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Antibiotic therapy in necrotizing soft tissue infections: a narrative review of the greater Paris SURFAST consortium

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Abstract
Necrotizing soft tissue infections (NSTIs) are uncommon, yet rapidly progressive and potentially fatal conditions. However, evidence-based guidance on antibiotic therapy remains limited. Current recommendations emphasize the need for broad-spectrum empirical coverage, including gram-positive, gram-negative, anaerobes, and *Streptococcus pyogenes* when clinically indicated. We aimed at developing a practical, evidence-based framework for empirical antibiotic therapy in NSTIs. This narrative review is informed by a comprehensive literature search of PubMed, without date restrictions. We propose a structured decision-making algorithm for empirical antibiotic selection in NSTIs, integrating key clinical parameters: infection site, healthcare-associated versus community-acquired origin, risk factors for extended-spectrum β-lactamase-producing *Enterobacterales* and methicillin-resistant *Staphylococcus aureus*, and signs of sepsis or septic shock. Alternative regimens are provided for patients with severe β-lactam allergies. Special considerations for immunocompromised and other vulnerable host populations are also addressed. This review offers clinicians a pragmatic, stepwise approach to antibiotic therapy in NSTIs, while identifying critical knowledge gaps and priorities for future research.

Keywords Necrotizing skin and soft tissue infections, Necrotizing fasciitis, Antibiotics

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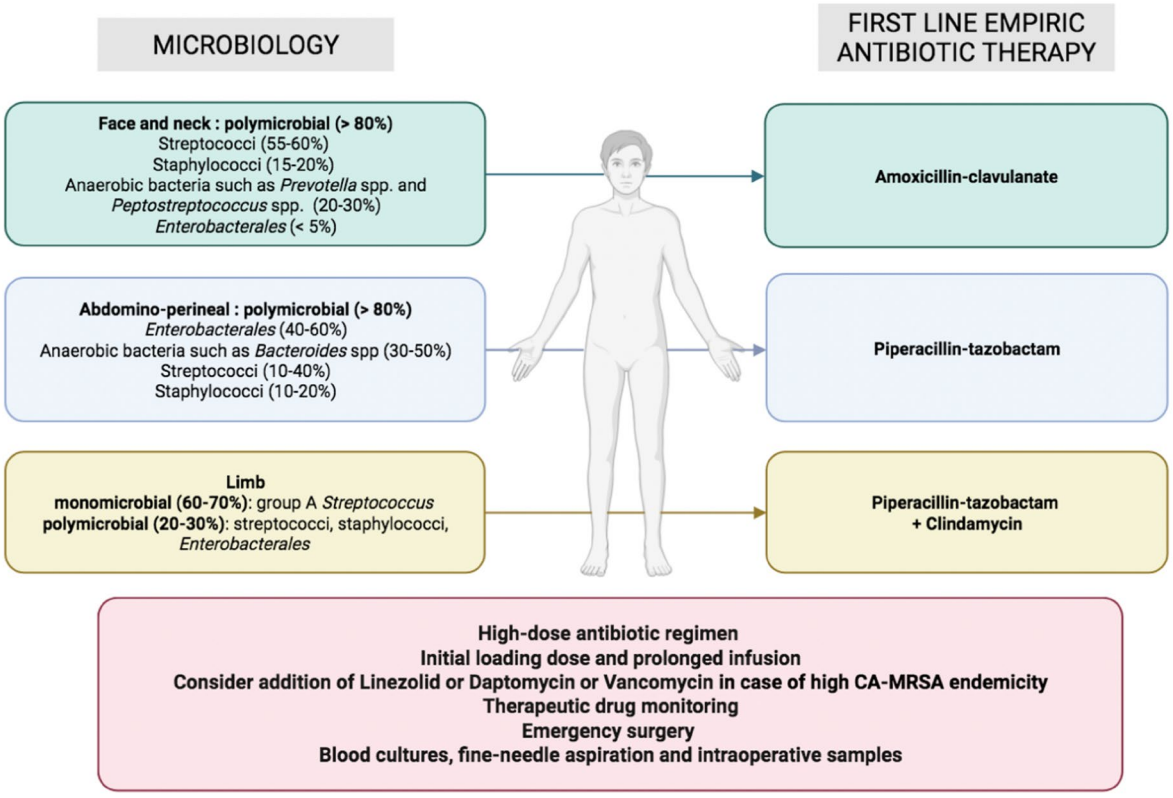
Graphical abstract



Key concepts in the management of necrotizing soft tissue infections. First-line empirical therapy refers to the suggested antibiotic if the patient has no β-lactam allergy, no sepsis or septic shock, no risk factors for ESBL-E or MRSA infection, the infection is community-acquired, and there has been no prior systemic antibiotic use within 1 month.

