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Clinical Reviews

Necrotizing Soft Tissue Infections (NSTI): Pearls and Pitfalls for the Emergency Clinician

Jessica Pelletier,* Michael Gottlieb,† Brit Long,‡,§ and John C. Perkins Jr.*

*Department of Emergency Medicine, Virginia Tech Carilion School of Medicine, Roanoke, Virginia, †Department of Emergency Medicine, Rush University Medical Center, Chicago, Illinois, ‡San Antonio Uniformed Services Health Education Consortium (SAUSHEC), and §Department of Emergency Medicine, Brooke Army Medical Center, Fort Sam Houston, Texas
Reprint Address: Brit Long, MD, Brooke Army Medical Center, 3841 Roger Brooke Dr., Fort Sam Houston, TX 78234.

□ **Abstract—Background: Skin and soft tissue infections are common emergency department (ED) presentations. These infections cover a wide spectrum of disease, from simple cellulitis to necrotizing fasciitis. Despite the commonality, a subset of skin and soft tissue infections known as necrotizing soft tissue infections (NSTIs) can cause significant morbidity and mortality. Objective: This review evaluates the current evidence regarding the presentation, evaluation, and management of NSTI from the ED perspective. Discussion: NSTIs are commonly missed diagnoses. History and physical examination findings are inconsistent, and the risk factors for this high mortality disease are common amongst ED populations. Laboratory evaluation and the Laboratory Risk in Necrotizing Fasciitis (LRINEC) score is helpful but is insufficient to rule out the disease. Imaging modalities including ultrasound, computed tomography, and magnetic resonance imaging are highly sensitive and specific, but may delay definitive management. The gold standard for diagnosis includes surgical exploration. Surgical intervention and empiric broad-spectrum antibiotic coverage are the foundations of treatment. Adjuvant therapies including hyperbaric oxygen and intravenous immunoglobulin have not yet been proven to be beneficial or to improve outcome. Conclusion: NSTIs are associated with significant morbidity and mortality. Knowledge of the history, examination, evaluation, and management is vital for emergency clinicians. © 2021 Published by Elsevier Inc.**

□ **Keywords—necrotizing soft tissue infections; LRINEC; necrotizing fasciitis; pyomyositis; Fournier gangrene**

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Clinical Scenarios

Case 1

A 55-year-old man with a history of diabetes mellitus presents with subjective fever and left lower leg pain, erythema, edema, and warmth for 3 days. His pain is severe today, resulting in his presentation to the Emergency Department (ED). Examination reveals a heart rate of 110 beats/min, blood pressure 108/63 mm Hg, respiratory rate 21 breaths/min, and temperature 38.1°C. Physical examination of the left lower extremity demonstrates palpable warmth, and diffuse erythema appears consistent with cellulitis. There is no induration, fluctuance, or crepitus; however, the patient's tenderness to palpation seems out of proportion to the severity of skin changes. Lower-extremity radiograph reveals no acute findings. Laboratory analysis reveals a white blood cell count of 16,000/μL, C-reactive protein of 8 mg/dL, hemoglobin of 11.5 g/dL, hyperglycemia with a glucose of 285 mg/dL (but no diabetic ketoacidosis), creatinine of 1.5 mg/dL,

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and sodium of 132 mEq/L. The emergency clinician administers analgesics and antibiotics and plans to admit the patient to the hospital with a diagnosis of sepsis and cellulitis.

Case 2

A 42-year-old woman with a history of alcoholism is brought in by emergency medical services for redness along the perineal region. She endorses pain that has worsened over 1 day. Examination reveals fever and redness in the perineal region with tenderness to palpation. The rest of her vital signs and examination are normal. The emergency clinician is concerned for necrotizing soft tissue infection and consults the surgeon, who asks what the laboratory analysis reveals.

1. Introduction

Skin and soft tissue infections are common ED presentations, with an incidence of 29.7 per 1000 ED encounters and accounting for approximately 10% of hospital admissions (1,2). Although the majority of these are simple abscesses and cellulitis, necrotizing soft tissue infections (NSTIs), including necrotizing fasciitis, pyomyositis, clostridial myonecrosis, and Fournier gangrene, are a dangerous subset that can result in widespread tissue destruction and septic shock (3). The incidence of NSTI varies widely based on source location and the definition of the NSTI used, but literature suggests an incidence of 0.024–0.045 per 1000 per year, which seems to be increasing over time (4). Potential reasons for the increase include rising rates of diabetes, immunocompromised states, obesity, and improved education leading to increased detection (4). Affected individuals are typically 50–60 years of age (5,6). Although rare, these infections have a rate of limb loss of 15.9% (7). The mortality rate ranges from 20–35% up to 70% (or even 100% if source control via surgery is not obtained) (3–5,7–10). Mortality is higher in patients who develop septic shock or toxic shock syndrome (7,11).

