CHEST®
Official publication of the American College of Chest Physicians

Necrotizing Fasciitis

Ronald J. Green, Donald C. Dafoe and Thomas A. Raffin

Chest 1996;110;219-229
DOI 10.1378/chest.110.1.219

ISSN:0012-3692

Necrotizing Fasciitis*

Ronald J. Green, MD; Donald C. Dafoe, MD; and Thomas A. Raffin, MD, FCCP

Necrotizing fasciitis is an uncommon soft-tissue infection, usually caused by toxin-producing, virulent bacteria, which is characterized by widespread fascial necrosis with relative sparing of skin and underlying muscle. It is accompanied by local pain, fever, and systemic toxicity and is often fatal unless promptly recognized and aggressively treated. The disease occurs more frequently in diabetics, alcoholics, immunosuppressed patients, IV drug users, and patients with peripheral vascular disease, although it also occurs in young, previously healthy individuals. Although it can occur in any region of the body, the abdominal wall, perineum, and extremities are the most common sites of infection. Introduction of the pathogen into the subcutaneous space occurs via disruption of the overlying skin or by hematogenous spread from a distant site of infection. Polymicrobial necrotizing fasciitis is usually caused by enteric pathogens, whereas monomicrobial necrotizing fasciitis is usually due to skin flora. Tissue damage and systemic toxicity are believed to result from the release of endogenous cytokines and bacterial toxins. Due to the paucity of skin findings early in the disease, diagnosis is often extremely difficult and relies on a high index of suspicion. Definitive diagnosis is made at surgery by demonstration of a lack of resistance of normally adherent fascia to blunt dissection. Treatment modalities include surgery, antibiotics, supportive care, and hyperbaric oxygen. Early and adequate surgical debridement and fasciotomy have been associated with improved survival. Initial antibiotic therapy should include broad aerobic and anaerobic coverage. If available, hyperbaric oxygen therapy should be considered, although to our knowledge, there are no prospective, randomized clinical trials to support this. Mortality rates are as high as 76%. Delays in diagnosis and/or treatment correlate with poor outcome, with the cause of death being overwhelming sepsis syndrome and/or multiple organ system failure. ***(CHEST 1996; 110:219-29)***

Key words: Fournier's gangrene; hyperbaric oxygen; necrotizing fasciitis; review; soft-tissue infection; Streptococcus organisms

Abbreviations: HBO=hyperbaric oxygen; NSAIDs=nonsteroidal anti-inflammatory drugs

Necrotizing fasciitis is an uncommon soft-tissue infection, usually caused by toxin-producing, virulent bacteria, which is characterized by widespread fascial necrosis with relative sparing of skin and underlying muscle. It is often associated with severe systemic toxicity and is usually rapidly fatal unless promptly recognized and aggressively treated.[1,2]

Because of differing prognoses and treatment modalities, it is helpful to distinguish the various skin and soft-tissue infections. Figure 1 illustrates this spectrum of skin and soft-tissue infections, which can be best classified anatomically. The common superficial pyodermas do not extend beyond the skin (epidermis and dermis), and include erysipelas, impetigo, folliculitis, ecthyma, furunculosis, and carbunculosis.[3,4] Cellulitis is a deeper skin infection than erysipelas. Necrotizing fasciitis primarily involves superficial fascia, subcutaneous fat (which contains vascular structures and nerves), and deep fascia. Myonecrosis (clostridial or nonclostridial) refers to a condition resulting in rapid necrosis of muscle, with delayed involvement of overlying skin and soft tissues.[3]

This report focuses on necrotizing fasciitis, an uncommon but devastating disease managed in ICUs. After an historic background, we will discuss its epidemiology, etiology, clinical presentation, pathophysiology, microbiology, histology, and diagnosis. Next, we will touch on the reported correlation between necrotizing fasciitis and the use of nonsteroidal anti-inflammatory agents. We will conclude with a discussion of treatment modalities and mortality.

Historical Background

Like many diseases that have been "discovered" in our modern medical era, necrotizing fasciitis was actually first described by Hippocrates in the 5th century BC. He discussed it as a complication of "erysipelas:"[5]

*From the Divisions of Pulmonary and Critical Care Medicine (Drs. Green and Raffin) and Transplant Surgery (Dr. Dafoe), Stanford (Calif) University School of Medicine.
Manuscript received November 7, 1995; revision accepted January 24, 1996.
Reprint requests: Dr. Raffin, Division of Pulmonary and Critical Care Medicine, Room H3149, Stanford University School of Medicine, Stanford, CA 94305-5236

