOUND INFECTIONS

**WOUND MANAGEMENT** Wound closure is controversial in bite injuries. Many authorities prefer not to attempt primary closure of wounds that are or may become infected, preferring to irrigate these wounds copiously, debride devitalized tissue, remove foreign bodies, and approximate the wound edges. Delayed primary closure may be undertaken after the risk of infection is over. Small uninfected wounds may be allowed to close by sec-

**TABLE e15-1 MANAGEMENT OF WOUND INFECTIONS FOLLOWING ANIMAL AND HUMAN BITES**

| Biting Species | Commonly Isolated Pathogens | Preferred Antibiotic(s)[a] | Alternative in Penicillin-Allergic Patient | Prophylaxis Advised for Early Uninfected Wounds | Other Considerations |
|---|---|---|---|---|---|
| **Dog** | *Staphylococcus aureus*, *Pasteurella multocida*, anaerobes, *Capnocytophaga canimorsus* | Amoxicillin/clavulanate (250–500 mg PO tid) or ampicillin/sulbactam (1.5–3.0 g IV q6h) | Clindamycin (150–300 mg PO qid) plus either TMP-SMX (1 DS tablet PO bid) or ciprofloxacin (500 mg PO bid) | Sometimes[b] | Consider rabies prophylaxis. |
| **Cat** | *P. multocida*, *S. aureus*, anaerobes | Amoxicillin/clavulanate or ampicillin/sulbactam, as above | Clindamycin plus TMP-SMX as above or a fluoroquinolone | Usually | Consider rabies prophylaxis. Carefully evaluate for joint/bone penetration. |
| **Human, occlusional** | Viridans streptococci, *S. aureus*, *Haemophilus influenzae*, anaerobes | Amoxicillin/clavulanate or ampicillin/sulbactam, as above | Erythromycin (500 mg PO qid) or a fluoroquinolone | Always | |
| **Human, clenched-fist** | As for occlusional plus *Eikenella corrodens* | Ampicillin/sulbactam as above or imipenem (500 mg q6h) | Cefoxitin[c] | Always | Examine for tendon, nerve, or joint involvement. |
| **Monkey** | As for human bite | As for human bite | As for human bite | Always | For macaque monkeys, consider B virus prophylaxis with acyclovir. |
| **Snake** | *Pseudomonas aeruginosa*, *Proteus* spp., *Bacteroides fragilis*, *Clostridium* spp. | Ampicillin/sulbactam as above | Clindamycin plus TMP-SMX as above or a fluoroquinolone | Sometimes, especially with venomous snakes | Antivenin for venomous snake bite |
| **Rodent** | *Streptobacillus moniliformis*, *Leptospira* spp., *P. multocida* | Penicillin VK (500 mg PO qid) | Doxycycline (100 mg PO bid) | Sometimes | |

[a]Antibiotic choices should be based on culture data when available. These are suggestions for empirical therapy and need to be tailored to individual circumstances and local conditions. IV regimens should be used for hospitalized patients. A single IV dose of antibiotics may be given to patients who will be discharged after initial management.
[b]Prophylactic antibiotics are suggested for severe or extensive wounds, facial wounds, and crush injuries; when bone or joint may be involved; and when comorbidity is present (see text).
[c]May be hazardous in patients with immediate-type hypersensitivity reaction to penicillin.
***Note:*** TMP-SMX, trimethoprim-sulfamethoxazole; DS, double-strength.

ondary intention. Puncture wounds due to cat bites should be left unsutured because of the high rate at which they become infected. Facial wounds are usually sutured after thorough cleaning and irrigation because of the importance of a good cosmetic result in this area and because anatomic factors such as an excellent blood supply and the absence of dependent edema lessen the risk of infection.