Early diagnosis and management can improve outcomes, but diagnosis can be challenging due to subtle early history and physical examination findings and nonspecific laboratory and imaging results. Once discovered, NSTIs require aggressive resuscitation, broad-spectrum antibiotic coverage, and emergent surgical intervention. There are several pitfalls associated with this condition. This narrative review will highlight pearls and pitfalls in the evaluation and management of NSTIs.

2. Methods

The authors searched PubMed for articles using a combination of the keywords "necrotizing soft tissue infection" or "necrotizing fasciitis." The search was conducted from the database's inception to January 2020. PubMed yielded 2886 articles. Authors evaluated case reports and series, retrospective and prospective studies, randomized controlled trials, systematic reviews and meta-analyses, and other narrative reviews. Authors also reviewed guidelines and supporting citations of included articles. The literature search was restricted to studies published in English, with focus on the emergency medicine and critical care literature. Three authors decided which studies to include for the review by consensus. When available, systematic reviews and meta-analyses were preferentially selected. These were followed sequentially by randomized controlled trials, prospective studies, retrospective studies, case reports, and other narrative reviews when alternate data were not available. A total of 46 resources were selected for inclusion in this narrative review from the original 2886 articles identified on literature search. Of these 46 resources, there were seven systematic reviews and meta-analyses, zero randomized controlled trials, four prospective studies, 18 retrospective studies, six case reports and case series, and 11 narrative reviews or expert consensus documents.

3. Discussion

Pearl #1: NSTI is a spectrum of diseases, of which necrotizing fasciitis is only one subtype.
Pitfall: Failure to understand the spectrum of pathology in NSTI.

As with many disease processes, NSTIs are better defined as a spectrum of disease rather than a single diagnosis. The terminology of NSTI is now the accepted nomenclature by surgical and critical care specialties to describe the subset of skin and soft tissues infections that require surgical management (Table 1) (5,12–15).

The pathophysiology underlying NSTI differs somewhat by subtype (Table 2) (16–18). Type I NSTI tends to be atraumatic and occurs in older, sicker patients with multiple comorbidities, especially diabetes mellitus (7,13,19). In type II NSTI, a monomicrobial infection occurs. This is most commonly *Streptococcus*, but can also be due to *Staphylococcus*, typically, methicillin-resistant *Staphylococcus aureus* (3,11,13). Streptococcal type II NSTI exhibits a somewhat unique pathophysiology, as its surface molecule M-protein acts as a superantigen that has the ability to hyperstimulate the immune response (13). These bacteria also release pyrogenic toxins responsible

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Table 1. NSTI Classification by Infectious Milieu (5,13–15)

Type I	Polymicrobial
	Most common
	Risk factors: Immunosuppressed, pre-existing disease, and elderly
Type II	Monomicrobial
	Less common
	Risk factors: Trauma, surgery, intravenous drug use
	Group A *Streptococcus* most common pathogen
	Methicillin-resistant *Staphylococcus aureus* (MRSA) second most common
Type III	Monomicrobial
	Very rare
	Risk factor: Contaminated water exposure
	Vibrio or *Clostridium* spp.
	Hemodynamic collapse prior to cutaneous manifestations
Type IV	Rare
	Risk factors: Immunocompromised or penetrating trauma
	Candida or *Zygomycetes* spp.
	Very rare

Table 2. Risk Factors for Development of NSTI

Risk Factors for NSTI	Adjusted Odds Ratio for NSTI (95% Confidence Interval, $p < 0.001$)		Prevalence (%) in NSTI Population
	Chen et al., 2017 (18)	Liu et al., 2019 (16)	
Diabetes mellitus	2.93 (2.77–3.11)	3.23 (3.07–3.41)	42-57 (16–18)
Alcoholism	2.64 (2.27–3.08)	2.94 (2.55–3.40)	–
Chronic kidney disease	1.98 (1.84–2.14)	2.61 (2.43–2.79)	21–33 (16,17)
Stroke	–	1.54 (1.45–1.64)	26 (16)
Hypertension	–	1.50 (1.42–1.58)	56–62 (16,17)
Cirrhosis	1.47 (1.39–1.57)	1.80 (1.70–1.91)	29 (16)
Tuberculosis	1.44 (1.27–1.64)	1.82 (1.61–2.05)	–
Valvular heart disease	1.17 (1.06–1.30)	1.35 (1.23–1.49)	–
Ischemic heart disease	–	1.35 (1.28–1.43)	33 (16)
Gout	–	1.26 (1.19–1.34)	25 (16)
Immunocompromised status	–	–	58 (18)
Vascular disease	–	–	45 (18)
Hepatitis	–	–	31 (17)
Obesity	–	–	25 (18)

NSTI = necrotizing soft tissue infection.

for the strong association of type II NSTI with toxic shock syndrome (13).