Background

Necrotizing soft tissue infections (NSTIs) are rare, life-threatening conditions characterized by extensive necrosis of the skin and subcutaneous tissue [1]. Although they can affect any part of the body, NSTIs most commonly involve the lower extremities. Studies have estimated the incidence of NSTIs from 0.2 to 15/100.000/year [2–5]. NSTIs primarily affect individuals with pre-existing comorbidities, such as diabetes, obesity, cardiovascular disease, intravenous drug use, and immunosuppression [1, 6–9]. NSTIs can also develop following traumatic injury, minor skin breaches, mucosal injury, or even non-penetrating soft tissue damage [10, 11]. Most infections are polymicrobial, involving a combination of anaerobic flora and gram-positive and/or gram-negative bacteria, predominantly streptococci and *Enterobacterales* [7, 9, 12]. Monomicrobial infections, primarily caused by *Streptococcus pyogenes* (Group A Streptococcus, GAS) and most commonly affecting limbs [7, 13], have been reported in approximately 30% of cases, with an increasing incidence in the post-COVID-19 era, associated with the spread of the $M1_{UK}$ lineage [14]. *Staphylococcus aureus*, *Vibrio vulnificus or Aeromonas hydrophila* have also been isolated, although more rarely [8, 9, 15, 16]. Mortality rates range from 10% to 30% [7, 9], depending on the severity at presentation, and survivors often face significant long-term morbidity, including amputations and reduced quality of life [7, 9, 17].

Urgent initial management of NSTIs includes broad-spectrum antibiotic therapy, rapid surgical debridement of infected tissue, and intensive care for associated organ failure [1, 8, 18]. While there is strong agreement on the principles of management, antibiotic management remains heterogeneous. Data on optimal antibiotic treatment are limited, and current guidelines are largely based on observational studies and experimental data [18, 19].

We have established a multidisciplinary reference network at Assistance Publique-Hôpitaux de Paris, called the SURFAST consortium, which includes intensivists, dermatologists, infectious disease physicians, pediatricians, surgeons, and microbiologists, all experts in the management of NSTIs. This consortium oversees all cases of

NSTIs referred from the greater Paris area, a large region of France with a population of over 12 million.

As a part of this consortium, we have implemented antibiotic management consensus statement to standardize practice. Here, we aim to present these practice recommendations and review the evidence in support.

Methods

Expert panel

A multidisciplinary panel made of experts involved in the management of patients with NSTIs (infectious diseases, dermatology, intensive care medicine, microbiology, pediatric, ear-nose-throat) met three times to elaborate the content of this procedure. A writing committee conducted an extensive non-systematic review limited to the English language using the PubMed database and wrote the article. A reading committee made an independent reviewing.

Definitions

Risk factors for extended spectrum β-lactamase- producing Enterobacterales (ESBL-E) infection

- For community acquired NSTIs, the presence of at least one of the following criteria will be considered at risk for ESBL-E infection: hospitalization in the previous six months, exposure to ß-lactams or fluoroquinolones in the previous six months, ESBL-E colonization or infection in the previous twelve months, travel to areas exhibiting high ESBL-E endemicity in the last six months (Asia, Africa, Caribbean, Central America, South America) [20, 21].
- For healthcare-associated setting, in addition to the previously mentioned risk factors, the local epidemiological context in case of high endemicity, should be considered as a risk factor for ESBL-E infection.
- Importantly, as ESBL-E account for less than 10% of NSTIs in regions with low endemicity [22, 23], empiric carbapenem therapy should not be initiated based on a single risk factor alone. Clinical decision-making should consider both the number of risk factors and the patient's severity.

Risk factors for Methicillin-resistant Staphylococcus aureus (MRSA) infection

The presence of at least one of the following criteria is at risk for MRSA: residency in post-acute care facility, chronic hemodialysis, long-term transcutaneous intravascular devices, MRSA colonization or infection in the last twelve months, exposure to ß-lactams or fluoroquinolones in the previous 3 months, immunosuppression (such as ongoing malignancy, transplantation, chemotherapy, corticosteroids (prednisone ≥ 25 mg/day), splenectomy, immunosuppressive therapies, autoimmune diseases), complex home care and chronic wound [24, 25].

In the US, risk factors for community-acquired MRSA are as follows: neonates, children beyond the neonatal period, athletes, household contacts of MRSA skin and soft tissue infection patients, emergency department patients, urban undeserved communities, indigenous populations, detainees in jail or prison, cystic fibrosis patients, military personnel, men who have sex with men, HIV patients, veterinarians, livestock handlers, and pet owners [26]. Travelers from America, North Africa, Western Asia, Southern Europe, Asia and Oceania are also at risk for MRSA colonization for twelve months following return [27]. In settings with high endemicity of CA-MRSA, empirical antibiotic coverage targeting MRSA is warranted, in line with previous guidelines [18, 19]. Healthcare-associated infections are considered as risk factors in settings where the prevalence of MRSA is high [28].

In pediatric population, approximately 30% of Panton-Valentin leucocidin (PVL)-producing strains are MRSA and the higher prevalence of community-acquired MRSA in children supports the inclusion of anti-MRSA coverage in empirical antibiotic therapy for this specific population [29].

Severe allergy to β-lactams

Defined by anaphylaxis and/or severe delayed hypersensitivity cutaneous reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction (or rash) with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis, bullous exanthemas, or maculopapular exanthema [30, 31].

Sepsis

Defined by a Sepsis-related Organ Failure Assessment (SOFA) score >2 in adults. In children, it is assessed using the Phoenix sepsis score ≥ 2 [24].

Septic shock

Defined, in adults, by a serum lactate level ≥ 2 mmol/L and the need for vasopressor therapy to maintain a mean arterial pressure of 65 mmHg. In children, it is defined by a Phoenix hemodynamic score ≥ 1 point (need for vasoactive treatment, lactate level ≥ 5 mmol/L, or age-specific hypotension) [24].

