Winning the Race With Necrotizing Soft Tissue Infection

The patient with a nonspecific surface presentation that merely hints at necrotizing soft tissue infection may in fact be hurtling along an extremely fulminant course with a poor prognosis. The authors explain how to proceed quickly through the necessary assessments so you can get your patient to the operating room before it's too late.

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The emergent condition commonly referred to as *necrotizing fasciitis* is a rapidly progressing, potentially lethal form of infection affecting skin, subcutaneous tissue, and underlying fascia. It requires stat workup and aggressive surgical debridement. First described in Western medicine following the American Civil War, the condition still presents a formidable challenge in diagnosis and management.[1,2]

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The term *necrotizing fasciitis* has evolved as a descriptive convenience. A variety of infections of this general type have been described as *necrotizing erysipelas*, *streptococcal gangrene*, *gas gangrene*, *Fournier's gangrene*, and *suppurative fasciitis*.[2,3] This terminology differentiates the diseases primarily on the basis of anatomical location, cutaneous depth, and microbial source. More recently, it has been suggested that all of these infections be referred to as necrotizing soft tissue infection (NSTI), reflecting their common pathology and disease management strategy.[3]

Necrotizing soft tissue infections affect about 500 to 1500 patients per year in the United States.[3] Even with early, aggressive treatment, the reported mortality is in the 30% to 40% range or higher and has

not changed significantly in the past 30 years.[1,2,4] In outcome studies, delaying surgical treatment of NSTI for more than 24 hours after presentation significantly increased mortality. Without treatment, NSTI usually leads to sepsis and multiple organ failure within 24 hours.[2,5]

Reports suggest that less than half (with some suggesting as few as 14%) of patients with NSTI are admitted with a correct initial diagnosis.[1] It is clear that early recognition, proper emergency department management, and rapid referral to appropriate surgical services are vital to prevent the loss of life or limb. Failure to promptly recognize and treat NSTIs may lead to litigation, as illustrated in a case series by Fink and colleagues.[6]

VARIED AND ELUSIVE CAUSES

As previously mentioned, NSTI is rare in the United States, with an estimated prevalence of about 0.04 cases per 1000. Its incidence increased from 1980 to 2000, most likely due to a larger population of immunocompromised patients.[1,4]

Necrotizing soft tissue infections are generally separated into polymicrobial versus monomicrobial etiologies. Polymicrobial NSTI is the most commonly encountered type, accounting for more than 70% of infections. Monomicrobial infections are usually caused by group A *Streptococcus* but may also be caused by single strains of *Bacteroides* or *Clostridium*.[1,3,7] A third class of NSTIs, resulting from exposure to *Vibrio vulnificus* in warm seawater, has been suggested in some literature. Although rare, this form of fasciitis is associated with considerable morbidity and mortality.[1] The most common microbial causes of NSTI are summarized in Table 1.[3]

Many patients presenting to the emergency department with an NSTI will report a history of soft tissue trauma to the affected area or an operation followed by poor wound care. In adults, it is most prevalent among intravenous drug users and immunocompromised individuals.[3,4] Among the former, "black tar" heroin use has been directly associated with necrotizing fasciitis.[4] Elderly patients and those with diabetes mellitus, HIV, peripheral vascular disease, and obesity should be screened aggressively for NSTI.

Knowing the mechanism of trauma provides little help in diagnosing NSTI, except when the mechanism is intravenous drug use. In some patients, the precipitating insult is as trivial as a minor abrasion, insect bite, or boil.[1,3,8]

In addition to external trauma, the spread of microbes from an untreated perirectal abscess, an infected pilonidal cyst, or a perforated colon, rectum, anus, or urogenital organ can cause NSTI. Commonly affected areas are the perineum and lower extremities. Perineal NSTI, especially in males, is often referred to as *Fournier's gangrene* or *Fournier's disease*.[1] In diabetic patients, the foot is a common site for NSTI.