Although type III NSTI technically constitutes a monomicrobial infection, it is categorized as a separate subtype from type II because these infections are rarer. Organisms producing NSTI of this category include *Vibrio, Clostridium, Bacteroides*, or *Escherichia* species, which require special circumstances for infection not seen in type I or II infections (11). *Vibrio* infections usually require salt water or uncooked oyster exposure, and there is also an association with chronic liver disease (3,5,7,11,15). *Clostridium* infections are associated with penetrating trauma, crush injuries, or intravenous drug use (3,5,11,15). Spontaneous atraumatic NSTI with *Clostrid-*

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ium species, usually with *Clostridium septicum*, is thought to arise via bacteremia from gastrointestinal sources (3,11). *Bacteroides* or *Escherichia* (Gram-negative) infections are associated with significant pre-existing organ dysfunction (5,11,15). *Aeromonas* infections are sometimes classified as type III or type IV infections. These are thought to arise from traumatic injury in freshwater (3,7,14,15). More classically, type IV infections involve fungal organisms such as *Candida* or *Zygomycetes*, which often involve penetrating injury (14).

Pearl #2: Chronic illness or recent surgery should raise clinician suspicion for NSTI.

Pitfall: Discounting NSTI in the patient without a classic history.

It is important for physicians to understand that NSTI can occur with or without an inciting injury. Inoculation via a skin wound or penetrating trauma is an obvious potential source for bacterial entry into tissues. In atraumatic cases, it is hypothesized that a local inflammatory reaction in response to injury, even as simple as muscle strain, induces increased vascular permeability within tissues (11). Transient bacteremia could lead to seeding of those tissues with bacteria. Sources of transient bacteremia include the genitourinary or gastrointestinal tract (11,20).

Among those diagnosed with NSTI, 80% have a clear point of inoculation such as a bite, surgical incision, injection site, or perianal source (11). Type II infections have a clear inoculation only half of the time and are often associated with nonpenetrating trauma or muscle strains (20). Sources of inoculation for type II infections can include intravenous drug use and recent surgery (14). Recent surgery is a risk factor that should make the clinician suspicious for NSTI rather than simple cellulitis (11).

It is important to note that one-fourth of patients diagnosed with NSTI have no risk factors for the disease (Table 2) (6). Common comorbidities in patients with NSTI include obesity, hypertension, tobacco use, malignancy, immunocompromised status, and heart disease (4,11,16,17). Chronically ill and immunocompromised patients are also at risk for severe disease regardless of the disease process (Tables 1 and 2). Nonsteroidal anti-inflammatory drug use is controversial, demonstrating an association but no evidence of causation (7,11).

Pearl #3: There is wide variability in the clinical presentation of NSTI.

Pitfalls: Performing an incomplete skin examination and prematurely excluding the diagnosis in the absence of major skin findings.

NSTI is a clinical diagnosis, but early in the course of the disease the diagnosis can be challenging. Nonspecific symptoms such as diarrhea, fatigue, loss of appetite, or malaise may precede the onset of skin findings in NSTI (6). Pain out of proportion to examination is a classic finding in NSTI, though this may be absent in patients with encephalopathy or neuropathy (11,14). Pain is reported as the initial complaint in only 79% of cases (7).

There may not be obvious skin findings initially, especially in cases of deep tissue involvement where the skin is spared. In fact, 41–96% of NSTI cases are initially misdiagnosed as simple cellulitis or abscess, as early symptoms are not specific. Early skin findings may include mild erythema or edema (14). Literature suggests swelling is the most common finding, followed by pain and erythema (Table 3) (7,8,18,21,22). Warmth, bullae, skin necrosis, and crepitus are less common findings, in decreasing order of prevalence (6,7). The most common sites of involvement cited throughout the literature are the lower extremities followed by the perineum (6,18,23). Cervicofacial NSTI should be considered in the differential diagnosis of patients with sore throat and neck pain (19). Although fever has a specificity of 77%, it is found in fewer than half of NSTI cases, with a sensitivity of 40–46% (7,24). The finding of hemorrhagic bullae, often touted to be classic for NSTI, is highly specific (96%) but is seen in only 25% of cases (8).

Fournier gangrene may present somewhat differently than other subtypes of NSTI. Initial symptoms include perineal pruritus and pain. Anxiety, encephalopathy, and tachypnea may precede fulminant shock (5). There are often no initial skin changes until the perineum suddenly develops bullae and crepitus, which are typically late findings (5).

Many patients with NSTI will not initially present with obvious signs of shock, and hypotension is found in only 21% of cases (8). Toxic shock syndrome (with hypotension, macular rash, and palm and sole desquamation) is associated with up to half of group A *Streptococcus*-associated NSTI cases (15). Multisystem organ failure is a common complication of this disease process (14).