Key concepts

1. Intravenous antibiotic therapy is the cornerstone of medical management of NSTIs and must be combined with early surgical debridement of all infected tissue [18, 32].
2. Antibiotic therapy should be initiated without delay upon suspicion of NSTIs without waiting for surgical debridement or intraoperative samples [22].
3. The initial empiric antibiotic regimen should be broad-spectrum, targeting gram-positive (including streptococci and staphylococci), anaerobic bacteria and, depending on the location of the NSTI, gram-negative bacteria including *Enterobacterales* [33].
4. Group A Streptococcus (GAS) is often involved in NSTIs, and its toxin-mediated virulence warrants the early addition of an antibiotic with anti-toxin activity when GAS infection is suspected or confirmed by early microbiological findings [34]. We recommend a combination of β-lactam and anti-toxin antibiotics for the first 48–72 h of treatment. Linezolid is non-inferior to clindamycin as adjunctive therapy for invasive GAS infection [35, 36]. To date, there is no evidence supporting the use of daptomycin or vancomycin as antitoxin agents.
5. The high incidence of septic shock at presentation (over 50% of cases) combined with the extensive tissue necrosis at the site of infection leads to significant pharmacokinetic alterations such as increased volume of distribution, hypoalbuminemia and impaired tissue diffusion in the necrosis [37]. Therefore, we favor (i) high-dose antibiotic regimens, (ii) prolonged β-lactam infusion (extended or continuous) and (iii) therapeutic drug monitoring to optimize efficacy [38].
6. Aminoglycosides may be added to the antibiotic therapy of patients with sepsis/septic shock to broaden its spectrum. The choice of drug (e.g., amikacin or gentamicin) should be based on local epidemiology and the targeted pathogens (i.e. Gram-negative versus Gram-positive).
7. Although no studies have specifically addressed this issue in NSTIs, it seems safe to recommend antibiotic de-escalation based on the site of infection, blood cultures and/or per operative sample cultures.
8. Antibiotic treatment until clinical improvement, including apyrexia, and for 48–72 h after the last surgical debridement is likely to be sufficient [18, 39, 40].

Antibiotic choice according to the site of infection

NSTIs are commonly classified based on microbiological findings. The most widely accepted classification distinguishes between type I and type II NSTIs [41]. Type I infections are polymicrobial and typically occur in elderly patients or individuals with underlying comorbidities. A portal of entry, such as a skin ulcer or mucosal breach, is often identified. In contrast, type II NSTIs are monomicrobial, most frequently caused by GAS or *S. aureus*, and can affect patients of any age, including those without pre-existing conditions. Some authors also describe a type III category, encompassing infections caused by organisms such as *Aeromonas hydrophila*, *Vibrio vulnificus* or clostridial species.

In our protocol, we chose to categorize NSTIs according to the anatomical location of the infection rather than on microbiological documentation. This pragmatic approach is intended to help clinicians select the correct empirical antibiotic therapy for patients with suspected NSTIs, before microbiological results are available.

Antibiotic dosing regimens for adults and children are presented in Table 1. Adult dosages follow the 2025 European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations for high-dose therapy [42]. Pediatric dosages follow the Red Book recommendations, except for levofloxacin, for which higher doses are proposed based on recent pediatric pharmacokinetic–pharmacodynamic (PK/PD) analyses and the recommendations of the Société de Pathologie Infectieuse de Langue Française (SPILF) for pediatric use [43, 44].

Limb

It is the most common site of NSTIs, being involved in 57 to 70% of cases [45]. Approximately 50% of documented monomicrobial GAS NSTI is associated with skin breaches, including post-traumatic wounds, injection drug use, surgical procedures or pre-existing skin lesions. In the remaining 50% of cases, no obvious portal of entry is identified, but approximately 25% of patients report recent trauma without visible skin breaches [1]. Common risk factors include diabetes, chronic liver disease, obesity, cardiovascular disease, peripheral arterial disease, and immunosuppression, although up to 25% of patients have no underlying comorbidity [3]. The Choice of initial empirical therapy is shown in Fig. 1 and depends on (i) whether the infection is community-acquired or healthcare-associated, (ii) β-lactam allergy, (iii) signs of sepsis or septic shock, (iv) comorbidities and (v) microbiological evidence of gram-positive cocci. Other factors are also considered, including risk factors for ESBL-E and MRSA. Importantly, the decision to start a carbapenem should not be based on the presence of a single risk factor but should take into account both the number of risk factors and the severity of the patient. The combination of an aminoglycoside (e.g., amikacin) to the empirical antibiotic regimen may allow carbapenems to be used sparingly while still covering ESBL-E. In

Table 1 Recommended antibiotic dosages and administration in adults and children for the first 24 h, regardless of initial renal function, then adjust according to creatinine clearance and residual antibiotic concentration monitored before the 5th dose (or at 48 h)