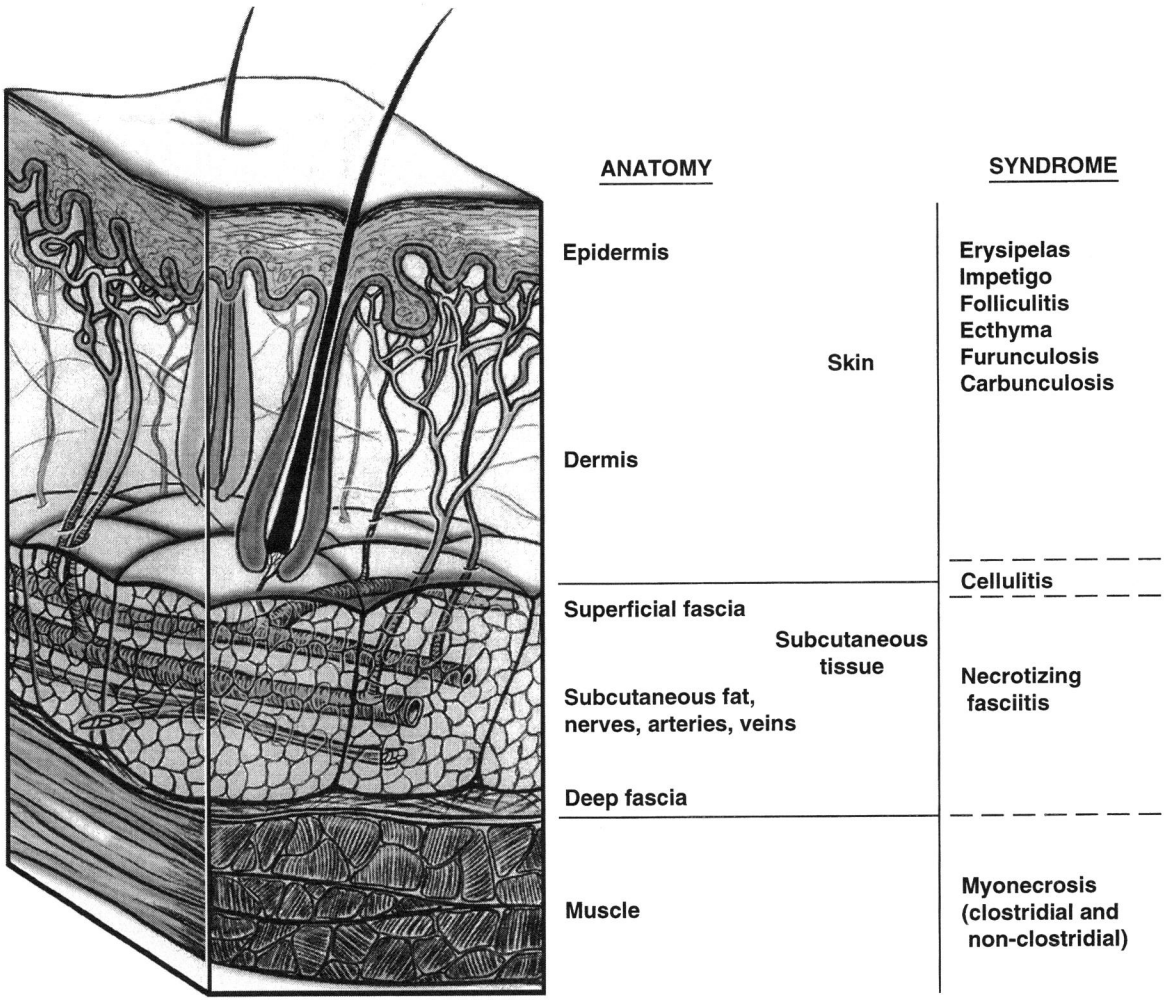

FIGURE 1. Anatomic and clinical classification of soft-tissue infections.

> . . . the erysipelas would quickly spread widely in all directions. Flesh, sinews and bones fell away in large quantities . . . Fever was sometimes present and sometimes absent . . . There were many deaths. The course of the disease was the same to whatever part of the body it spread.

In the early 19th century, necrotizing fasciitis was variously known as the malignant ulcer, gangrenous ulcer, putrid ulcer, phagedena ("eating away"), phagedenic ulcer, phagedena gangraenosa, and hospital gangrene.[6] By the mid-19th century, hospital gangrene and phagedena were the preferred names.[6]

The first detailed descriptions in English were provided by a British naval surgeon, Leonard Gillespie, and two British naval physicians, Sir Gilbert Blane and Thomas Trotter, in the late 18th century.[6] In England, from the 1780s through the 1850s, the disease was known as one of the most dreaded to befall those serving in the army and navy.[6] Hospital gangrene was rare in civilian hospitals despite the fact that surgical wound infections, puerperal fever, and erysipelas were quite common in the preantiseptic era.[6]

The first description of necrotizing fasciitis in the United States occurred in 1871 by Joseph Jones,[7] a Confederate Army surgeon, who called it hospital gangrene. By the beginning of the 20th century, it was thought that hospital gangrene was a disease of the past. As stated by Park in 1908, "Hospital gangrene so-called . . . is now practically never seen."[6] In 1924, Meleney[8] described an outbreak of hospital gangrene in a hospital in Peking, where it was considerably more common than in the West, calling it hemolytic streptococcal gangrene. The term currently in use, necrotizing fasciitis, was first utilized by Wilson[9] in 1952 and most accurately describes the most consistent feature of the infection, fascial necrosis.

Recent outbreaks, which have been publicized by the lay press variously as the "Killer Bug," "Flesh-eating Bacteria," and "Galloping Gangrene," have once again piqued people's interest in this uncommon but often fatal disease.[6,10,11] The resurgence of interest was fueled by a 1989 report by Stevens and colleagues[12] of 20 patients with group A streptococcal toxic shock syndrome, 11 of whom had necrotizing fasciitis. From

1989 to 1991, an estimated 10,000 to 15,000 cases of invasive group A streptococcal infections occurred annually in the United States, with necrotizing fasciitis developing in 5 to 10% of patients with a case-fatality rate of 28%.[13] Since 1991, there has been no active surveillance for invasive group A streptococcal infections in the United States.[13] In England and Wales, the number of laboratory reports of systemic infection with group A streptococci has remained stable over the past 3 years.[14] Hence, it remains unclear whether the incidence of necrotizing fasciitis is actually increasing or whether renewed interest has sparked an increase in published reports.

Epidemiology

There has been confusion in the literature as to the precise definition of necrotizing fasciitis,[15] which has been compounded by the use of multiple terms, including hemolytic streptococcal gangrene, progressive synergistic bacterial gangrene, necrotizing erysipelas, suppurative fasciitis, acute dermal gangrene, and Fournier's gangrene (necrotizing fasciitis of the male genitalia).[3,16,17] Postoperative necrotizing fasciitis has also been called progressive postoperative bacterial synergistic gangrene, which usually occurs at the edge of previous wounds and spreads cutaneously, sparing the deep fascia.[18] The presence of clostridial infection need not exclude a diagnosis of necrotizing fasciitis if the clinical and histologic picture is otherwise consistent.[15] In contrast, clostridial gas gangrene spares the fascia but produces rapid necrosis of the muscle.[18]

There is no age or sex predilection for necrotizing fasciitis. The disease occurs more frequently in diabetics, alcoholics, immunosuppressed patients, IV drug users, and patients with peripheral vascular disease.[4,17] However, necrotizing fasciitis also occurs in young, previously healthy individuals.[12,19] In this population, the pathogenic organism is commonly a virulent strain of group A β-hemolytic streptococcus, with the clinical presentation commonly being that of streptococcal toxic shock syndrome.[12,19]

Etiology

Although it can occur in any region of the body, necrotizing fasciitis most commonly occurs in the abdominal wall, extremities, and perineum (Table 1).[4,15,17,20-22] Introduction of the pathogen into the subcutaneous space can occur via any disruption of the overlying skin, such as a cut, abrasion, burn, laceration, contusion, bite, injection, or surgical incision. Reported etiologies of soft-tissue injury leading to necrotizing fasciitis include blunt or penetrating trauma,[20-26] postoperative complications,[21,22] cutaneous infections or ulcers,[20-23,25,27] illicit IV or subcutaneous drug injections,[21-23,25] perirectal abscesses,[21-23] animal or insect bites,[21] incarcerated hernias,[21,22] subcutaneous insulin injection,[23] colocutaneous fistula,[23] renal calculi,[20] and idiopathic causes.[20,22-25,28,29]

In addition to direct inoculation of the subcutaneous tissues from a superficial site, hematogenous spread from a distant site of infection can probably occur.[30] There are numerous reports[1,19] of patients developing *Streptococcus pyogenes* necrotizing fasciitis where the

Table 1—*Etiology of Necrotizing Fasciitis*

Etiology
Soft-tissue injury
General and extremities
Animal or insect bite
Blunt or penetrating trauma
Cutaneous infections or ulcers
Illicit IV, IM, or subcutaneous drug injections
Postoperative complication
Sprained ankle
Subcutaneous insulin injection
Abdominal
Appendicitis
Colocutaneous fistula
Incarcerated hernia
Perforated viscus
Renal calculus
Perineal
Anal dilatation
Fungating rectal carcinoma
Hemorrhoidal banding
Perirectal or ischiorectal abscess
Pilonidal abscess
Genitourinary
Bartholin's gland duct abscess
Cervical or pudendal nerve block
Coital injury
Genitourinary infections superimposed on
Urethral stricture
Traumatic instrumentation
Urethral calculus
Neoplasm
Prostatic massage
Postepisiotomy
Septic abortion
Vulvar abscess
Head and neck
Face and neck
Cervical adenitis
Otologic etiologies
Peritonsillar abscess
Salivary gland infections
Scalp and periorbital
Blunt or penetrating trauma
Pruritus
Suppurative dental infections
Percutaneous catheter placement
Abscess drainage catheter
Percutaneous endoscopic gastrostomy tube placement
Tube thoracostomy
Special circumstances
Idiopathic
Hematogenous spread

only identifiable source was an antecedent sore throat, presumed to be streptococcal pharyngitis.