>>FAST TRACK<<

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DECEPTIVE PRESENTATIONS

Necrotizing infection can spread at the rate of up to 1 inch per hour with few signs of distress visible on skin examination,[1] even as the infection destroys the underlying subcutaneous tissues and fascia. Fulminant NSTI may result in systemic shock and cardiovascular collapse before it shows significant skin manifestations.[1] Tissue necrosis caused by bacterial toxins

TABLE 1. Microbes Recovered in NSTI

Organism	Percentage of patients*
Streptococcus spp	42.5
Staphylococcus aureus	35.6
Klebsiella spp	23.3
Enterococcus spp	19.2
Acinetobacter baumannii	17.8
Escherichia coli	16.4
Pseudomonas aeruginosa	13.7
Enterobacter spp	8.2
Proteus spp	8.2
Bacteroides spp	8.2
fungi (*Candida* spp)	6.8
Peptostreptococcus spp	5.5
Clostridium spp	2.7
others	13.7

*n = 73
Data extracted from Anaya and Dellinger. 2007.[3]

TABLE 2. Clinical Findings in NSTI

Usually observed	Sometimes observed
swelling/edema	hypotension
erythema	crepitus
pain	skin necrosis
tachycardia	induration
diaphoresis	blisters/bullae
fever	ecchymosis
orange peel appearance	subcutaneous emphysema on x-ray

TABLE 3. Differential Diagnosis for Suspected NSTI

Disorder	Characteristics/symptoms
non-necrotizing cellulitis/adipositis	erythema, edema, induration, with normal subcutaneous fascia and fat
myonecrosis	noninfectious inflammation and necrosis of muscle only
lymphedema	induration and edema of extremity without systemic infectious signs
noninfectious fasciitis (eosinophilic fasciitis)	chronic disorder, diagnosed by biopsy, treated with steroids
phlegmasia cerulea dolens	pain, bluish discoloration and edema of entire affected extremity from iliofemoral vein thrombosis
myxedema	systemic manifestations of severe thyroid disease
pyoderma gangrenosum	pustular skin necrosis commonly associated with inflammatory bowel disease

Data extracted from Sarani et al. 2009.[1]

leads to the release of local and systemic inflammatory agents. Endothelial vascular damage, activation of the coagulation cascade, and thrombosis induce additional tissue ischemia and further progression of the infection. The possible end results include septic shock, systemic intravascular coagulation, multiple organ dysfunction, and death.[5,8]

Signs and symptoms differ depending on microbial colonization, location, and a patient's preexisting conditions. Tables 2 and 3 summarize the more and less common clinical findings and the differential diagnosis,[1] respectively. The classic presentation includes pain out of proportion to the physical findings, anxiety, and excessive sweating.[2,3] In only 10% to 40% of cases can the patient immediately associate the pain of an infection with recent trauma.[1] It is useful to note that as a result of localized ischemia, pain may lessen as infection progresses.[1]

On physical exam, most patients with NSTI display erythema and edema, as well as pain and tenderness.[1,2,4] Edema is often accompanied by an appearance and texture resembling those of an orange peel *(peau d'orange)*, caused by obstruction of the superficial lymphatics.[1,2,4] Systemic findings of tachycardia and fever are also common, and hypotension is sometimes a feature. Necrosis and crepitus, the most classic dermal signs, are present in less than 30% of patients. Other possible dermal signs include induration and bullae.[1-3,9] Usually, the patient will place onset at 2 to 7 days prior to emergency department presentation.[10]

In children, the presentation of NSTI is similar to that in adults,[11] and there is clearly a similar benefit associated with early intervention. However, timely diagnosis can be even more challenging in a child, because pediatric NSTI usually develops in a previously healthy patient with no chronic comorbid conditions. Suspicion for NSTI should be high when a neonatal presentation suggests suspected omphalitis or abdominal wall infections associated with umbilical structures, as these conditions are linked to an increased incidence of particularly virulent NSTI.

LIMITED DIAGNOSTIC AIDS

It is important to note that the standard of definitive diagnosis for NSTI is an exploratory operation. Due to the propensity for rapid spread, extensive diagnostic testing should not delay surgery.