	Adults	Children
Amoxicillin/clavulanate	IV: Amoxicillin/clavulanate 2 g/8 h of amoxicillin over 60 min Oral: Amoxicillin/clavulanate 1 g × 3/day + Amoxicillin 1 g × 3/day	IV: 150 mg/kg/24 h in 3 administrations over 30 min, not exceeding 6 g/24 h If < 4 kg: 100 mg/kg/24 h in 2 administrations
Cefazolin	IV: 2 g/8 h or 6 g/24 h by continuous infusion after 2 g loading dose	IV: 150 mg/kg/24 h in 4 to 6 injections, not exceeding 12 g/24 h
Imipenem/cilastatin	Loading dose*: 1 g IVL over 30 min 1 g/6 h IVL over 30 min	IV: 60–100 mg/kg/24 h in 4 administrations over 30 min if < 500 mg or over 60 min if > 500 mg, not exceeding 4 g/24 h
Meropenem	Loading dose*: 2 g IV over 30 min 2 g/8 h by prolonged infusion over 4 h	IV: 90–120 mg/kg/24 h in 3 administrations over 30 min or continuous IV infusion, not exceeding 6 g/24 h
Oxacillin/cloxacillin	IV: 150 mg/kg/24 h in 4 to 6 injections over 30 min	IV: 150–200 mg/kg/24 h in 4 to 6 injections, not exceeding 12 g/24 h
Piperacillin/tazobactam	Loading dose*: 4 g IV in 30 min Prolonged infusion: 4 g/6 h over 4 h Or continuous infusion: 16 g/24 h after a loading dose	400 mg/kg/24 h in 4 administrations over 30 min or continuous IV infusion, not exceeding 16 g/24 h
Clindamycin	IV or oral: 600 mg/6 h or 900 mg/8 h in at least 30 min	IV: 40 mg/kg/24 h in 3 to 4 administrations over 30 min, not exceeding 2,7 g/24 h
Daptomycin	10 mg/kg/24 h by IV infusion over 30 min	From 1 to 6 years old: 12 mg/kg/24 h From 7 to 17 years old: 10 mg/kg/24 h Systematic therapeutic drug monitoring
Linezolid	IV or oral: 600 mg/12 h	IV or oral: < 12 years old: 30 mg/kg/24 h in 3 administrations > 12 years old: 20 mg/kg/24 h in 2 administrations Not exceeding 1200 mg/24 h
Vancomycin	Loading dose: 30 mg/kg not exceeding an infusion rate of 1 g/h Followed by a maintenance dose of 30 mg/kg/24 h by continuous IV infusion	Loading dose: 20 mg/kg Followed by a maintenance dose of 50–60 mg/kg/24 h by continuous IV infusion
Amikacin	25 mg/kg/24 h IV over 30 min	25–30 mg/kg/24 h IV over 30 min
Gentamicin	5–7 mg/kg/24 h IV over 30 min	7–8 mg/kg/24 h IV over 30 min
Ciprofloxacin	IV: 400 mg/8 h Oral: 750 mg/12 h	IV: 30–45 mg/kg/24 h in 2 to 3 administrations over 60 min, not exceeding 1,2 g/24 h
Levofloxacin	IV or oral: 500 mg/12 h	IV: From 6 months to 5 years old: 20 mg/kg/24 h in 2 administrations over 60 min After 5 years old: 15 mg/kg/24 h in 1 administration over 60 min Not exceeding 1 g/24 h
Metronidazole	IV or oral: 500 mg/8 h or IV 1500 mg/24 h in a single IV injection	30 mg/kg/24 h in 3 to 4 administrations over 30–60 min, not exceeding 1,5 g/24 h If < 7 days: 7,5 mg/kg/12 h

* In case of sepsis or septic shock; IV: intravenous

case of community-acquired limb NSTI in patients without comorbidities, when preliminary microbiological evidence is available (positive direct examination from blood culture or subcutaneous needle aspiration revealing Gram-positive cocci in chains), amoxicillin–clavulanic acid may be considered as the empirical β-lactam agent of choice.

Abdomino-perineal

Predisposing factors for perineal NSTIs, also known as Fournier's gangrene, include trauma, pressure ulcers, hemorrhoids, local abscess, digestive perforation, urinary tract infection or kidney stone, and surgery or other instrumentation [46]. Over 80% of cases are polymicrobial, typically involving *Enterobacterales*, anaerobic bacteria (such as *Bacteroides* spp.), streptococci, and staphylococci [7, 47]. Initial antibiotic therapy is shown in Fig. 2. The choice of initial empirical therapy depends on (i) β-lactam allergy and (ii) signs of sepsis or septic shock.

Face and neck

Within the spectrum of NSTIs, head and neck involvement is rare. A literature review conducted in 2017 compiled 1,235 case reports. The most common portals of entry are odontogenic (47%), pharyngo-laryngeal (28%),