Involvement of the abdominal wall is usually a postoperative complication of abdominal surgery.[22] In one series, all instances of postoperative necrotizing fasciitis occurred after contaminated or clean-contaminated surgery, mainly in patients with extensive fecal contamination of the abdominal cavity.[22]

Necrotizing fasciitis of the extremity is most often secondary to trauma, illicit drug use, or insect bite. It may even develop at the site of a trivial scratch or wound or even in seemingly intact skin.[19] In the perineum, it can develop as a postoperative complication, from a pilonidal abscess[22] or a neglected perineal or ischiorectal abscess.[17,31] Retroperitoneal necrotizing fasciitis is usually fatal,[32] although there are case reports of survivors.[33,34]

The overwhelming majority of cases of necrotizing fasciitis of the vulva occur in obese diabetics and often begin as a Bartholin's gland duct abscess or a vulvar abscess.[35-39] Other etiologies include development of necrotizing fasciitis as a postoperative wound infection following cesarean section,[40] episiotomy,[41] hysterectomy,[41] or minilaparotomy for bilateral partial salpingectomy;[42] in a previously irradiated area of the pelvis, often with a fatal outcome;[43] after septic abortion;[41] and following cervical or pudendal nerve block.[41]

When necrotizing fasciitis involves the male genitalia, it is known as Fournier's gangrene,[44] named after Jean Alfred Fournier, who described cases of scrotal gangrene in 1843.[31,45] Some authors expand the definition of Fournier's gangrene to include necrotizing fasciitis of the perineal region in both men and women.[31,41] The most common causes of necrotizing fasciitis of the male genitalia are genitourinary infections and trauma.[41] A urinary tract infection superimposed on a urethral stricture with or without extravasation of urine, traumatic instrumentation, urethral calculus, neoplasm, prostatic massage, surgery, or even coital injury can lead to necrotizing fasciitis.[31,41,46]

Necrotizing fasciitis of the head and neck is rare.[15,21,22,24] Cases can be separated into two groups: those originating on the scalp or periorbital region and those originating on the face or neck.[47] Blunt or penetrating trauma is the most common etiology of scalp involvement while the etiology of periorbital involvement is usually trauma, eyelid infection, or pruritus.[47,48] Patients with scalp or periorbital involvement tend to have monomicrobial infections, particularly with *S pyogenes*,[48-50] and a more benign course,[47,48] although there is one case report of a fatality.[51] Facial and cervical necrotizing fasciitis usually results from progressive, suppurative dental infections.[52-55] Other etiologies include peritonsillar abscess, salivary gland infections, cervical adenitis, and otologic and dermatologic sources.[56,57] The infections may easily spread via natural fascial planes into deep cervical spaces or vascular compartments.[55] Many complications of cervical necrotizing fasciitis have been described, including airway obstruction, jugular venous thrombosis, rupture of the great vessels, aspiration pneumonia, mediastinitis, empyema, and lung abscess.[52,57,58] Given the etiology and anatomic patterns of spread, it is not surprising that facial and cervical necrotizing fasciitis tends to be polymicrobial and is associated with significant mortality.[47]

Necrotizing fasciitis can occur as a complication of percutaneous catheter placement. Reported cases include development of necrotizing fasciitis following tube thoracostomy for empyema drainage,[59] percutaneous endoscopic gastrostomy tube placement,[60] and percutaneous drainage of an intra-abdominal abscess.[61]

The inciting event leading to necrotizing fasciitis is often unknown. In various retrospective case series, an idiopathic cause was reported in anywhere from 13 to 31% of patients.[20,22-25,28,29] In these cases, absence of an obvious source can make the diagnosis challenging.[30] Idiopathic necrotizing fasciitis is more likely to be due to *S pyogenes* and occur in the extremities as opposed to necrotizing fasciitis from known etiologies.[22] It is thought to result from either inoculation via undetected breaks in the epidermis or hematogenous spread from another source.[30]

Clinical Presentation and Pathophysiology

Necrotizing fasciitis usually begins with the development of characteristic skin changes within 7 days of the inciting event.[62] An erythematous, tender, swollen, hot area of cellulitis, accompanied by local pain and fever, is commonly the first sign.[21,25,62] Leukocytosis with a left shift is usually present at the time of hospital admission.[25,28,63] Early necrotizing fasciitis is very painful.[21,64] In fact, pain out of proportion to physical findings in a patient who appears to have a systemically toxic condition should raise the clinical suspicion of necrotizing fasciitis.[4,19,20] Following the initial cellulitic skin changes, the skin becomes smooth, shiny, and tensely swollen as the erythema spreads diffusely.[62] Induration or distinct margins are absent, with the diseased area gradually fading into normal skin. In a few days, the skin darkens to a patchy, dusky blue as blisters and bullae develop.[65] Initially, the bullae are filled with serous fluid, which later becomes hemorrhagic.[66] By this time, the infection is well established in the subcutaneous space. Necrosis of the superficial fascia and fat takes place, producing a watery, thin, and often foul-smelling fluid known as "dishwater pus."[62] The precise mechanism resulting in liquefactive necrosis is not known. Some investigators believe it is caused by bacterial enzymes, including hyaluronidase

and lipases, which degrade fascia and fat, respectively.[62] Normal-appearing skin is undermined while underlying muscle usually remains intact.[15] The extent of fascial necrosis is more widespread than changes in the overlying skin.[20] If thrombosis of the skin's nutrient arteries occurs, focal areas of necrosis form, appearing as deep thermal burns.[4,9,21] Lymphangitis and lymphadenitis are rare.[25,67,68] Four or 5 days into the illness, the purplish skin becomes frankly gangrenous.[62] The subcutaneous nerves are then destroyed by the infectious process and the previously tender skin becomes hypesthetic or anesthetic.[69] As organisms and toxins are liberated into the bloodstream, the patient develops signs and symptoms of sepsis syndrome. Hypocalcemia can develop from extensive fat necrosis.[4] Occasionally, septic emboli can be seen.[62] There are reports of metastatic abscess formation in liver, lungs, spleen, brain, and pericardium from necrotizing fasciitis.[70,71] During the second week, the skin may slough spontaneously. Untreated, the disease is almost invariably fatal. However, there are a few untreated patients who spontaneously recovered after sloughing of necrotic skin.[8]

Microbiology

No single organism is responsible for the fascial necrosis and systemic toxicity seen in necrotizing fasciitis.[62,63] In fact, the synergistic action of facultative aerobic and anaerobic bacteria could be responsible for the often fulminant course of the disease.[63] Table 2 lists the organisms that have been implicated in necrotizing fasciitis.