**ANTIBIOTIC THERAPY** **Established Infection** Antibiotics should be administered in all established bite-wound infections and should be chosen in light of the most likely potential pathogens, as indicated by the biting species and by Gram's stain and culture results **(Table e15-1)**. For dog and cat bites, antibiotics should be effective against *S. aureus*, *Pasteurella* spp., *C. canimorsus*, streptococci, and oral anaerobes. For human bites, agents with activity against *S. aureus*, *H. influenzae*, and β-lactamase-positive oral anaerobes should be used. The combination of an extended-spectrum penicillin with a β-lactamase inhibitor (amoxicillin/clavulanic acid, ticarcillin/clavulanic acid, ampicillin/sulbactam) appears to offer the most reliable coverage for these pathogens. Second-generation cephalosporins (cefuroxime, cefoxitin) also offer substantial coverage. The choice of antibiotics for penicillin-allergic patients (particularly those in whom immediate-type hypersensitivity makes the use of cephalosporins hazardous) is more difficult and is based primarily on in vitro sensitivity since data on clinical efficacy are inadequate. The combination of an antibiotic active against gram-positive cocci and anaerobes (such as clindamycin) with trimethoprim-sulfamethoxazole or a fluoroquinolone, which is active against many of the other potential pathogens, would appear reasonable. In vitro data suggest that azithromycin alone provides coverage against most commonly isolated bite-wound pathogens.

Antibiotics are generally given for 10–14 days, but the response to therapy must be carefully monitored. Failure to respond should prompt a consideration of diagnostic alternatives and surgical evaluation for possible drainage or debridement. Complications such as osteomyelitis or septic arthritis mandate a longer duration of therapy.

Management of *C. canimorsus* sepsis requires a 2-week course of IV penicillin G (2 million units IV every 4 h) and supportive measures. Alternative agents for the treatment of *C. canimorsus* infection include cephalosporins and fluoroquinolones. Serious infection with *P. multocida* (e.g., pneumonia, sepsis, or meningitis) should also be treated with IV penicillin G. Alternative agents include second- or third-generation cephalosporins or ciprofloxacin.

Bites by venomous snakes (Chap. 391) may not require antibiotic treatment. Because it is often difficult to distinguish signs of infection from tissue damage caused by the envenomation, many authorities continue to recommend treatment directed against the snake's oral flora—i.e., the administration of broadly active agents such as ceftriaxone (1–2 g IV every 12–24 h) or ampicillin/sulbactam (1.5–3.0 g IV every 6 h).

Seal finger appears to respond to doxycycline (100 mg twice daily for an interval guided by the response to therapy).

**Presumptive or Prophylactic Therapy** The use of antibiotics in patients presenting early after bite injury (within 8 h) is controversial. Although symptomatic infection frequently will not yet have manifested at this point, many early wounds will harbor pathogens, and many will become infected. Studies of antibiotic prophylaxis for wound infections are limited and have often included only small numbers of cases in which various types of wounds have been managed according to various protocols. A meta-analysis of eight randomized trials of prophylactic antibiotics in patients with dog-bite wounds demonstrated a reduction in the rate of infection by 50% with prophylaxis. However, in the absence of sound clinical trials, many clinicians base the decision to treat bite wounds with empirical antibiotics on the species of the biting animal; the location, severity, and extent of the bite wound; and the existence of comorbid conditions in the host. All human- and monkey-bite wounds should be treated presumptively because of the high rate of infection. Most cat-bite wounds, particularly those involving the hand, should be treated. Other factors favoring treatment for bite wounds include severe injury, as in crush wounds; potential bone or joint involvement; involvement of the hands or genital region; host immunocompromise, including that due to liver disease or splenectomy; and prior mastectomy on the side of an involved upper extremity. When prophylactic antibiotics are administered, they are usually given for 3–5 days.

**Rabies and Tetanus Prophylaxis** Rabies prophylaxis, consisting of both passive administration of rabies immune globulin (with as much of the dose as possible infiltrated into and around the wound) and active immunization with rabies vaccine, should be given in consultation with local and regional public health authorities for many wild-animal (and some domestic-animal) bites and scratches as well as for certain nonbite exposures (Chap. 188). Rabies is endemic in a variety of animals, including dogs and cats in many areas of the world. Many local health authorities require the reporting of all animal bites. A tetanus booster immunization should be given if the patient has undergone primary immunization but has not received a booster dose in the past 5 years. Patients who have not previously completed primary immunization should be immunized and should also receive tetanus immune globulin. Elevation of the site of injury is an important adjunct to antimicrobial therapy. Immobilization of the infected area, especially the hand, is also beneficial.

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