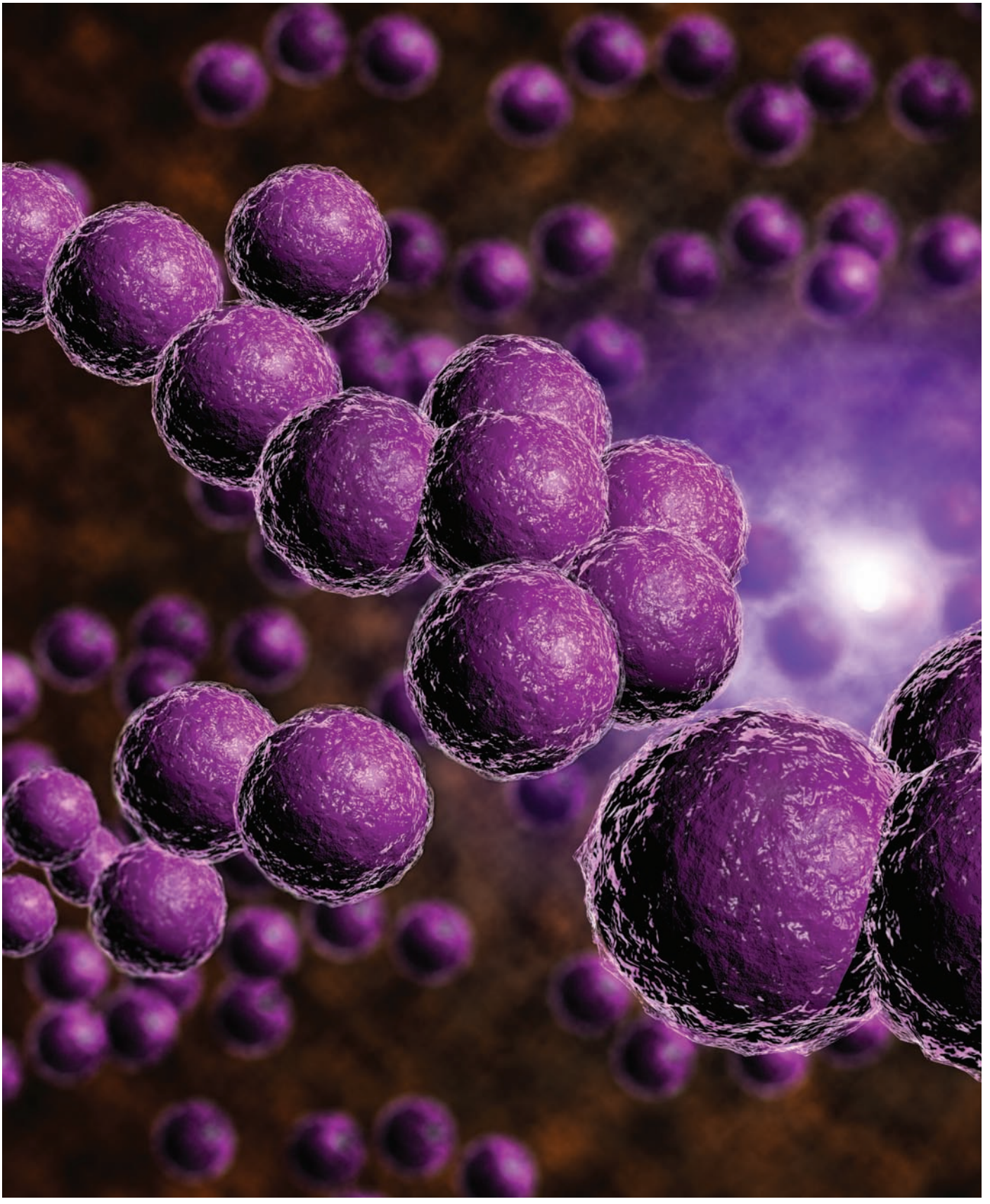
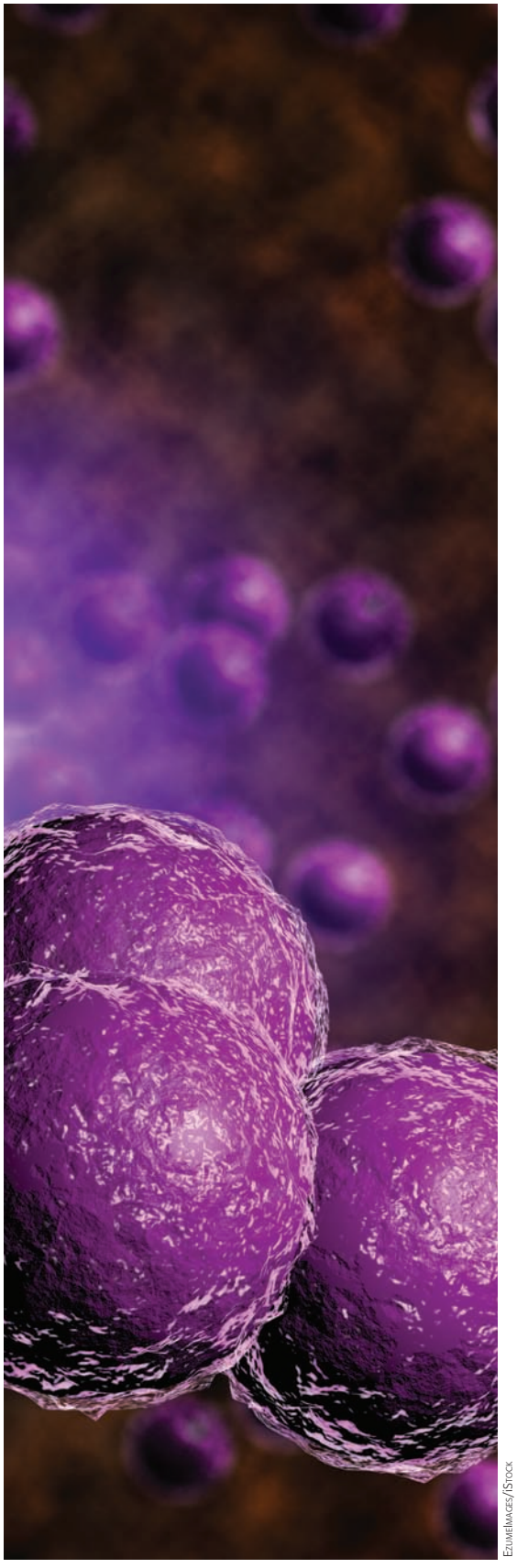