Subacute NSTI may also occur. There have been reported cases of slowly progressing cases of NSTI, taking weeks to fully manifest (5). There is no evidence that the rapidity of spread of NSTI influences mortality rate; therefore, this disease process should be treated the same regardless of acute vs subacute presentation (5).

Pearl #4: Laboratory testing cannot be used to rule out NSTI due to its low sensitivity.

Pitfall: Waiting for results of laboratory testing when NSTI is suspected.

There is no single laboratory test with adequate sensitivity and specificity to differentiate NSTI from other infectious processes or exclude the diagnosis. The ED evaluation of NSTI should begin with a detailed history and physical examination. Laboratory testing is important but should not delay surgical consultation when there is a strong suspicion for NSTI. However, adjunctive laboratory testing can be valuable in determining severity of illness (i.e., to identify end-organ damage) and shap-

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Table 3. Physical Examination Findings in NSTI

Finding	Sensitivity	Specificity
Swelling	92% (23) 83% (24) 81% (7) 62% in patients with early intervention, 46% in patients with late intervention (22)	–
Pain/tenderness	92% (23) 83% in patients with early intervention, 78% in patients with late intervention (22) 79% (7) 76% (24)	–
Erythema	94% in patients with early intervention, 85% in patients with late intervention (22) 75% (23) 71% (7)	–
Fever	67% (23) 55% in patients with early intervention, 41% in patients with late intervention (22) 46% (8) 40% (7)	77% (8)
Warmth	44% (7)	–
Bullae	26% (7) 25% (8)	96% (8)
Skin necrosis	65% in patients with early intervention, 58% in patients with late intervention (22) 24% (7)	–
Hypotension	21% (7) 21% (8)	98% (8)
Crepitus	20% (7)	–
Induration	21% in patients with early intervention, 18% in patients with late intervention (22)	–

NSTI = necrotizing soft tissue infection.

ing the pretest probability of NSTI. Laboratory testing for possible NSTI should include complete blood count, complete metabolic panel, C-reactive protein, and blood cultures.

Several scoring systems incorporating laboratory analysis have been studied for use in NSTI. The components of the Laboratory Risk in Necrotizing Fasciitis (LRINEC) score are all markers of systemic illness (Table 4) (18). Although higher LRINEC scores tend to be found in sicker patients and those with more advanced disease, a recent systematic review and meta-analysis found that the LRINEC score was only 68.2% sensitive and 84.8% specific with a score of 6, and 40.8% sensitive and 94.9% specific with a score of 8 (8). There have been case reports of patients with NSTI having LRINEC scores of 0 (25).

The LRINEC score can assist the provider in effectively communicating with surgical consultants to convey a concern for NSTI if it is significantly elevated. Much like the adjunctive laboratory values, the LRINEC score adds to the overall clinical picture and assists in formulating pretest probability of disease. This may be of particular benefit to clinicians who may need to transfer the patient for surgical evaluation, but a low score should not be used to exclude the diagnosis.

Pearl #5: Imaging has variable sensitivity for NSTI and can delay definitive operative management.

Pitfall: Relying on imaging to secure a diagnosis.

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Table 4. Laboratory Risk in Necrotizing Fasciitis (LRINEC) Score (18)

Test	Value	Score
C-reactive protein	$\geq$ 150 mg/L	+4
White blood cell count	15–25 $\times$ 10^9/L	+1
	$>$ 25 $\times$ 10^9/L	+2
Hemoglobin	$<$ 11 g/dL	+2
Sodium	$<$ 135 mmol/L	+2
Creatinine	$>$ 141 μmol/L	+2
Glucose	$>$ 180 mg/dL	+1

Interpretation: Score $\geq$ 6 further evaluation needed.
Score $\geq$ 8 is high risk.
NSTI = necrotizing soft tissue infection.

It is important to remember that NSTI is a clinical diagnosis and that imaging is not required for the diagnosis. Plain radiographs have poor sensitivity for soft tissue air, and computed tomography (CT) or magnetic resonance imaging (MRI) can be time consuming and may not be universally available. If the emergency physician has a high clinical suspicion of NSTI, immediate consultation to the surgical specialist is recommended prior to advanced imaging such as CT or MRI. If imaging is pursued, several modalities are available in the evaluation of NSTI, including plain radiographs, ultrasound, CT, and MRI (Table 5) (8,26–30).

Plain radiographs are reasonable to obtain as they can be performed at the bedside and occasionally may help secure a diagnosis when soft tissue gas is visualized. As the sensitivity of this modality is only 49% (and has been cited as low as 25%), it should not be used to exclude NSTI, but it may aid in accelerating disposition of the patient to the surgical suite (6–8,14). Additionally, it is important to note that many NSTIs are not caused by gas-forming organisms (31).