Radiographic studies may help provide confirmation that a patient has NSTI, but they have

limited use in primary detection. Imaging studies should be used in conjunction with vigilant examination and laboratory testing to help confirm ambiguous or questionable findings. Plain films can detect or confirm subcutaneous gas and swelling. A finding of subcutaneous emphysema is specific for the diagnosis of NSTI. However, the absence of this sign does not necessarily rule out NSTI.[1,3]

CT radiography is more sensitive and can show inflammatory signs, such as deep fascial gas, edema, soft tissue thickening, and abscesses.[1,4] Common but nonspecific findings in patients with NSTI include thickening of affected fascial planes. The presence of subcutaneous gas along the fascial planes is highly specific for NSTI.[4] One study reported that CT or x-ray detected subcutaneous gas in 73% of individuals.[1] Note that the addition of IV contrast is of little added benefit[1] and should be avoided due to the risk of renal failure.

MRI has a high reported sensitivity for NSTI but is limited by its low specificity. It also has the potential to cause unacceptable delays in treatment and should never be used in critically ill or unstable patients. If used, it will commonly show soft tissue thickening on a T_2-weighted image (which may be enhanced with contrast). More specific findings include fascial hyperintensity, which may be enhanced with contrast in T_1-weighted studies.

Ultrasound can be used to detect superficial fluid collections and abscesses, but this method is neither specific nor sensitive and should not normally be used. However, it may be helpful in guiding needle aspiration of fluid for culture of suspected pathogens.[1,9]

Scoring systems predictive of NSTI have been proposed, although studies validating these scoring systems have been limited.[12,13] In the useful risk-indicator scoring system devised by Wong and colleagues (Table 4), a score greater than or equal to 6 indicates high risk for NSTI with a positive predictive value of 92% and a negative predictive value of 96%.[13] It is important to note that this score is helpful only in the context of a strongly suspected necrotizing infection.[3]

Needle aspiration can retrieve samples of fluid collections for microbiological analysis.[1,7,9] Gram stain and culturing should be performed rapidly and should also be accompanied by an expedited blood culture.[9] When aspirating, the needle should be inserted into the advancing margin of the infection where live pathogens are most plentiful. Frozen section biopsy, if available, is also suggested for rapid identification. Histologic findings include obliterative capillary vasculitis, tissue necrosis, and acute inflammation.[9]

If definitive diagnosis is necessary in a case of suspected necrotizing fasciitis, an excisional deep skin biopsy may be performed. Samples for histology and culture can be taken at this time.

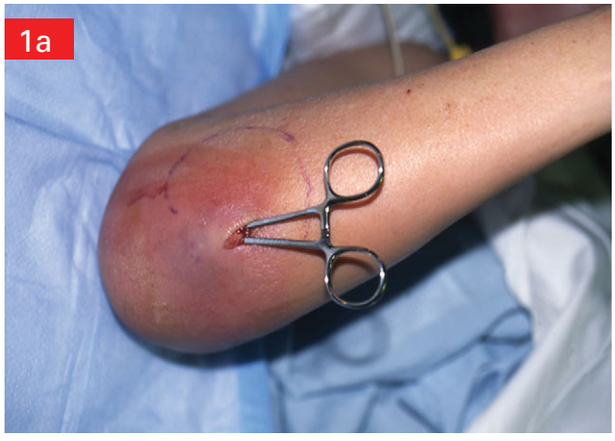
A reported bedside diagnostic maneuver is the "finger test."[3,9] A small incision is made in the skin and subcutaneous tissue down to the level of deep fascia.