EZUMEIMAGES/ISTOCK

CE 1.0 ANCC CONTACT HOUR

Rx 1.0 PHARMACOLOGY CREDIT

Necrotizing fasciitis:
A comprehensive review

BY LEON L. CHEN, DNP, AGACNP-BC, FCCP, FAANP, FNYAM;
BRIAN FASOLKA, PhD, RN, CEN; AND CAITLIN TREACY, MS, AGACNP-BC

Abstract: Necrotizing soft-tissue infections (NSTIs) are rare but rapidly progressive, life-threatening bacterial infections with high morbidity and mortality. NSTIs include necrotizing forms of fasciitis, myositis, and cellulitis. This article focuses on necrotizing fasciitis (NF) and discusses NF classifications, clinical features, diagnostic approaches, evidence-based treatments, and nursing interventions.

Keywords: bacterial infection, necrotizing fasciitis, necrotizing soft-tissue infections, NF, NSTIs, sepsis, toxic shock syndrome

NECROTIZING soft-tissue infections (NSTIs) are rare but rapidly progressive, life-threatening bacterial infections that can destroy the epidermis, dermis, subcutaneous tissue, fascia, and muscle.[1-4] Patients with certain comorbidities such as diabetes are at a higher risk for NSTIs. Described as far back as Hippocrates, NSTIs continue to be associated with significant mortality.[3,5] Prompt recognition of signs and symptoms, targeted diagnostic testing, and timely treatment are crucial to avoid poor patient outcomes, including sepsis, amputation, and death.[2]

Although NSTIs include necrotizing forms of fasciitis, myositis, and cellulitis, this article will focus on the most common type, necrotizing fasciitis (NF).