CT can assist in the evaluation. A systematic review and meta-analysis from 2019 evaluating 23 studies identified the sensitivity and specificity of CT to be 88.5% and 93.3%, respectively (8). However, other studies have demonstrated sensitivity as low as 80% for CT diagnosis of NSTI (27). CT can be nondiagnostic in NSTI due to identification of nonspecific inflammatory changes such as swelling, especially early in the course of the disease. Soft tissue gas, with a specificity as high as 98%, is not typically present until late in the course of the disease (6,14,28). Extra care should be taken when using CT imaging in cases of cervicofacial NSTI, as imaging findings can mimic comparatively benign pathology (19).

MRI has a sensitivity of 90–100% for NSTI when looking specifically at fascial thickening with T2 weighting (13). Specificity with T2-weighted images is much lower, cited as 50–85% (29,30). T1 weighting is reportedly more specific for NSTI (13). However, the limited accessibility of MRI in many EDs, as well as the significant amount of time required to obtain and interpret these images, limits its utility in the setting of a disease that can progress along a rapidly deteriorating course. In most contexts, obtaining MRI imaging would delay definitive management with surgical debridement, making it impractical as a diagnostic tool in the ED.

Pearl #6: POCUS may support the diagnosis of NSTI but is insufficient to exclude the condition.

Pitfall: Not utilizing POCUS in NSTI evaluation.

Point-of-care ultrasound (POCUS) can assist in the diagnosis of NSTI. Case reports describe the rapidity with which POCUS has allowed clinicians to make the diagnosis of NSTI, in some cases where CT and MRI imaging was nondiagnostic (12,32–34). There is a growing body of literature aimed at adding a bedside imaging component to the rapid diagnosis of NSTI. The POCUS findings can be easily recalled with the "STAFF" mnemonic: subcutaneous thickening, air, and fascial fluid (Figures 1A, B, C, D) (5). Free air is often a late finding and may be absent when the NSTI is not due to a gas-forming organism. Irregular and thickened fascial layers, when compared with the contralateral side, have been shown to be useful. Fluid accumulation has been demonstrated to be the most sensitive POCUS finding for NSTI, with a sensitivity of 88.2% and a specificity of 93.3% when using a 4-mm cutoff (35). A recent retrospective study with prospective enrollment was not able to reproduce these numbers, finding a sensitivity of 42.3% and a specificity of 93.6% with a 4-mm cutoff point. In this study, evaluating for fascial fluid with a cutoff of 2 mm had a much higher sensitivity of 75%, with specificity of 70.2% (36). It has been demonstrated that as the cutoff for fluid accumulation on ultrasound increases, sensitivity for NSTI decreases while specificity increases.

Pearl #7: Ensure that the patient is hemodynamically optimized and has received antibiotics prior to transfer to the surgical suite.

Pitfall: Withholding antibiotic therapy if the diagnosis of NSTI is not entirely clear.

While awaiting surgical management of the patient with an NSTI, patients should receive aggressive fluid resuscitation, early broad-spectrum antibiotics, and initiation of vasopressors if fluid resuscitation does not maintain adequate perfusion (3,19). Although appropriate medical resuscitation of the unstable patient is critical from the emergency medicine standpoint, one must be cautious not to create excessive delays to surgical exploration while resuscitating the NSTI patient, as surgical management is the definitive therapy (3,36). Delays to the surgical suite may lead to worsened spread of the underlying infection and subsequent increase in risk for amputa-

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Table 5. Imaging for NSTI

Imaging Modality	Sensitivity(with 95% CI if Available)	Specificity(with 95% CI if Available)
Radiograph	48.9% (8)	94.0% (8)
Point-of-care ultrasonography	88% (26)	93% (26)
Computed tomography	80% (27)	93.3% (95% CI 80.8%–97.9%) (8)
	88.5% (95% CI 55.5–97.9%) (8)	
	100% (95% CI 72–100%) (28)	98% (95% CI 94–99%) (28)
Magnetic resonance imaging	90–100% (29,30)	50–85% (29,30)

NSTI = necrotizing soft tissue infection; CI = confidence interval.