Giuliano et al[72] divided bacteriologic culture results seen in necrotizing fasciitis into two distinct groups. Type 1 is polymicrobial and involves non-group A streptococci plus anaerobes and/or facultative anaerobes, often with involvement of enterobacteriaceae. In type 2, also known as hemolytic streptococcal gangrene, the pathogen is group A β-hemolytic streptococci alone or in combination with a staphylococcus. As many as 11 organisms were isolated from each patient in their series. Of the anaerobic species isolated, none was present as the sole organism. No differences in clinical course, morbidity, or mortality were demonstrated between the groups. Other studies[70,71] support the findings of Giuliano et al.[72]

The number and type of organisms present in necrotizing fasciitis tend to depend on the site of infection. Abdominal and perineal infections, particularly postoperatively, tend to be polymicrobial and grow enteric pathogens (type 1 in the classification of Giuliano et al[72]).[15,22,31] These postoperative infections grow an average of three bacterial isolates.[22,23,73] The predominant organisms in these polymicrobial infections are aerobic and anaerobic Gram-negative enteric bacilli, enterococci, and, less commonly, staphylococcal and streptococcal species.[15,25,32] The anaerobes include Bacteroides and clostridial species.

Table 2—*Organisms Identified in Necrotizing Fasciitis*

Organisms
Gram-positive aerobic bacteria
Group A, β-hemolytic streptococcus
Group B streptococcus
Enterococci
Coagulase-negative staphylococci
Staphylococcus aureus
Bacillus sp
Gram-negative aerobic bacteria
Escherichia coli
Pseudomonas aeruginosa
Enterobacter cloacae
Klebsiella sp
Proteus sp
Serratia sp
Acinetobacter calcoaceticus
Citrobacter freundii
Pasteurella multocida
Anaerobic bacteria
Bacteroides sp
Clostridium sp
Peptostreptococcus sp
Marine Vibrio sp
Vibrio vulnificus
Vibrio parahemolyticus
Vibrio damsela
Vibrio alginolyticus
Fungi
Candida sp
Aspergillus sp
Rhizopus

Extremity lesions more commonly are monomicrobial and involve skin flora (type 2 in the classification of Giuliano et al[72]).[19,22] Almost half of the monomicrobial infections described by McHenry et al[22] were caused by *S pyogenes* whereas *S pyogenes* was isolated from only 2 of 45 patients with polymicrobial infections.

A third type of necrotizing fasciitis is caused by the marine vibrios (Gram-negative rods), particularly *Vibrio vulnificus, Vibrio parahemolyticus, Vibrio damsela,* and *Vibrio alginolyticus.*[4,74-77] *V vulnificus* is believed to be the most virulent.[75,77] The usual portal of entry is a puncture wound caused by a fish, or a cut or insect bite exposed to sea water, shellfish, or fish in tropical waters.[4,76,77] The pathogenic vibrios are believed to synthesize an extracellular toxin that mediates much of the soft-tissue damage in necrotizing fasciitis.[77]

Many case reports have described other pathogens. These include group B streptococcus,[27] *Pasteurella multocida,*[78] and postoperative infection with candidal species.[23,79]

There is good correlation between the Gram's stain

Table 3—*Diagnostic Features*

Features
Severe local pain
Paucity of skin findings
Fever
Signs and symptoms of systemic toxicity
Nonspecific results of physical examination findings
Soft-tissue gas is uncommon

of surgical or aspirated material from the area of fascial necrosis and organisms eventually cultured.[62] The necrotic center of the lesion is the preferred site for obtaining culture material and Gram's stain.[72,80] This is in distinction to cellulitis, where the leading edge of the lesion is aspirated. Anaerobic and aerobic cultures should be obtained.

Soft-tissue gas almost exclusively occurs in anaerobic infections. The notable exception to this is necrotizing fasciitis in diabetic patients. In diabetics, small-vessel disease, altered leukocyte function, and elevated tissue glucose levels predispose to an environment low in oxygen tension and rich in substrate for bacterial growth.[62]

The tissue damage and systemic toxicity of necrotizing fasciitis are believed to be due to the release of bacterial toxins and endogenous cytokines.[81,82] Exotoxins A and B have been implicated in invasive group A streptococcal infections.[11] Exotoxin A has been demonstrated in cases of invasive streptococcal A infections whereas it was not present in cases of noninvasive streptococcal A infections.[83] In addition, Talkington et al[84] found that strains of streptococcus associated with necrotizing fasciitis and myositis secrete abnormally high levels of a cysteine protease dubbed exotoxin B, an enzyme that destroys tissue by breaking down protein.

There is a recent debate whether new strains of more virulent group A streptococcus have evolved, resulting in an increased number of cases of fatal skin and soft-tissue infections, such as necrotizing fasciitis.[11,12,82] As evidence against increased virulence, McHenry et al[22] found mortality rates in those patients with *S pyogenes* to be similar to the 20% mortality rate reported by Meleney[8] in 1924. Hence, it is still unclear whether the recent apparent increase in mortality is real or simply due to a resurgence of interest in the disease leading to an increase in published reports.

Histopathology

The histopathologic features of necrotizing fasciitis are necrosis of the superficial fascia with blood vessel thrombosis and suppuration.[15,67] Other consistent features include the following: severe subcutaneous fat necrosis; severe inflammation of the dermis and subcutaneous fat; vasculitis, often with endarteritis; and local hemorrhage.[15,67]

Umbert and colleagues[15] reported details of the histopathologic findings in necrotizing fasciitis. In most cases, the epidermis showed no major changes. Dilated blood vessels in the papillary dermis were found in biopsy specimens of acute lesions. In the papillary and reticular dermis, a perivascular, predominantly lymphohistiocytic, infiltrate containing plasma cells was present as was lobular and septal panniculitis. The reticular dermis, subcutaneous fat, and fascia were edematous and contained an inflammatory infiltrate. All levels of tissue contained noninflammatory intravascular coagulation of vessels. Some patients demonstrated necrosis of eccrine glands and ducts as a result of thrombosis and infarction. The fasciae were suppurative and edematous, with necrosis and thrombosis of vessels in advanced lesions. In most patients, microorganisms were seen easily between collagen bundles and in fat lobules. Some specimens showed myonecrosis of underlying skeletal muscle.