Epidemiology

NSTIs are relatively rare. The incidence of NF is estimated to be 0.3 to 15 cases per 100,000 population.[1] However, due to difficulty in diagnosis and underreporting, this is likely an underestimation.[6,7]

Certain factors place patients at a higher risk for NF and other NSTIs, including any skin or mucosal breach and various surgical procedures. Patients with comorbidities such as immunosuppression, malignancy, vascular disease, diabetes, alcoholism, and obesity are at an increased risk of NSTIs with progression to severe sepsis and septic shock.[6]

Despite increased awareness and treatment advances for NF and other NSTIs, mortality remains high at 25% to 35%.[2] The reasons relate to both the rapid progression of disease and the subtlety of early signs and symptoms, which may delay diagnosis and intervention.[6]

NF classifications

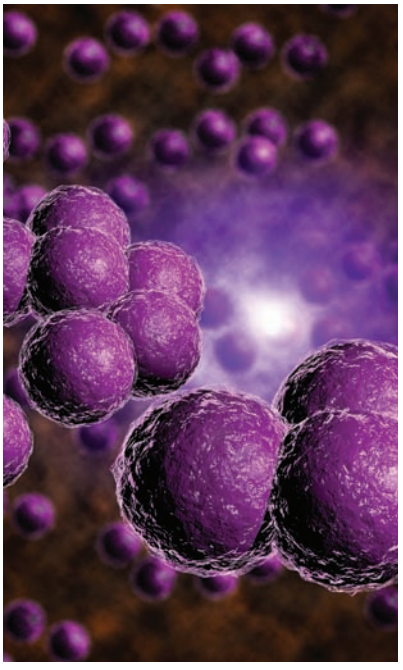
NF is an infection of the deep soft tissues causing progressive destruction of the muscle fascia and overlying subcutaneous fat. Two major classifications of NF are generally

accepted, and several new classifications have been proposed to create further subdivisions.[1] The following classifications are based on the underlying bacteria that initiated the cascade of injury.[1,8]

- Polymicrobial (type I) NF. Type I NF stems from polymicrobial infection identified via microbiological culture. This type of infection is caused by both aerobic and anaerobic bacteria. The complex microbiological profile of offending organisms leads to gaseous infiltration of subcutaneous tissue similar to gas gangrene.[3,9] Type I NF accounts for most reported cases of NF and is more prevalent in older adults with chronic diseases.
- Monomicrobial (type II) NF is most commonly associated with Gram-positive organisms such as group A *Streptococcus* (GAS) and methicillin-resistant *Staphylococcus aureus* (MRSA). Endotoxins released by type II NF organisms are responsible for some clinical presentations, including toxic shock syndrome.[3,6,9] Type II NF is not associated with a specific age group. Some patients do not have comorbidities or an obvious portal of entry that predisposes them to severe infection.[3,6]

Several other species of organisms have been implicated in NF, including *Pseudomonas*, *Klebsiella*, *Clostridium*, *Aeromonas*, and *Vibrio vulnificus*. These organisms, while rare, are more virulent and produce more severe clinical manifestations. The identification of these microbes has led some experts to propose a third type classification of NF, but no consensus has been reached.[3,10]

The two forms of NF are also differentiated by the site of the infection. Necrotizing microbial infiltration into the submandibular space



NF is an infection of the deep soft tissues causing progressive destruction of the muscle fascia and overlying subcutaneous fat.

fascia leading to tissue damage is called *Ludwig angina*. An oropharyngeal infection leading to secondary septic thrombophlebitis of the internal jugular vein is termed *Lemierre syndrome*. *Fournier gangrene*, described as bacterial infiltration into the gastrointestinal or urethral mucosa, can progress rapidly into the perineal region.[6,11] These alternate classifications and nomenclatures may not have significant impact on immediate clinical management of NF but are important nevertheless for epidemiologic purposes.