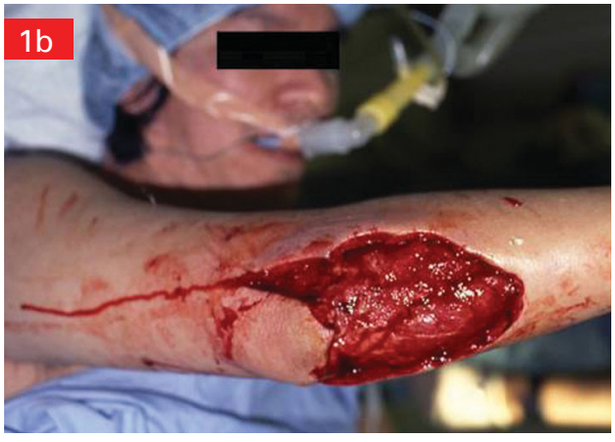
TABLE 4. NSTI Risk Score Based on Laboratory Tests

Measure	Score*
C-reactive protein (mg/L)	
>150	0
≥150	4
white blood cell count (cells/mm^3)	
<15	0
15-25	1
>25	2
hemoglobin (g/dL)	
>13.5	0
11-13.5	1
<11	2
sodium (mmol/L)	
≥135	0
<135	2
creatinine (µg/L)	
≤141	0
>141	2
glucose (mg/dL)	
≤180	0
>180	1

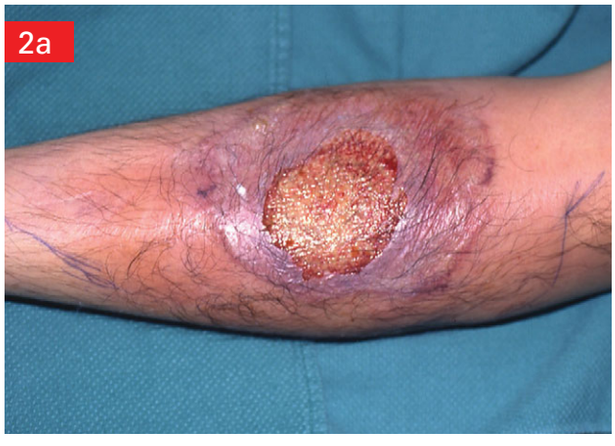
* Score of 6 or higher indicates high risk.
Data extracted from Wong et al. 2004.[13]

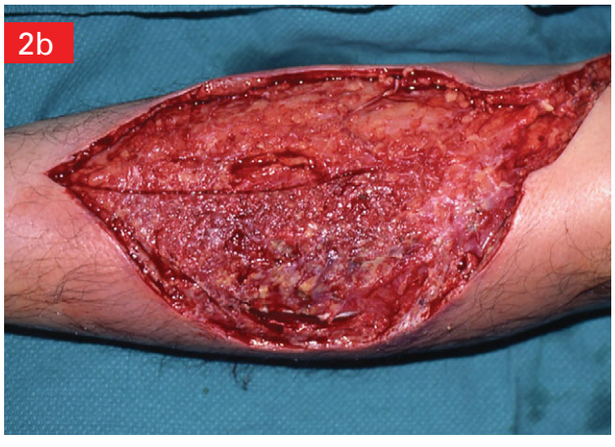
>>FAST TRACK<<
The presence of subcutaneous gas along the fascial planes is highly specific for NSTI.





FIGURES 1a & b. Presentation, testing, and treatment of NSTI.
1a. Preoperative exploration of a suspected NSTI with a blunt hemostat. **1b.** The same patient after surgical debridement.





FIGURES 2a & b. Full debridement revealing extent of NSTI.
2a. Superficial presentation of NSTI of the calf. **2b.** The same patient postoperatively with all necrotic tissue removed.

There may be a lack of bleeding as a result of ischemic necrosis, indicative of NSTI. Sometimes, a foul discharge with a "dishwater" appearance is evident. With a sterile gloved finger or blunt hemostat, the clinician gently probes the incision at the level of the deep fascia (Figure 1a). If the fascia and tissues readily separate with blunt finger dissection or the probe tracks easily along the subcutaneous fascial plane, the test is positive for NSTI and mandates immediate transfer to the operating room, where the incision can then be extended for surgical debridement (Figure 1b).