Diagnosis

Owing to the paucity of skin findings early in the disease, diagnosis is often extremely difficult and relies on a high clinical index of suspicion. Diagnostic clues include severe local pain, fever, and signs of systemic toxicity with otherwise nonspecific history and physical examination findings (Table 3). If there is a high index of suspicion, a clinical diagnosis of necrotizing fasciitis can be made, prompting early surgical exploration to confirm the diagnosis and perform appropriate debridement. Lack of resistance of normally adherent fascia to blunt dissection is diagnostic of necrotizing fasciitis.[4,19,27] Some investigators even advocate immediate surgical exploration with biopsy and frozen section examination when the diagnosis is suspected but not accompanied by clinical findings.[22] A less invasive manner in which to make a tissue diagnosis has been advocated by Stamenkovic and Lew,[85] namely full-thickness biopsy, which, if performed early, has been shown to significantly improve outcome.

Radiologic studies, including plain radiographs,[22,63,86] CT,[22,87] ultrasonography,[88] and MRI[89,90] have been used to aid in diagnosing necrotizing fasciitis. Detection of soft-tissue gas by plain radiograph is more sensitive than by physical examination.[22,86] Furthermore, it has been suggested that CT scanning is more accurate in detecting soft-tissue gas than plain radiographs.[87] CT scanning can also be helpful in delineating the extent of spread of the infection, especially in cervical necrotizing fasciitis.[52,56,58] Ultrasonography has been used to aid in delineating the extent of

Fournier's gangrene and to differentiate it from other causes of "acute scrotum."[41,88]

Beyond simply recognizing the less common sign of soft-tissue gas, MRI is able to demonstrate good tissue contrast, sensitively detect soft-tissue fluid, and actually visualize the pathologic process. Using MRI, Rahmouni et al[90] were able to differentiate necrotizing soft-tissue infections, which warrant immediate surgical intervention, from nonnecrotizing cellulitis, which can be treated medically.[90] However, their study did not address whether the use of MRI had a significant impact on morbidity or mortality. These issues need to be examined before MRI is adopted as standard of care in the diagnosis and treatment of necrotizing fasciitis. Furthermore, in this age of cost-conscious medicine, its use should be reserved for cases where the diagnosis is uncertain and the findings would change management.

Use of Nonsteroidal Anti-inflammatory Drugs

There have been several reports over the past 10 years associating the use of nonsteroidal anti-inflammatory drugs (NSAIDs) with the development of necrotizing fasciitis, usually involving group A β-hemolytic streptococcus, in previously healthy, young people who are being treated for minor injuries, aches and pains, or arthritis.[64,91-95] Given their efficacy in treating such ailments, NSAIDs are some of the most commonly ingested medications known. There are millions, if not billions, of instances when these medications were taken for the aforementioned indications with a benign result. Hence, it is much more likely that there is simply a correlation, rather than a cause-and-effect relationship, between the use of nonsteroidal anti-inflammatory agents (an extremely common event) and the development of necrotizing fasciitis (an extremely uncommon event). However, given that there is evidence to support the immunosuppressive nature of NSAIDs,[40] to be cautious, some have advocated that they should be used with discretion in cases of soft-tissue inflammation when infection cannot be ruled out.[92,94]

Treatment

Treatment modalities include antibiotics, surgery, supportive care, and hyperbaric oxygen (Table 4).

Antibiotics: The goal of initial antibiotic therapy is to assure broad coverage of aerobic Gram-positive and Gram-negative organisms and anaerobes. Specific initial antibiotic recommendations vary. They include the combination of a penicillin or cephalosporin, an aminoglycoside, and anaerobic coverage with either clindamycin or metronidazole.[4,63,96] Antimicrobial therapy should then be appropriately tailored to culture and susceptibility results. High-dose penicillin remains the drug of choice for necrotizing fasciitis due to *S pyogenes*.[97]

Table 4—*Treatment Fundamentals*

Treatment
Early and definitive surgery
Antibiotics
Supportive care
Hyperbaric oxygen therapy should be considered

Even with appropriate and early antibiotic use, infection may progress due to the fact that thrombosis of superficial vessels in necrotizing fasciitis precludes effective antibiotic penetration to the site of infection[67,69,77] and tissue hypoxia impairs the oxidative killing mechanism of leukocytes.[69] Accumulation of bacteria and bacterial toxins occurs, which contributes to the development of sepsis syndrome and its sequelae. Therefore, early surgical intervention is crucial.

Surgery: Treatment of necrotizing fasciitis is first and foremost surgical. Adequate surgery includes early debridement of all necrotic tissue and drainage of involved fascial planes via extensive fasciotomy until healthy fascia is encountered. The goal is to perform definitive surgery, regardless of how radical, at the first operation.[14] Early and adequate surgical debridement and fasciotomy have been associated with improved survival compared to delayed surgical intervention.[17,20,22,25,26,29,98] Survival has been documented after excision of as much as 45% of a patient's surface area.[14] Postoperatively, because of the potential for rapid progression, the surgical wound must be reevaluated frequently for evidence of disease extension. Some investigators advocate routine surgical reexamination of the infected area within 24 h to ensure adequate debridement of infected and necrotic tissue.[20-22,73] Extension of fascial necrosis is an indication for repeated fasciotomy and further debridement. In many instances, two or more major debridements, carried out in the operating room under general anesthesia, are indicated.[21,73] In cases of extremity involvement, amputation is often warranted to control infection, particularly in patients with peripheral vascular disease and/or diabetes.[22] In cases of perineal necrotizing fasciitis, diverting colostomy and/or urinary diversion are often needed to control infection definitively.[22,32]

Supportive Care: As in any critically ill patient, adequate nutritional support and prompt recognition and treatment of nosocomial infections have been shown to improve outcome.[70,98] Aggressive fluid resuscitation, analgesia, and early intensive care involvement are the mainstays of therapy.[20]

After initial debridement, the cooperation of multiple specialists, including intensivists, general surgeons, and infectious disease specialists, is crucial for optimal

patient treatment. After the patient's condition is stabilized and the patient begins to recover, plastic surgery evaluation is almost always warranted for reconstruction and skin grafting.[99]

Hyperbaric Oxygen: Hyperbaric oxygen (HBO) therapy refers to a treatment modality in which the entire patient is placed in a chamber and breathes oxygen at increased atmospheric pressure.[100] The feature of HBO that is believed to be responsible for its therapeutic efficacy is hyperoxia (elevated partial pressure of oxygen in tissues).[101] The physiologic effects of HBO at the tissue level have been shown to include increased killing ability of leukocytes, killing of certain anaerobes, reduction of tissue edema, stimulation of fibroblast growth, and increased collagen formation.[101,102] Justification for its use is based on animal studies, case reports, and retrospective studies.[103] The Undersea and Hyperbaric Medical Society includes necrotizing soft-tissue infection as one of only 12 reimbursable indications for the use of HBO.[104]

In a retrospective analysis, Riseman and colleagues[96] reported on 29 patients with necrotizing fasciitis, 12 of whom received conventional surgical and antibiotic therapy and 17 of whom received adjunctive HBO. HBO consisted of 90 min in a monoplace chamber at 2.5 atm every 8 h the first day, then twice daily for a total of 10 treatments. All HBO-treated patients received their first treatment within 24 h of hospital admission. Patient demographics, wound bacteriology, and antibiotic therapy were similar between the groups. The HBO group contained more diabetics (47% vs 33%), more patients in shock (29% vs 8%), and more patients with perineal or truncal infections (71% vs 50%). Mortality was 66% in the non-HBO group vs 23% in the HBO group ($p<0.025$), and the HBO group required an average of 1.16 debridements whereas the non-HBO group required 3.25 ($p<0.03$). This study has been criticized because the groups were treated successively, with all non-HBO group patients being treated prior to the acquisition of the chamber (before 1980).[101,105] The authors themselves state that as the study progressed, clinicians prescribed earlier and more extensive debridements.[96] Hence, the HBO group may simply have benefited from the more efficacious therapy of early and extensive debridement.