Pathophysiology

The pathophysiology characteristic of both types of NF is widespread. Diffuse damage to superficial tissue extends to the deep muscular plane and fascia, with certain unique features depending on the offending organism.[11] Due to its complex polymicrobiological profile, Type I NF is likely to be especially severe in older adults with existing comorbidities. The presence of both aerobic and anaerobic organisms causes extensive tissue necrosis and hemodynamic compromise. Some organisms of the *Clostridium* species produce alpha toxins that further degrade tissue. It is not unusual for the organisms of Type I NF to have synergistic effects, producing more profound local and systemic damage.[6,7,9,11]

Type II NF associated with GAS causes tissue damage by releasing exotoxins, which often initiate a complex cascade of immune-related responses including cytotoxic T-cells, cytokine release, and toxic shock syndrome. Microvascular damage or thrombosis may lead to tissue ischemia and subsequent necrosis.[12]

Signs and symptoms

Many patients with NF present to the ED exhibiting signs and symptoms of an infection. Superficial findings may not be distinct beyond erythema and edema.[1] Clinicians must quickly recognize the distinction between cellulitis manageable with antimicrobial therapy and NF requiring surgical intervention. Delays in appropriate management of NF can have devastating consequences, including limb loss, organ damage, and a significantly increased risk of death.[3,13]

Like NF, cellulitis is characterized by skin erythema, edema, and warmth. Fever is sometimes present but patients with cellulitis are typically hemodynamically stable. Along with superficial erythema, warmth,

ecchymosis, fever, and soft tissue edema, patients with NF may experience extreme tenderness or pain and eventually progress to hemodynamic instability and tissue necrosis.[3] Elevated concentrations of creatine kinase or aspartate aminotransferase also suggest deep tissue infection.[1]

Unfortunately, the critical diagnostic distinction between cellulitis and NF is typically difficult to discern, as the initial clinical presentation of NF is often vague.[3] Presentation can be further distorted by factors such as the use of nonsteroidal anti-inflammatory drugs, which can mask signs such as fever and classic symptoms of NF such as crescendo-like pain. Severe pain that is disproportionate to the degree of apparent injury is considered a classic symptom of NF, but patients with diabetic neuropathy may not experience the same level of pain as those without preexisting neuropathy.[2,5,10]

In NF, the site of injury impacts the severity of clinical manifestations due to local bacterial flora and proximity to vital organs. For example, NF of the head and neck region are more likely to have polymicrobial infection and progress to mediastinitis.[1]

At early stages, patients can be largely asymptomatic or have only mild localized signs and symptoms that can be attributed to benign disorders such as skin irritation or self-limiting inflammation.[9,11] If the initial presentation is mild, the patient may not be alarmed enough to seek immediate help.[11]

Most patients experience superficial erythema, edema, tenderness or pain, and fever regardless of the extent of the infection into deep fascia. With Type II NF, patients' initial superficial injury may be undetectable and severe signs and symptoms may not manifest until the underlying tissue damage has progressed extensively and the patient is already at extreme risk for a poor outcome.[8,9,11,12] Patients with extensive comorbidities who develop NF caused by organisms that release exotoxins tend to have more severe systemic signs and symptoms consistent with severe sepsis and septic shock, such as hemodynamic instability and lactic acidosis.[6]

Organisms that are gas-producing may cause subcutaneous crepitus that can be detected upon palpation of the affected region. Skin lesions such as bullae and blisters occur when the infection is in advanced stages. While these may help clinicians differentiate the disease from relatively benign disorders such as cellulitis, they do not have a high diagnostic sensitivity. The clinician should remain suspicious of a more severe underlying infection even if these overt signs are not present.[2,5,8,9,11,12]

Despite the various classifications of NF and subtle differences in etiology and microbiology, the overall diagnostic and treatment approach is similar.[3,13]