>>FAST TRACK<<
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MEDICAL AND SURGICAL MANAGEMENT

A patient presenting with NSTI needs fluid resuscitation, appropriate supportive care, and emergent referral for surgical evaluation and debridement of the infected areas.[2,9-11] An infectious disease specialist may also be consulted. Immediate treatment with broad-spectrum intravenous antibiotics to slow the spread of the infection and prevent systemic shock and sepsis is imperative.[3] However, antibi-

otics alone are inadequate for treatment of NSTI, as thrombotic occlusion prevents medication from penetrating the infected tissue.[3] Moreover, persistent hypotension and capillary leakage are common in NSTI, so saline fluid replacement is required in conjunction with antibiotics.[1,3,10] The most common complications associated with NSTI infection are acute renal failure, acute respiratory distress syndrome, and septicemia.[10]

Antibiotic selection and treatment. Since most NSTIs are polymicrobial, it is important that antibiotics have gram-negative, gram-positive, and anaerobic coverage.[1,9] The initial antibiotic treatment recommended by Edlich and colleagues is penicillin G, 24 million units per day intravenously, divided into doses every 4 to 6 hours; clindamycin, 900 mg intravenously every 8 hours; and gentamicin, 1 mg/kg intravenously every 8 hours.[9] Renal function must be closely monitored after antibiotics are administered, especially in elderly, immunocompromised, or diabetic patients. In patients with penicillin allergy, high-dose metronidazole can be substituted. Imipenem and meropenem are recommended in some cases for broad-spectrum polymicrobial coverage.[3] In all cases, once microbiological analysis of the infection has been completed, antibiotic therapy should be specifically tailored to specific organisms and antibiotic sensitivities. If multiple antibiotic-resistant strains of bacteria are involved in the infection, as is becoming common, vancomycin or daptomycin may be given.[1]

>>FAST TRACK<<

Definitive treatment for NSTI can be accomplished only in the operating room.

Surgical debridement. Definitive treatment for NSTI can be accomplished only in the operating room. All necrotic or ischemic tissues and fascia that can be easily elevated should be removed, leaving only viable (actively bleeding) tissue behind (Figures 2a & 2b).[2,8,9,10] Although some tissues may appear normal, at the microscopic level thrombosis and vasculitis may render them unsalvageable. Experience

Clinical Pearls and Pitfalls

PEARLS

- Rapid surgical treatment is essential.
- Stat x-rays and labs may help, but findings on physical exam should primarily alert a physician to NSTI.
- Maintain a high index of suspicion with:
  - diabetic or immunocompromised patients
  - IV drug users
  - crepitus
  - erythema and edema of affected area
  - signs of sepsis
  - pain out of proportion to the physical findings
  - subcutaneous emphysema on plain film x-ray
  - sites most likely to be affected by necrotizing fasciitis, such as the perineum and lower extremities

PITFALLS

- A slight delay in treatment can result in loss of life or limb.
- Laboratory testing should not slow surgical debridement.
- Antibiotic treatment requires wide-spectrum coverage as most NSTIs are multi-microbial.
- Antibiotic therapy needs to account for drug allergies and patients with compromised renal systems.

NSTI = necrotizing soft tissue infection; IV = intravenous

shows that normal-appearing tissues that overlie or are adjacent to an infection site are usually subject to full-thickness loss. As a result, sequential debridement surgeries are frequently necessary until the infection is cleared and only viable tissue remains.[10] Affected extremities sometimes must be amputated if the infection involves major structures, especially vessels or nerves.[3] Consultation with a plastic surgeon for wound closure and reconstruction is recommended.

Other treatments. Contradictory studies have been published regarding the utility of hyperbaric oxygen therapy.[1,3,9,10] Furthermore, few centers have the equipment and facilities to provide it. Where it is available, hyperbaric oxygen therapy in conjunction with surgery has shown potential for improving outcomes in patients with severe infections.[10] Studies have also demonstrated that intravenous immunoglobulin treatment may be a useful adjuvant to standard therapy. However, experimental treatments should not jeopardize or delay standard surgical treatment.[1] □

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