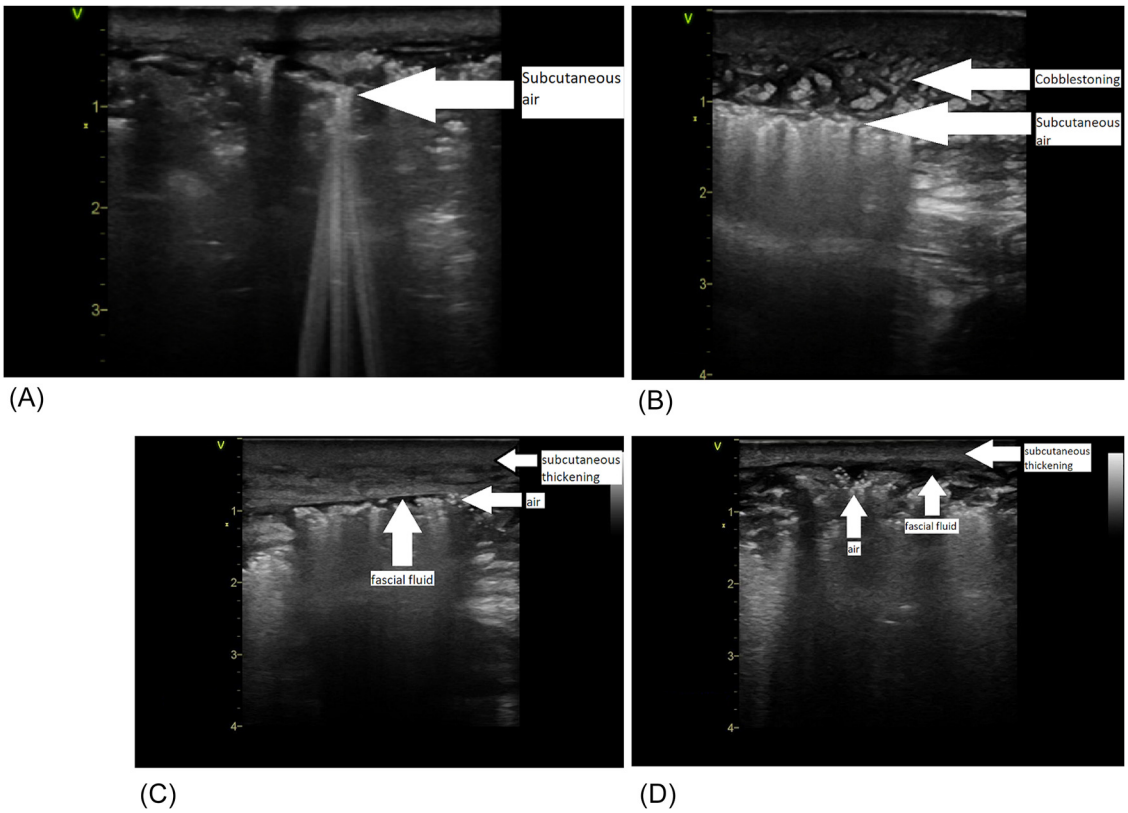

Figure 1. (A) Subcutaneous air noted on bedside ultrasound in a patient with necrotizing soft tissue infection (NSTI). (B) Subcutaneous air noted on bedside ultrasound in a patient with NSTI. Note that there is overlying cobblestoning, a nonspecific finding seen in soft tissue edema. Were it not for the subcutaneous air, this could easily have been misdiagnosed as cellulitis based on the image alone. (C) Subcutaneous thickening, air, and free fluid in the fascial plane. (D) Subcutaneous thickening, air, and free fluid in the fascial plane. Courtesy of Dr. Jonathan Nogueira, DO.

tion, hospital length of stay, and mortality (3,24,36). There is, thus, a fine balance that must be reached between medical resuscitation and definitive surgical treatment. Close communication is necessary between the emergency clinician and the surgical team concerning appropriate timing for operative exploration (36).

Broad-spectrum antibiotic coverage should be initiated empirically if NSTI is suspected, using appropriate loading doses and the local antibiogram (3). Coverage for methicillin-resistant *Staphylococcus aureus* (MRSA), Gram-positive, Gram-negative, and anaerobic bacteria is necessary. This will vary based on local resistance patterns, but may include vancomycin or linezolid for MRSA coverage with piperacillin-tazobactam or cefepime and metronidazole. In addition to this broad-spectrum coverage, clindamycin should be added for its anti-toxin effect, which has been associated with improved survival in group A *Streptococcus* type II infections. Risk

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Table 6. Empiric Antibiotic Regimen for NSTI

Carbapenem (ertapenem, imipenem, or meropenem 1 g i.v. every 8 h in adults) (37)
OR
Beta lactam-beta lactamase inhibitor (such as piperacillin-tazobactam 4.5 g every 6 h in adults) for activity against Gram-negative bacilli and anaerobes (37)
OR
Cefotaxime + metronidazole (1–2 g every 6–8 h + 0.5 g every 8 h) (37)
PLUS
Clindamycin (600–900 mg i.v. every 8 h in adults) for its activity against Gram-positive organisms and anaerobes, as well as its antitoxin effects (37)
PLUS
Vancomycin (20–25 mg/kg bolus, 25–35 mg/kg/24 h continuous infusion) (6,9,37), **daptomycin (9)**, or **linezolid** (600 mg every 12 h) for activity against Gram-positive organisms and MRSA (6,9)
In patients with severe hypersensitivity to carbapenems or beta lactam-beta lactamase inhibitors, consider substituting:
Aminoglycoside
OR
Fluoroquinolone (such as ciprofloxacin 500 mg every 12 h)
PLUS
Metronidazole (0.5 g every 8 h) (3)
In patients with salt or freshwater exposure and significant risk for *Vibrio vulnificus* or *Aeromonas hydrophila* involvement, consider adding:
Doxycycline (100 mg every 12 h) (6)
In patients with significant risk for fungal involvement, consider adding:
Amphotericin B or **fluoroconazoles** (5 mg/kg/day for amphotericin B lipid complex) (38)