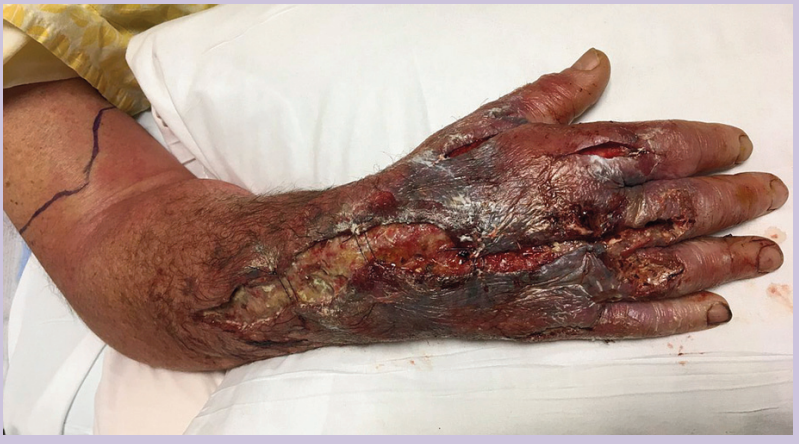
Diagnosis

No specific lab studies have been proven to be reliable for the diagnosis of NF.[14] Wong and colleagues developed the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) to help clinicians screen for NF using serum levels of the total white blood cell count, hemoglobin, sodium, glucose, creatinine, and C-reactive protein.[15] LRINEC scores of 6 or more were thought to be associated with NF. However, in subsequent reports LRINEC scores failed to accurately predict NF.[16,17]

Lab studies should include a complete blood cell count, complete metabolic panel, coagulation profile, lactate level, creatine kinase,

Minor injury, major complication

A healthy man, age 60, developed NF after scratching his hand on a piece of metal.



Source: Chung KC. *Grabb and Smith's Plastic Surgery*. 8th ed. Philadelphia, Pa.: Wolters Kluwer; 2019.

C-reactive protein, and erythrocyte sedimentation rate. Confirmatory diagnosis of the causative bacteria is based upon a culture and Gram stain of specimens collected from deep tissue, or by positive blood cultures. Cultures collected from superficial sites may not have clinical value if the causative organism is within the deep tissue.[13]

Plain radiography has not been shown to provide adequate diagnostic accuracy and is not recommended as an initial or definitive imaging study for NF.[10] Computed tomography (CT) and MRI may show edema extending along the fascial plane, although these findings may be absent in early stages of NF.[13]

Although MRI may provide superior results, CT is favored as the initial imaging choice because is generally more readily available for emergent imaging than MRI.[10] Another benefit is that CT can be rapidly assessed by nonradiologist providers before a formal imaging report is available. However, because clinical presentation is the most important factor for NF diagnosis, surgical intervention should not be delayed in order to facilitate diagnostic imaging.[13] Surgical exploration is the only way to establish the diagnosis of necrotizing infection.

Medical management

Initial pharmacotherapy should include empiric broad-spectrum antibiotics until soft tissue Gram stain, culture, and sensitivity results are available.[3] The most recent Infectious Disease Society of America guideline recommends either vancomycin or linezolid in combination with piperacillin-tazobactam, a carbapenem, or ceftriaxone-metronidazole.

Because clinical presentation is the most important factor for NF diagnosis, surgical intervention should not be delayed.

Clindamycin should also be included in empiric therapy due to its effect on toxins released by certain organisms, including *S. aureus* and GAS.[3,13] Penicillin plus clindamycin is recommended to treat documented GAS necrotizing infections.[13] As soon as the sampled specimen's microbiology is determined, the clinician can tailor therapy to the specific organism while utilizing local antibiograms in order to determine local resistance patterns. Additional medical management includes supportive measures such as aggressive I.V. fluid resuscitation and vasopressor support for septic shock.[4]

The role of hyperbaric oxygen therapy and I.V. immunoglobulin G (IVIG) for management of NF remains controversial.[3] IVIG is thought to achieve therapeutic benefit through neutralization of streptococcal toxins and in cases of severe infection or streptococcal toxic shock syndrome, it may be beneficial. However, its therapeutic benefit has not been demonstrated in large randomized studies.[6]

Surgical management

Surgery is the gold standard treatment when NF is either suspected or diagnosed. Surgical exploration and debridement of the affected tissue should be performed promptly. Initial tissue findings may include discoloration, gross edema or ecchymosis, and signs of necrosis. Specimens for Gram stain and culture should be obtained during surgical exploration.