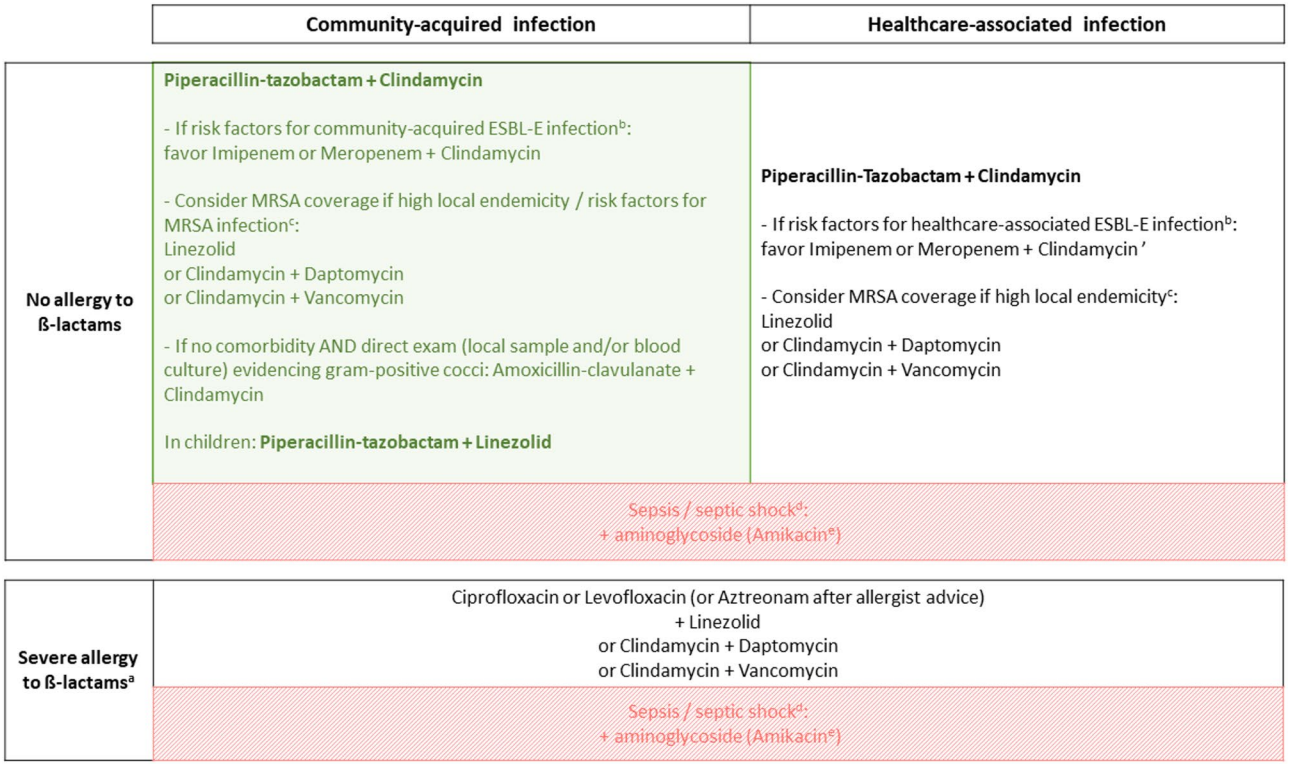


Fig. 1 Initial empiric therapy for limb necrotizing soft tissue infections. ESBL-E: extended spectrum β-lactamase producing *Enterobacterales*; MRSA: Methicillin-resistant *S. aureus*; [a, b,c, d] For severe allergy to β-lactams, risk factors for community and healthcare associated ESBL-E infection, risk factors for MRSA infection, sepsis and septic shock definitions, refer to the definitions' section; [e] Amikacin is suggested over gentamicin for optimal coverage of Gram-negative bacilli

tonsillar/peritonsillar (6%), traumatic/iatrogenic/postoperative (5%), salivary gland (2%), skin (1.7%) or unidentified (9%). In addition to the above risk factors, poor oral and dental hygiene are also frequently reported [48].

These infections are typically polymicrobial, with frequent involvement of streptococci (55–60%) and staphylococci (15–20%). Anaerobic bacteria are identified in 20–30% of cases, although probably underestimated by their difficult growth, with *Prevotella* spp. and *Peptostreptococcus* spp. being the most commonly isolated. *Enterobacterales* are identified in less than 5% of cases [48, 49].

Initial antibiotic therapy is outlined in Fig. 3. The choice of initial empiric therapy depends on (i) the risk of multidrug resistance (ESBL-E, MRSA), (ii) β-lactam allergy, and (iii) signs of sepsis or septic shock.

Specific hosts

Intensive care units (ICU) patients

The management of ICU patients with severe infections follows standard critical care principles: early and appropriate antibiotic therapy, surgical source control, and conventional management of organ failure and comorbidities. A key challenge is the altered pharmacokinetics of water-soluble antibiotics (e.g., ß-lactams, aminoglycosides, lipopeptides) in sepsis, which affect distribution, tissue penetration, and renal clearance due to microcirculation changes [38]. As a result, plasma and tissue drug concentrations can be highly variable and unpredictable. It is recommended that an initial full daily dose be administered based on patient weight (regardless of creatinine clearance), followed by daily therapeutic drug monitoring for adjustments (Table 1) [50–52].

Neutropenic patients

Neutropenic patients with NSTIs are more severe on admission to the ICU than non-neutropenic patients with NSTIs, they have more positive blood cultures (about 60% of cases), hospital-acquired NSTIs and abdominal-perineal locations. Hospital mortality ranges from 58% to 76% [53, 54]. Monomicrobial documentation is more common than in patients with non-neutropenic NSTIs (66% vs. 40%), including predominantly gram-negative bacteria (*Enterobacterales* and non-fermenting bacteria) [54, 55]. In contrast, GAS and other streptococcal species are rarely documented. Empiric antibiotic treatment in these patients should include a ß-lactam with anti-pseudomonal activity such as piperacillin-tazobactam (or a carbapenem if risk factors for ESBL-E infection are present), combined with an aminoglycoside if sepsis/