NSTI = necrotizing soft tissue infection.

for type I infections (polymicrobial) and multidrug-resistant organisms is higher in diabetics (6). Table 6 lists specific considerations with regard to the suspected organism causing NSTI and necessary antibiotic coverage (3,6,9,37,38). Thus, careful consideration must be made to the susceptibility of the individual patient for particular organisms and risks of certain bacteria. Early broad-spectrum coverage should be administered and should not be delayed by cultures, consultation, or imaging.

Adjunctive therapies include hyperbaric oxygen and intravenous immunoglobulin (IVIG), but they remain controversial. Hyperbaric oxygen (HBO) therapy is proposed to assist by increasing the oxygen concentration in the relatively hypoxic fascial tissues. These tissues have poor oxygenation at baseline, but this is enhanced by the microvascular thrombosis and subsequent compromised blood flow that occurs in NSTI. It is hypothesized that by maximizing tissue oxygenation, HBO could both inhibit anaerobic bacterial growth and increase cytokine activity. Studies have not shown convincing improvement in patient-centered outcomes, and the limited availability of HBO prevents routine use (15,39). IVIG is proposed to bind unbound superantigens in superantigen-mediated toxic shock syndrome associated with some *Staphylococcus* and *Streptococcus* species. Multiple studies have shown no difference in patient-centered outcomes, including death and function, for this expensive intervention (15,40). Additionally, IVIG is not a benign therapy, with risks including allergic reaction, aseptic meningitis, hemolytic anemia, kidney injury, transmission of pathogens, and thrombosis (20). There are not currently evidence-based guidelines to endorse the use of either of the adjuvant therapies, and they should be considered on a case-by-case basis when and if available.

Pearl #8: A definitive diagnosis can be made at bedside with a scalpel in some patients.

Pitfall: Failing to explore all avenues to help the patient with an NSTI achieve early surgical consultation and source control.

Emergency physicians, especially those who work in a setting where transfer is mandatory for a patient with an NSTI, should consider utilizing a scalpel to secure a bedside diagnosis of NSTI. The pathophysiology of NSTI involves tissue death at the microvascular level with rapid spread along fascial planes (11). Consequently, clinicians can perform bedside incision after local anesthesia to as-

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Table 7. Summary of Pearls and Pitfalls

Pearls	Pitfalls
NSTI is a spectrum of diseases, of which necrotizing fasciitis is only one subtype.	Failure to understand the spectrum of pathology in NSTI.
Chronic illness or recent surgery should raise clinician suspicion for NSTI.	Discounting NSTI in the patient without a classic history.
There is wide variability in the clinical presentation of NSTI.	Performing an incomplete skin examination and prematurely excluding the diagnosis in the absence of major skin findings.
Laboratory testing cannot be used to rule out NSTI due to its low sensitivity.	Waiting for results of laboratory testing when NSTI is suspected.
Imaging has variable sensitivity for NSTI and can delay definitive operative management.	Relying on imaging to secure a diagnosis.
POCUS may support the diagnosis of NSTI but is insufficient to exclude the condition.	Not utilizing POCUS in NSTI evaluation.
Ensure the patient is hemodynamically optimized and has received antibiotics prior to transfer to the surgical suite.	Withholding antibiotic therapy if the diagnosis of NSTI is not entirely clear.
A definitive diagnosis can be made at bedside with a scalpel in some patients.	Failing to explore all avenues to help the patient with an NSTI achieve early surgical consultation and source control.
Source control in NSTI is the most significant factor in reducing mortality.	Failure to appreciate the importance of early and aggressive source control.

NSTI = necrotizing soft tissue infection.

sess for 'dishwater' fluid or the ability to use one's finger to 'probe' the necrotic tissue without impedance usually encountered with intact fascia (11).

This can be performed by making a small incision (i.e., enough to insert a gloved finger) at the location of suspected NSTI (i.e., area is anesthetic, has dusky coloration, hemorrhagic bullae, or other signs of NSTI) (11,41). If 'dishwater'-appearing fluid exits this wound, the diagnosis is confirmed (11,41). If no fluid exits the wound, the physician should 'probe' the wound, and if a finger can be used to explore the wound freely in all directions with minimal resistance, a diagnosis is secured (11,41). Although this may not be necessary at a hospital where General Surgery is readily available for rapid consultation, this technique can confirm the diagnosis and expedite transfer for definitive surgical management in hospitals where surgical consultation is not possible. Considering the significant impact on mortality with delayed surgical intervention, a small incision at bedside offers limited downside.