Within 24 hours of the initial debridement, the patient should return to surgery for subsequent debridement.[6] This should continue daily until the surgical team determines that all necrotic tissue has been removed and only healthy tissue remains.[13] Amputation may be required to manage the infection in severe cases involving the extremities.

Discrete pus is generally absent, but surgical wounds often drain copious volumes of tissue fluid. Consequently, patients may need aggressive fluid volume replacement after surgery.[13]

Nursing considerations

Given the subtlety in presentation and lack of confirmatory physical findings, timely diagnosis of NF may be difficult. It is crucial for nurses to maintain a high index of suspicion for NF, especially in patients who are at high risk. In particular, nurses should assess for localized erythema,

warmth, tenderness disproportionate to the affected area, skin sclerosis, and signs of sepsis and septic shock including fever and hemodynamic instability.[6]

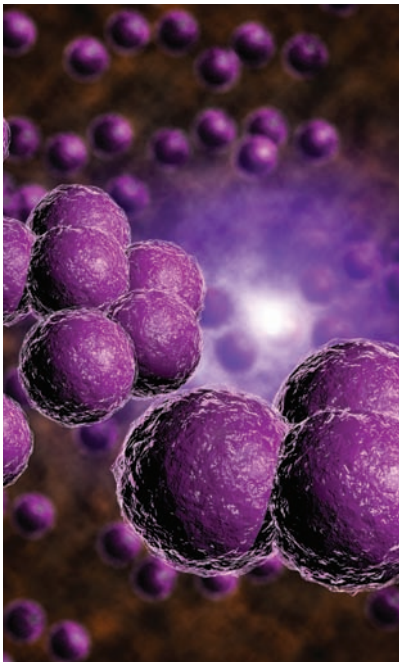
Nurses who suspect NF should promptly notify a provider and prepare for additional workup and management. This may include further imaging and lab studies.

Nurses should also be prepared to initiate treatment for NF in a timely manner. Interventions include administration of I.V. antimicrobials and fluids and correction of metabolic derangements. For some patients, transfer to the ICU may be indicated for frequent assessments and invasive hemodynamic monitoring.

Given the risk for septic shock, the nurse must frequently monitor vital signs and other the physical assessment findings for signs of decompensation. The nurse must immediately notify the provider and/or call the rapid response team of signs and symptoms of impending shock and be prepared to administer I.V. fluids, both crystalloids and colloids, and possibly vasoactive agents such as I.V. norepinephrine, as prescribed.[1] Given the severe pain often associated with NF, nursing care includes frequent pain assessments and appropriate pain management interventions.

Pre-op care should include medication reconciliation and the patient's informed consent. Intraoperatively, nurses must be prepared to assist with the collection of deep tissue culture specimens according to institutional protocol.

Nurses who care for patients in the post-op setting will have to carefully monitor them for surgical wound integrity, bleeding, and



Nonspecific presentations can make NF diagnosis difficult. Clinical judgment and a high index of suspicion expedite recognition.

electrolyte imbalances. Nurses must be diligent about administering prescribed antimicrobials as scheduled to maintain serum drug levels.

In the post-op setting, nursing care also includes hemodynamic monitoring, pain management, and nutritional support. Due to the large surgical wounds and increased metabolic demand experienced by patients with NF, the expected caloric requirement may be twice that of a typical patient in order to replace protein and fluid loss.[6] The nurse should anticipate that multiple surgical procedures will be performed as definitive NF treatment.

Along with standard precautions, nurses caring for patients with invasive GAS infection with soft tissue involvement should initiate droplet and contact precautions. Droplet and contact precautions may be discontinued after 24 hours of antimicrobial therapy.[1,18]

Patient education and support

The nurse should assess the patient's understanding of NF and provide additional teaching as necessary. Additional elements of patient teaching include pain management, antimicrobial therapy, surgical procedures, and wound care. As the patient prepares for discharge from acute care, the nurse must provide patient education regarding home medications, follow-up care, and signs and symptoms of normal healing versus those suggesting possible complications.