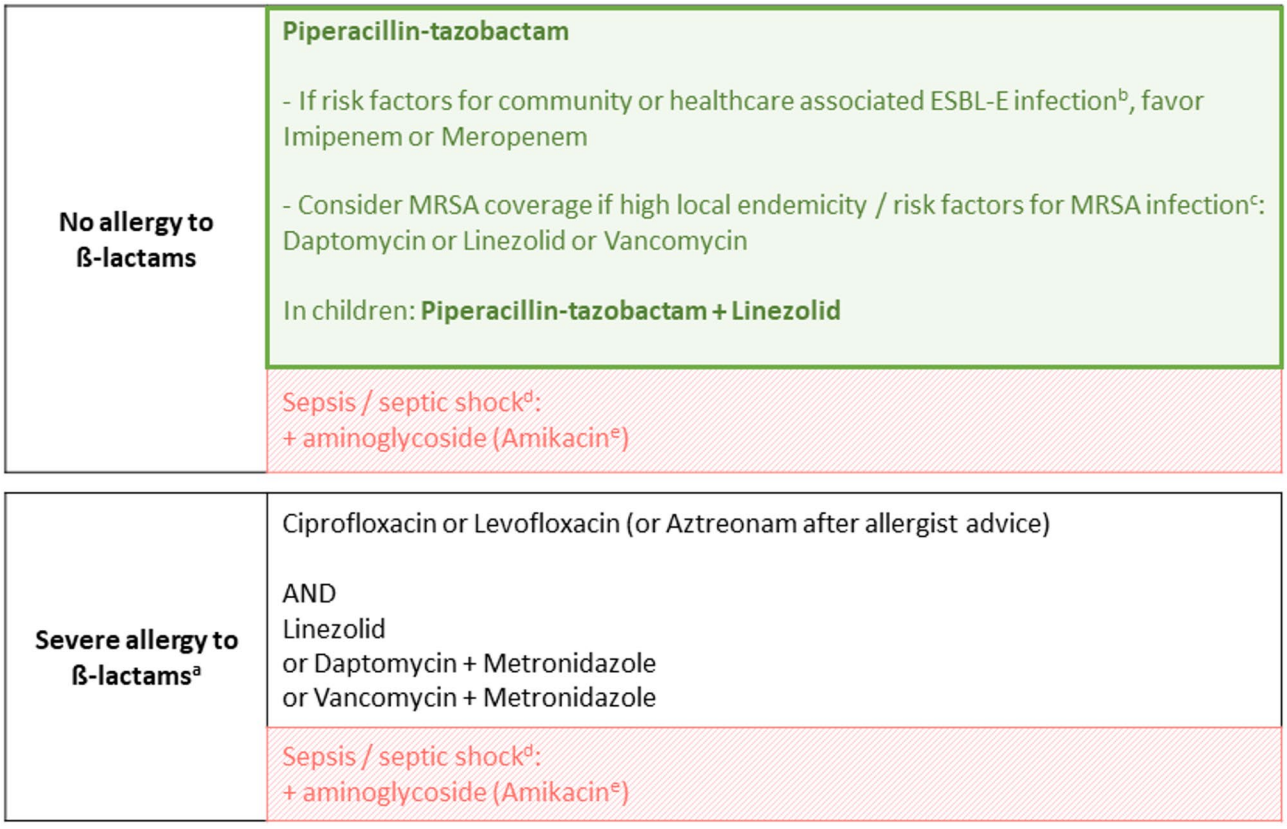


Fig. 2 Initial empiric therapy for abdomino-perineal necrotizing soft tissue infections. ESBL-E: extended spectrum β-lactamase producing *Enterobacterales*; MRSA: Methicillin-resistant *S. aureus*; [a, b,c, d] For severe allergy to β-lactams, risk factors for community and healthcare associated ESBL-E infection, risk factors for MRSA infection, sepsis and septic shock definitions, refer to the definitions' section; [e] Amikacin is suggested over gentamicin for optimal coverage of Gram-negative bacilli

septic shock. MRSA coverage should be broad for hospital-acquired/healthcare-associated NSTIs, patients with sepsis or septic shock, and those with other risk factors of MRSA as defined above. Clindamycin combination is not recommended in this population due to the low likelihood of GAS isolation.

In patients with suspected NSTIs with persistent/recurrent fever and neutropenia, empirical therapy should be broadened to include anti gram-positive agents if not already started (i.e., vancomycin, linezolid or daptomycin); an antifungal should be considered (e.g., caspofungin, amphotericin B) [18].

Pregnancy

All β-lactams are considered safe during pregnancy. Amikacin and gentamicin have no fetal toxicity at standard doses and can be prescribed, preferably once daily. Vancomycin should be preferred to daptomycin and linezolid, as there is limited data available on the latter two antibiotics in pregnant patients. Among fluoroquinolones, ciprofloxacin has the most extensive safety data and should be preferred to levofloxacin [56].

Specific pathogens

Infections caused by *Vibrio* spp. (primarily *V. vulnificus* but also occasionally *V. alginolyticus* non-serogroup 01, *V. cholerae*, and *V. parahaemolyticus*), can complicate traumatic wound sustained in saltwater (or brackish inland waters) or from exposure to drippings from raw seafood and subsequently progress to NSTIs [57]. A rapidly progressive primary bacteremia caused by *V. vulnificus* may occur after entry of the organism through the gastrointestinal tract (e.g., consumption of raw oysters) rather than through abraded skin. NSTI often occurs rapidly after the bacteremia [58]. Hepatic diseases are associated with infections and complications from *V. vulnificus* [59]. Tetracyclines have been considered for the treatment of *V. vulnificus* infections, with cefotaxime and ciprofloxacin as alternatives [60]. Infections caused by *V. vulnificus* should be considered when choosing the empirical antibiotic coverage for NSTIs occurring in warm coastal environments after the ingestion of shellfish. These infections are more frequent during the summer months and in patients with liver cirrhosis or other forms of immunosuppression.