Pearl #9: Source control in NSTI is the most significant factor in reducing mortality.

Pitfall: Failure to appreciate the importance of early and aggressive source control.

In all subtypes of NSTI, inflammation of local tissues leads to microvascular thrombosis (11,13,15). Subsequent decreased blood flow to the area of infection prevents host immune cells from responding to the front lines of infection and also leads to decreased tissue oxygenation with subsequent necrosis, further feeding bacterial propagation (11,13,15). Local ischemia causes damage to nervous tissue, thus producing pain out of proportion, which may eventually progress to anesthesia (5). It is important to realize that once this microvascular thrombotic process has progressed and local tissue perfusion is poor, antibiotics cannot effectively penetrate the infected tissues (15).

Source control in sepsis is an underappreciated yet crucial task for any physician caring for a septic patient. Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection (42). By removing the infectious source, the dysregulated host response should be dampened, which results in improved morbidity and mortality (43). For patients with an NSTI, this requires surgical intervention to excise the necrotic tissue. Source control (when compared with a cohort without source control) has been shown to improve mortality even when the cohort was older, had a higher prevalence of septic shock, and increased organ dysfunc-

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tion (43). When looking specifically at source control in NSTI, a 2017 retrospective review examining 60 patients with NSTI revealed a significant mortality reduction disparity in those patients who had surgical intervention (14.0%), when compared with patients who did not undergo surgical intervention (60%) (20). Survival in NSTI is optimal when patients are taken for surgical debridement within 6 h of diagnosis, but a survival benefit is still seen as long as surgery is performed within 24 h (36,44–46).

Table 7 summarizes pearls and pitfalls concerning the ED evaluation and management of NSTI.

4. Conclusion

NSTIs are common ED presentations, which can present in subtle ways but pose significant threats to life and limb. The emergency clinician must be poised to identify NSTIs early to ensure aggressive treatment with appropriate antibiotic therapy, medical resuscitation, and rapid transfer to the surgical suite for definitive surgical management via source control. The LRINEC score, POCUS, CT, and MRI can be useful adjuncts to aid in making this diagnosis, but ultimately, clinician judgment should supersede scoring tools and imaging techniques, as NSTI is a clinical diagnosis. If there is controversy, bedside incision with a scalpel and probing with a finger may be used to reveal fascial breakdown and "dishwater" fluid to secure the diagnosis. Ultimately, the patient's morbidity and mortality will be determined by the time to source control.

Clinical Bottom Line

Case 1

The patient continues to have severe pain, with increased heart rate and decreased blood pressure on reevaluation. The emergency clinician notes increased size of the erythema since the patient's arrival and consults the surgical specialist, who recommends broad-spectrum antibiotics including clindamycin. The surgical specialist evaluates the patient at the bedside, is concerned for NSTI, and takes the patient for surgical debridement.

In this case the LRINEC score was only a 3, which is considered low risk for NSTI (Table 4) (18). However, clinical judgment and re-evaluation of the patient dictated immediate surgical evaluation due to high concern for this life-threatening diagnosis.

Case 2

The emergency clinician repeats his concern for NSTI to the surgeon but states he will administer broad-spectrum antibiotics and perform imaging and laboratory testing. POCUS reveals subcutaneous thickening, air, and fascial fluid $>$ 4 mm. Laboratory evaluation reveals a C-reactive protein of 17 mg/dL, white blood cell count of 32,000/μL, hemoglobin of 9.5 g/dL, sodium of 129 mEq/L, creatinine of 2.4 mg/dL, and glucose of 200 mg/dL. He calls the surgeon, describes the POCUS findings, relays that the patient has a LRINEC score of 11, and repeats his concern that she has a high likelihood of NSTI. The surgeon agrees to take the patient for surgical exploration for definitive diagnosis and treatment.

Although NSTI is a clinical diagnosis, imaging modalities such as POCUS, as well as the LRINEC score, can serve as adjuncts to convince surgical consultants of the need for operative exploration.

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ARTICLE SUMMARY

1. Why is this topic important?

Necrotizing soft tissue infection (NSTI) can result in significant morbidity and mortality, especially when the diagnosis is delayed or the condition mismanaged.

2. What does this review attempt to show?

This review evaluates the current evidence regarding the emergency department (ED) diagnosis and management of NSTI.This review evaluates the current evidence regarding the emergency department (ED) diagnosis and management of NSTI.

3. What are the key findings?

NSTI is a spectrum of disease associated with a variety of risk factors. History, examination, and laboratory findings are inconsistent and should not be used to exclude a diagnosis of NSTI. Imaging can assist but should not delay definitive therapy. In the ED, treatment includes surgical consultation, resuscitation, and antibiotic administration.

4. How is patient care impacted?

Understanding the pearls and pitfalls associated with NSTI diagnosis and treatment can assist emergency clinicians in the care of these patients.

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