The patient should also receive targeted rehabilitation from the physiatry team to increase functional status. Given the severity of the condition, the nurse should prepare the patient and family for a prolonged hospital stay. If partial or full amputation was required to treat NF, the patient may experience significant disfigurement and associated psychological distress. In addition, patients who survive to hospital discharge are at increased risk for morbidity and mortality due to functional decline and impaired wound integrity. Nurses must provide patients and their families emotional support services, including social work and counseling if possible.[5]

Timely care improves outcomes

Despite advances in understanding, diagnosis, and treatment, NF still causes significant morbidity and mortality. Its microbiological profile remains complex and its classification

may evolve as our understanding of NSTI increases. Vague and nonspecific presentations can make diagnosis difficult. Clinical judgment and a high index of suspicion for NF will ultimately expedite recognition. Timely diagnosis and supportive therapies, including antimicrobials and timely referral to surgery, are crucial to improve patient outcomes. ■

REFERENCES

1. Stevens DL, Baddour LM. Necrotizing soft tissue infections. UpToDate. 2020. www.uptodate.com.

2. Wang J-M, Lim H-K. Necrotizing fasciitis: eight-year experience and literature review. *Braz J Infect Dis*. 2014;18(2):137-143.

3. Stevens DL, Bryant AE. Necrotizing soft-tissue infections. *N Engl J Med*. 2017;377(23):2253-2265.

4. Wessels MR. Streptococcal infections. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:1176.

5. Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. *Curr Probl Surg*. 2014;51(8):344-362.

6. Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machairas A. Current concepts in the management of necrotizing fasciitis. *Front Surg*. 2014;1:36.

7. Arif N, Yousfi S, Vinnard C. Deaths from necrotizing fasciitis in the United States, 2003–2013. *Epidemiol Infect*. 2016;144(6):1338-1344.

8. Jabbour G, El-Menyar A, Peralta R, et al. Pattern and predictors of mortality in necrotizing fasciitis patients in a single tertiary hospital. *World J Emerg Surg*. 2016;11:40.

9. Shiroff AM, Herlitz GN, Gracias VH. Necrotizing soft tissue infections. *J Intensive Care Med*. 2014;29(3):138-144.

10. Henry SM, Davis KA, Morrison JJ, Scalea TM. Can necrotizing soft tissue infection be reliably diagnosed in the emergency department? *Trauma Surg Acute Care Open*. 2018;3(1):e000157.

11. Kiat HJ, En Natalie YH, Fatimah L. Necrotizing fasciitis: how reliable are the cutaneous signs? *J Emerg Trauma Shock*. 2017;10(4):205-210.

12. Bystritsky R, Chambers H. Cellulitis and soft tissue infections. *Ann Intern Med*. 2018;168(3):ITC17-ITC32.

13. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(2):e10-e52.

14. Moskowitz E, Schroeppel T. Necrotizing fasciitis following abdominal gunshot wound. *Trauma Surg Acute Care Open*. 2018;3(1):e000163.

15. Wong C-H, Khin L-W, Heng K-S, Tan K-C, Low C-O. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med*. 2004;32(7):1535-1541.

16. Neeki MM, Dong F, Au C, et al. Evaluating the laboratory risk indicator to differentiate cellulitis from necrotizing fasciitis in the emergency department. *West J Emerg Med*. 2017;18(4):684-689.

17. Wilson MP, Schneir AB. A case of necrotizing fasciitis with a LRINEC score of zero: clinical suspicion should trump scoring systems. *J Emerg Med*. 2013(5);44:928-931.

18. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Centers for Disease Control and Prevention. 2019. https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html.

Leon L. Chen is a clinical assistant professor at New York University Rory Meyers College of Nursing in New York, N.Y., and the clinical program manager of research and simulated learning for the Department of Anesthesiology and Critical Care Medicine at Memorial Sloan Kettering Cancer Center in New York; Brian J. Fasolka is a clinical assistant professor at New York University Rory Meyers College of Nursing and an ED RN at Lenox Hill Hospital/Northwell Health in New York; and Caitlin Treacy is an NP with the Mobile Interventional Radiology Unit at Memorial Sloan Kettering Cancer Center in New York.

The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.

DOI-10.1097/01.NURSE.0000694752.85118.62