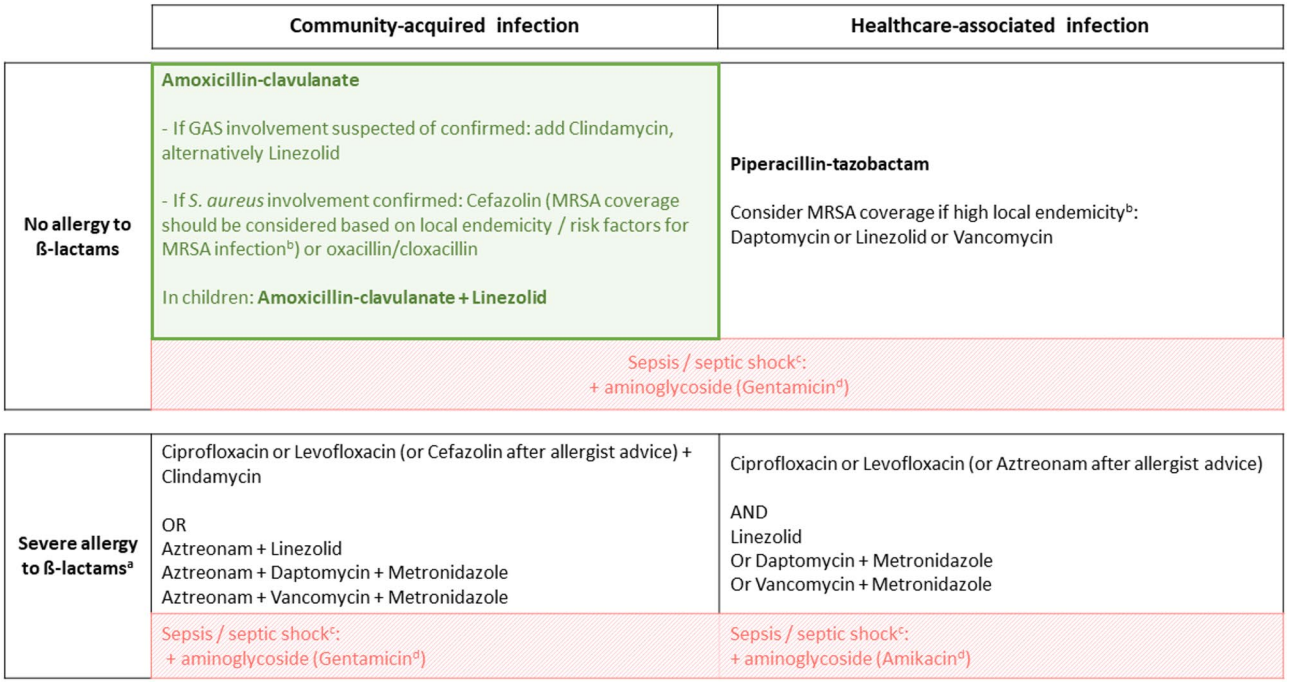


Fig. 3 Initial empiric therapy for necrotizing soft tissue infections of the face and neck. GAS: group A *Streptococcus*; MRSA: Methicillin-resistant *S. aureus*; [a, b, c] for severe allergy to β-lactams, risk factors for MRSA infection, sepsis and septic shock definitions, refer to the definitions' section; [d] Amikacin is suggested over gentamicin in healthcare-associated infections in patients with severe β-lactam allergy for optimal coverage against Gram-negative bacilli

A. hydrophila, an environmental gram-negative bacillus commonly found in lakes, rivers, and soil, may produce NSTIs following inoculation through a laceration sustained during freshwater exposure. Skin and soft-tissue infections due to *Aeromonas* sp. have been reported in Australia, Asia, South America, Europe and the Indian Ocean [61–64]. Most isolates of *Aeromonas* are susceptible in vitro to ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole, antipseudomonal aminoglycosides, third-generation cephalosporins, piperacillin-tazobactam, carbapenems and tetracyclines [65]. *Aeromonas* sp. Coverage should be considered for NSTIs occurring in aquatic environments.

Children

NSTIs are extremely rare pediatric infections in high-income countries, with an annual incidence of less than 0.1 per 100,000 patients under 18 years of age [66]. Although much lower than in adults, the overall mortality rate, approximately 6% [67–69], is notably higher than that typically observed in Pediatric Intensive Care Units (PICUs), particularly among patients with severe comorbidities. Predisposing conditions have shifted from varicella to healthcare-associated factors and trauma, with an apparent increase in cases developing secondarily due to medical care [69, 70].

The affected body areas are almost equally distributed among the arms, legs, head and neck, and chest and abdomen. Bacteria are identified in more than three-quarters of cases via blood cultures, skin biopsies or operative samples. Most pediatric NSTIs are monobacterial [71], and many are caused by gram-positive organisms, with MRSA accounting for an increasing number of patients.

Accordingly, the cornerstone of antibiotic therapy, although directly derived from the broader adult experience, should be tailored to account for all these pediatric-specific factors. In the pediatric population, *Staphylococcus aureus* producing Panton-Valentine leucocidin (PVL) plays a more significant role in severe community-acquired, non-necrotizing skin and soft tissue infections than it does in adults. Around 30% of PVL-producing strains are MRSA, and the higher prevalence of community-acquired MRSA in children suggests that anti-MRSA coverage should be included in empirical antibiotic therapy for this specific population [29].