In another study, Brown et al[103] performed a retrospective review of the efficacy of HBO. They looked only at truncal necrotizing infections and identified 30 patients treated with HBO and 24 patients who did not receive HBO. HBO consisted of 90-min treatments with 2.5 to 3.0 atm. Eighty percent of the HBO-treated patients received less than five treatments and the remainder received between five and seven, with discontinuation once patients' conditions stabilized and there was no evidence for ongoing necrosis. The HBO-treated group was younger (51 vs 62 years), had more clostridial infections (50% vs 17%), had longer ICU stays (7.3 vs 3.5 days; NS), and underwent more operations (mean of 3.2 vs 1.7; $p<0.0002$) and more debridements (mean of 2.4 vs 1.3; $p<0.004$) than the non-HBO group. Laparotomy was performed in 20 (66%) of the HBO group vs 10 (41%) of the non-HBO group ($p<0.007$). Hence, the HBO group was sicker and was treated more aggressively than the non-HBO group. This suggests that HBO was reserved for the sickest patients and/or that it actually improved patient outcome. There was a trend toward better survival in the HBO-treated group (30% vs 42% mortality), but because of the small study size, it did not reach statistical significance.

In summary, if HBO therapy is available, it should be considered as a treatment adjunct in patients with necrotizing fasciitis. Unfortunately, to our knowledge, there are no prospective, randomized, controlled trials demonstrating the efficacy of HBO in the treatment of necrotizing fasciitis. Importantly, whereas HBO treatment for clostridial gas gangrene should be instituted before surgical intervention,[101] its use in necrotizing fasciitis should not preclude early and definitive surgical debridement.[22,63]

Mortality

Mortality from necrotizing fasciitis has changed little since Meleney[8] first recognized the need for early surgical intervention. Mortality rates are as high as 76%.[22] In the largest series to date, the overall mortality rate was 29%.[22] McHenry and colleagues[22] found that delays in diagnosis and treatment (particularly adequate surgical debridement and fasciotomy) correlated with poor outcome. Other risk factors that have been shown to correlate with increased mortality include age over 50 years, diabetes mellitus, peripheral vascular disease and other systemic disorders, poor nutritional status, and anatomic site of infection involving the trunk.[21,23,26,70,71]

The proximate cause of death in patients with necrotizing fasciitis is usually either overwhelming sepsis or multiple organ system failure with or without the ARDS.[22,23,73] McHenry and colleagues[22] found that early deaths (defined as within the first 10 days after initial debridement) were due to the consequences of sepsis syndrome, whereas late deaths were attributable to multiple organ system failure.

Conclusion

Necrotizing fasciitis is an uncommon soft-tissue infection that is characterized by widespread fascial necrosis with relative sparing of skin and underlying muscle. It is often associated with severe systemic toxic reactions and is usually rapidly fatal if not promptly

recognized and aggressively treated. Given the paucity of initial skin findings, early diagnosis can be very difficult and relies on a high clinical index of suspicion. Diagnostic clues include severe local pain, fever, and signs of systemic toxicity with otherwise nonspecific history and physical examination findings. Radiologic procedures such as MRI can sometimes aid in diagnosis. If there is a high index of suspicion, a clinical diagnosis of necrotizing fasciitis can be made, prompting early surgical exploration to confirm the diagnosis and perform appropriate debridement. Lack of resistance of normally adherent fascia to blunt dissection is diagnostic of necrotizing fasciitis. Making the decision to subject a patient to such an operation can be very difficult when there is diagnostic uncertainty. This should be tempered by the fact that early and adequate surgical debridement and fasciotomy have been associated with improved survival in this often fatal disease. In addition to surgery, other treatment modalities include antibiotics and supportive care. If readily available, HBO therapy should be considered, but only after appropriate surgical intervention. A prospective, randomized, controlled clinical trial is needed to assess the efficacy of HBO therapy.