For all these reasons, referral to a PICU experienced in managing these complex clinical cases is justified to prioritize hemodynamic stabilization and the early initiation of broad-spectrum antibiotic therapy, before determining the optimal timing for surgical intervention by experienced pediatric surgeons [72, 73].

Follow-up antibiotic management

Although no studies have specifically addressed antibiotic de-escalation strategies in NSTIs, it appears reasonable to adjust therapy based on the anatomical site of infection (considering that abdominoperineal and

cervicofacial NSTIs are mostly polymicrobial, whereas limb NSTIs are monomicrobial in 60–70% of cases) as well as blood culture results and intraoperative microbiological samples. The optimal agent for oral step-down therapy has not been defined; oral de-escalation should be initiated after complete surgical debridement and we recommend selecting an antibiotic with good oral bioavailability and encourage lipophilic molecules with reliable skin tissue penetration. No randomized controlled trials have established the ideal duration of antibiotic therapy. Treatment is generally continued until surgical debridement is no longer required, the patient demonstrates clinical improvement and fever has been absent for at least 48 to 72 h [18, 39, 40].

After acute infection, we recommend careful surveillance, as recurrence —necrotizing or not—occurs in up to 35% of cases within one year of the initial NSTI [74].

Adjunctive non-antibiotic therapies

Intravenous immunoglobulins (IVIGs) are often used alongside standard treatments for severe invasive group A streptococcal (iGAS) NSTIs, because of their potential anti-toxin effects. Early studies, especially in streptococcal toxic shock syndrome, suggested a mortality benefit, but the evidence remains weak due to small sample sizes and study limitations, including bias, inconsistent use of clindamycin, and varying inclusion criteria [75, 76]. A recent randomized controlled trial by Madsen et al. found no significant benefit of IVIGs on physical quality of life, mortality, or complications at 180 days [77]. Limitations included low GAS prevalence and lower IVIG dosing. As most patients received clindamycin, which itself inhibits toxins, it remains unclear whether IVIGs add value. Therefore, IVIGs may be considered on a case-by-case basis for patients with persistent organ failure despite source control.

Although a pathophysiological rationale has been developed for hyperbaric oxygen therapy in clostridial infections, data on its benefits are conflicting [3], and hyperbaric oxygen is not consistently recommended in guidelines for NSTIs. Hyperbaric oxygen should not delay the initiation of other treatments.

Discussion

We present antibiotic management algorithm drawn up by a multidisciplinary group of experts. This expert consensus aims to homogenize antibiotic practice in patients with suspected or confirmed NSTIs treated in the SURFAST network, which comprises 11 hospitals in the Great Paris area.

Several aspects have been poorly studied in the literature and we could not agree on a clear position on them. There is little data on the optimal duration of antibiotic treatment, but most recent guidelines based on expert opinion suggest that antibiotics should be administered until debridement is no longer necessary and fever has resolved for 48–72 h [18, 19]. Procalcitonin-based strategies could be used to personalize the duration of antibiotic treatment [78]. Oral antibiotic switching could probably be performed after the last debridement in stable patients, but the safety of such a strategy has not been evaluated.

From a microbiological point of view, the advent of next-generation sequencing (NGS) methods is transforming medical diagnostics in infectious diseases. As in many other situations [79–81], shotgun metagenomics has demonstrated its superior ability to detect a wide range of pathogens, especially strict anaerobes compared to other methods [15]. The interest for this method is increased by the recent description of a complex pathobiome in NSTIs, which calls for the broad identification of all microorganisms present in both necrotic and macroscopically healthy tissues. Furthermore, ongoing developments in shotgun metagenomics may in the future add genomic information by detecting virulence or resistance determinants, which could improve clinical management [82, 83].

There are no data on the management of superinfection of the debrided skin. Deterioration of the local aspect with general signs should prompt collection of new microbiological samples and the initiation of empiric antibiotics if the patient presents sepsis or septic shock.

Our narrative review certainly has limitations: Firstly, our algorithms have not been graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) hierarchy criteria [84] and represent the position of the multidisciplinary experts involved in our clinical network. The most recent guidelines on the management of NSTIs were published in 2014 [18] and 2018 [19] and we felt there was a need to provide updated recommendations. Second, our framework has been designed for application in a French network (SURFAST) with our specific regional bacterial ecology, characterized by low MRSA endemicity, high ESBL-E endemicity, and < 10% GAS clindamycin resistance [85]. However, we have endeavoured to provide hierarchical criteria in the choice of antibiotic strategies to make them generalizable. We have also considered different clinical scenarios commonly encountered in the clinical practice (e.g., severe β-lactam allergy, pregnancy, paediatric and neutropenic patients) and have provided practical recommendations or alternatives for clinicians.

Conclusion

Urgent initial management of NSTIs includes broad-spectrum antibiotic therapy, rapid surgical debridement of infected tissue, and intensive care for associated organ failure. The SURFAST multidisciplinary reference

network provided targeted and pragmatic antibiotic management procedure to standardize practice.

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Author contributions
C.C., B.S. and N.D.P. contributed to the conception and design of the work, writing review, systematic search execution, literature review, drafted the work and approved the submitted version. S.D., P-L.W., A.B., M.C., O.C., C.B., C.H., G.M., A.T., T.U., B.V., P.M., and R.L. contributed to the conception and design of the work, writing review and approved the submitted version.

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