References

1 Weinbren MJ, Perinpanayagam RM. Streptococcal necrotising fasciitis. J Infect 1992; 25:299-302
2 Donaldson PMW, Naylor B, Lowe JW, et al. Rapidly fatal necrotising fasciitis caused by *Streptococcus pyogenes*. J Clin Pathol 1993; 46:617-20
3 Conly J. Soft tissue infections. In: Hall JB, Schmidt GA, Wood LDH, et al, eds. Principles of critical care. New York: McGraw-Hill, 1992; 1325-34
4 Canoso JJ, Barza M. Soft tissue infections. Rheum Dis Clin North Am 1993; 19:293-309
5 Descamps V, Aitken J, Lee MG. Hippocrates on necrotising fasciitis [letter]. Lancet 1994; 344:556
6 Loudon I. Necrotising fasciitis, hospital gangrene, and phagedena. Lancet 1994; 344:1416-19
7 Jones J. Investigations on the nature, causes and treatments of hospital gangrene as it prevailed in the Confederate armies 1861-1865. In: Hastings Hamilton F, ed. Surgical memoirs of the war of rebellion. New York: Sanitary Commission, 1871
8 Meleney FL. Hemolytic streptococcal gangrene. Arch Surg 1924; 9:317-64
9 Wilson B. Necrotizing fasciitis. Am Surg 1952; 18:416-31
10 Anonymous. Resurgent infections. Nature 1994; 369:344
11 Nowak R. Flesh-eating bacteria: not new, but still worrisome. Science 1994; 264:1665
12 Stevens DL, Tanner MH, Winship J, et al. Severe group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin A. N Engl J Med 1989; 321:1-7
13 CDC editorial note. Invasive group A streptococcal infections—United Kingdom, 1994. JAMA 1994; 272:16
14 Burge TS, Watson JD. Necrotising fasciitis: be bloody, bold, and resolute. BMJ 1994; 308:1453-54
15 Umbert IJ, Winkelmann RK, Oliver GF, et al. Necrotizing fasciitis: a clinical, microbiologic, and histopathologic study of 14 patients. J Am Acad Dermatol 1989; 20:774-81
16 Thibault GE. Clinical problem-solving: desperate appliance. N Engl J Med 1994; 330:623-26
17 Voros D, Pissiotis C, Georgantas D, et al. Role of early and extensive surgery in the treatment of severe necrotizing soft tissue infections. Br J Surg 1993; 80:1190-91
18 Barzilai A, Zaaroor M, Toledano C. Necrotizing fasciitis: early awareness and principles of treatment. Isr J Med Sci 1985; 21:127-32
19 Chelsom J, Halstensen A, Haga T, et al. Necrotising fasciitis due to group A streptococci in western Norway: incidence and clinical features. Lancet 1994; 344:1111-15
20 Ward RG, Walsh MS. Necrotizing fasciitis: 10 years' experience in a district general hospital. Br J Surg 1991; 78:488-89
21 Sudarsky LA, Laschinger JC, Coppa GF, et al. Improved results from a standardized approach in treating patients with necrotizing fasciitis. Ann Surg 1987; 206:661-65
22 McHenry CR, Piotrowski JJ, Petrinic D, et al. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg 1995; 221:558-65
23 Francis KR, Lamaute HR, Davis JM, et al. Implications of risk factors in necrotizing fasciitis. Am Surg 1993; 59:304-08
24 Thurber GM, Brantley SK Jr, Das SK. Necrotizing fasciitis. J Miss State Med Assoc 1991; 32:259-64
25 Wang K-C, Shih C-H. Necrotizing fasciitis of the extremities. J Trauma 1992; 32:179-82
26 Rea WJ, Wyrick WJ. Necrotizing fasciitis. Ann Surg 1970; 172:957-64
27 Riefler J III, Molavi A, Schwartz D, et al. Necrotizing fasciitis in adults due to group B streptococcus. Arch Intern Med 1988; 148:727-29
28 Tharakaram S, Keczkes K. Necrotizing fasciitis: a report of five patients. Int J Dermatol 1988; 27:585-88
29 Freischlag JA, Ajalat G, Busuttil RW. Treatment of necrotizing soft tissue infections: the need for a new approach. Am J Surg 1985; 149:751-55
30 McHenry CR, Brandt CP, Piotrowski JJ, et al. Idiopathic necrotizing fasciitis: recognition, incidence, and outcome of therapy. Am Surg 1994; 60:490-94
31 Stephens BJ, Lathrop JC, Rice WT, et al. Fournier's gangrene: historic (1764-1978) versus contemporary (1979-1988) differences in etiology and clinical importance. Am Surg 1993; 59:149-54
32 Woodburn KR, Ramsay G, Gillespie G, et al. Retroperitoneal necrotizing fasciitis. Br J Surg 1992; 79:342-44
33 Rush BM, Hood JS, McDonald JC, et al. Retroperitoneal necrotizing fasciitis. J La State Med Soc 1991; 143:23-4
34 Jayatunga AP, Caplan S, Paes TRF. Survival after retroperitoneal necrotizing fasciitis. Br J Surg 1993; 80:981
35 Farley DE, Katz VL, Dotters DJ. Toxic shock syndrome associated with vulvar necrotizing fasciitis. Obstet Gynecol 1993; 82:660-62
36 Adelson MD, Joret DM, Gordon LP, et al. Recurrent necrotizing fasciitis of the vulva: a case report. J Reprod Med 1991; 36:818-22
37 Nolan TE, King LA, Smith RP, et al. Necrotizing surgical infection and necrotizing fasciitis in obstetric and gynecologic patients. South Med J 1993; 86:1363-67
38 Roberts DB. Necrotizing fasciitis of the vulva. Am J Obstet Gynecol 1987; 157:568-71
39 Stephenson H, Dotters DJ, Katz V, et al. Necrotizing fasciitis of the vulva. Am J Obstet Gynecol 1992; 166:1324-27
40 Van Ammers PM, Moore PJ, Sacho H. Necrotising fasciitis after caesarean section—association with non-steroidal anti-inflammatory drugs. S Afr Med J 1991; 80:203-04
41 Laucks SS II. Fournier's gangrene. Surg Clin North Am 1994; 74:1339-52
42 Cederna JP, Davies BW, Farkas SA, et al. Necrotizing fasciitis

of the total abdominal wall after sterilization by partial salpingectomy. Am J Obstet Gynecol 1990; 162:138-39
43 Livengood CH III, Soper JT, Clarke-Pearson DL, et al. Necrotizing fasciitis in irradiated tissue from diabetic women: a report of two cases. J Reprod Med 1991; 36:455-58
44 Clayton MD, Fowler JE, Sharifi R, et al. Causes, presentation and survival of 57 patients with necrotizing fasciitis of the male genitalia. Surg Gynecol Obstet 1990; 170:49-55
45 Fournier JA. Gangrene foudroyante de la verge. Semaine Med 1883; 3:345-47
46 Efem SEE. The features and aetiology of Fournier's gangrene. Postgrad Med 1994; 70:568-71
47 Nallathambi MN, Ivatury RR, Rohman M, et al. Craniocervical necrotizing fasciitis: critical factors in management. Can J Surg 1987; 30:61-3
48 Overholt EM, Flint PW, Overholt EL, et al. Necrotizing fasciitis of the eyelids. Otolaryngol Head Neck Surg 1992; 106:339-44
49 Rose GE, Howard DJ, Watts MR. Periorbital necrotising fasciitis. Eye 1991; 5:736-40
50 Kronish JW, McLeish WM. Eyelid necrosis and periorbital necrotizing fasciitis. Ophthalmology 1991; 98:92-8
51 Kent D, Atkinson PL, Patel B, et al. Fatal bilateral necrotising fasciitis of the eyelids. Br J Ophthalmol 1995; 79:95-6
52 Maisel RH, Karlen R. Cervical necrotizing fasciitis. Laryngoscope 1994; 104:795-98
53 Kaddour HS, Smelt GJC. Necrotizing fasciitis of the neck. J Laryngol Otol 1992; 106:1008-10
54 Gillis AR, Gillis TM. Necrotizing cervical fasciitis of unknown origin. J Otolaryngol 1992; 21:171-73
55 Chow AW. Life-threatening infections of the head and neck. Clin Infect Dis 1992; 14:991-1004
56 Greinwald JH Jr, Wilson JF, Haggerty PG. Peritonsillar abscess: an unlikely cause of necrotizing fasciitis. Ann Otol Rhinol Laryngol 1995; 104:133-37
57 Moss RM, Kumpittaya S, Sorasuchart A. Cervical necrotizing fasciitis: an uncommon sequela to dental infections. Ann Otol Rhinol Laryngol 1990; 99:643-46
58 Langford FPJ, Moon RE, Stolp BW, et al. Treatment of cervical necrotizing fasciitis with hyperbaric oxygen therapy. Otolaryngol Head Neck Surg 1995; 112:274-78
59 Chen Y-M, Wu MF, Lee PY, et al. Necrotizing fasciitis: is it a fatal complication of tube thoracostomy? Report of three cases. Respir Med 1992; 86:249-51
60 Calton WC, Martindale RG. Complications of percutaneous endoscopic gastrostomy. Mil Med 1992; 157:358-60
61 Holley DT, McGrath PC, Sloan DA. Necrotizing fasciitis as a complication of percutaneous catheter drainage of an intra-abdominal abscess. Am Surg 1994; 60:197-99
62 Wilkerson R, Paull W, Coville FV. Necrotizing fasciitis: review of the literature and case report. Clin Orthop Related Res 1987; 216:187-92
63 Gozal D, Ziser A, Shupak A, et al. Necrotizing fasciitis. Arch Surg 1986; 121:233-35
64 Rietveld JA, Pilmore HL, Jones PG, et al. Necrotising fasciitis: a single centre's experience. N Z Med J 1995; 108:72-4
65 Webb HE, Hoover NW, Nichols DR, et al. Streptococcal gangrene. Arch Surg 1962; 85:969-73
66 Buchanan CS, Haserick JR. Necrotizing fasciitis due to group A β-hemolytic streptococci. Arch Dermatol 1970; 101:664-68
67 Barker FG, Leppard BJ, Seal DV. Streptococcal necrotising fasciitis: comparison between histological and clinical features. J Clin Pathol 1987; 40:335-41
68 Janevicius RV, Hann SE, Batt MD. Necrotizing fasciitis. Surg Gynecol Obstet 1982; 154:97-102
69 Cohen E, Korzets A, Tsalihin Y, et al. Streptococcal toxic shock syndrome complicating necrotizing fasciitis in a renal transplant patient. Nephrol Dial Transplant 1994; 9:1498-99
70 Rouse TM, Melangoni MA, Schulte WJ. Necrotizing fasciitis: a preventable disaster. Surgery 1982; 92:765-70
71 Freeman HP, Oluwole SF, Ganepola GAP, et al. Necrotizing fasciitis. Am J Surg 1981; 142:377-83
72 Giuliano A, Lewis F, Hadley K, et al. Bacteriology of necrotizing fasciitis. Am J Surg 1977; 134:52-7
73 Asfar SK, Baraka A, Juma T, et al. Necrotizing fasciitis. Br J Surg 1991; 78:838-40
74 Howard RJ, Pessa ME, Brennaman BH, et al. Necrotizing soft-tissue infections caused by marine vibrios. Surgery 1985; 98:126-30
75 Hung LK, Kinninmonth AWG, Woo ML. Vibrio vulnificus necrotizing fasciitis presenting with compartmental syndrome of the hand. J Hand Surg 1988; 13B:337-39
76 Maxwell EL, Mayall BC, Pearson SR, et al. A case of *Vibrio vulnificus* septicaemia acquired in Victoria. Med J Aust 1991; 154:214-15
77 Yuen K-Y, Ma L, Wong SSY, et al. Fatal necrotizing fasciitis due to *Vibrio damsela.* Scand J of Infect Dis 1993; 25:659-61
78 Hamamoto Y, Soejima Y, Ogasawara M, et al. Necrotizing fasciitis due to *Pasteurella multocida* infection. Dermatology 1995; 190:145-47
79 Cook DA, Heiner JP, Rao VK. Necrotizing candidal fasciitis following hip surgery. Orthopedics 1990; 13:768-70
80 Guibal F, Muffat-Joly M, Terris B, et al. Necrotising fasciitis [letter]. Lancet 1994; 344:1771
81 Yong JM. Necrotising fasciitis [letter]. Lancet 1994; 343:1427
82 Stevens DL. Invasive group A streptococcal infections. Clin Infect Dis 1992; 14:2-13
83 Belani K, Schlievert PM, Kaplan EL, et al. Association of exotoxin-producing Group A streptococci and severe disease in children. Pediatr Infect Dis J 1991; 10:351-54
84 Talkington DF, Schwartz B, Black CM, et al. Association of phenotypic and genotypic characteristics of invasive *Streptococcus pyogenes* isolates with clinical components of streptococcal toxic shock syndrome. Infect Immun 1993; 61:3369-74
85 Stamenkovic I, Lew PD. Early recognition of potentially fatal necrotizing fasciitis: the use of frozen section biopsy. N Engl J Med 1984; 310:1689-93
86 Fischer JR, Conway MJ, Takeshita RT, et al. Necrotizing fasciitis: importance of roentgenographic studies for soft-tissue gas. JAMA 1979; 241:803-06
87 Yamaoka M, Furusawa K, Uematsu T, et al. Early evaluation of necrotizing fasciitis with use of CT. J Craniomaxillofac Surg 1994; 22:268-71
88 Begley MG, Shawker TH, Robertson CN, et al. Fournier gangrene: diagnosis with scrotal US. Radiology 1988; 169:387-89
89 Kaufman JL. Clinical problem-solving: necrotizing fasciitis [letter]. N Engl J Med 1994; 331:279-80
90 Rahmouni A, Chosidow O, Mathieu D, et al. MR imaging in acute infectious cellulitis. Radiology 1994; 192:493-96
91 Rimailho A, Riou B, Richard C, et al. Fulminant necrotizing fasciitis and nonsteroidal anti-inflammatory drugs. J Infect Dis 1987; 155:143-46
92 Smith RJ, Berk SL. Necrotizing fasciitis and nonsteroidal anti-inflammatory drugs. South Med J 1991; 84:785-87
93 Krige JE, Spence RA, Potter PC, et al. Necrotizing fasciitis after diflunisal for minor injury. Lancet 1985; 2:1432-33
94 Frankish PD, Mason GH, Allen PR, et al. Acute streptococcal necrotising fasciitis. N Z Med J 1988; 101:625-26
95 Brun-Buisson CJL, Saada M, Trunet P, et al. Haemolytic streptococcal gangrene and non-steroidal anti-inflammatory drugs. BMJ 1985; 290:1786
96 Riseman JA, Zamboni WA, Curtis A, et al. Hyperbaric oxygen therapy for necrotizing fasciitis reduces mortality and the need for debridements. Surgery 1990; 108:847-50

97 Simpson AJH, Jumaa PA, Prentice MB. Necrotising fasciitis [letter]. Lancet 1994; 344:67
98 Majeski JA, Alexander JW. Early diagnosis, nutritional support and immediate extensive debridement improve survival in necrotizing fasciitis. Am J Surg 1983; 145:784-87
99 Ward RG. Necrotising fasciitis: immediate surgical opinion is essential [letter]. BMJ 1994; 309:341
100 Kindwall EP, Gottlieb LJ, Larson DL. Hyperbaric oxygen therapy in plastic surgery: a review article. Plast Reconstr Surg 1991; 88:898-908
101 Kindwall EP. Uses of hyperbaric oxygen therapy in the 1990s. Cleve Clin J Med 1992; 59:517-28
102 Cohn GH. Hyperbaric oxygen therapy: promoting healing in difficult cases. Postgrad Med 1986; 79:89-92
103 Brown DR, Davis NL, Lepawsky M, et al. A multicenter review of the treatment of major truncal necrotizing infections with and without hyperbaric oxygen therapy. Am J Surg 1994; 167:485-89
104 Kindwall EP. Hyperbaric oxygen. BMJ 1993; 307:515-16
105 Burge TS. Hyperbaric oxygen: still unproved in necrotising fasciitis [letter]. BMJ 1993; 307:936