Guidance

Central Administration of Pharmaceutical Care
General Administration For Drug Utilization and Pharmacy Practice

National Guidance of Rational Antimicrobial Use in the Management of Skin and Soft Tissue Infection

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Contents

The Scope of the Guidance

This guidance provides a practical framework for the rational antimicrobial use in the empiric treatment of skin and soft tissue infections (SSTIs), integrating the WHO AWaRe antibiotic classification to support antimicrobial stewardship and reduce antimicrobial resistance.

The AWaRe classification of antibiotics was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts at local, national and global levels, Antibiotics are classified into three groups, Access, Watch and Reserve, taking into account the impact of different antibiotics and antibiotic classes on antimicrobial resistance, to emphasize the importance of their appropriate use.

Access group antibiotics includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Selected Access group antibiotics are recommended as essential first or second choice empiric treatment options for the most infectious syndromes.[(2)]

Watch group antibiotics are the antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. These medicines should be prioritized as key targets of stewardship programs and monitoring. Selected Watch group antibiotics are recommended as essential first or second choice empiric treatment options for a limited number of specific infectious syndromes.[(2)]

Reserve group antibiotics includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as “last resort” options.[(2)]

N.B., the antibiotics highlighted in green fall under the Access category, those in yellow are classified as Watch antibiotics, and the ones in red belong to the Reserve group.

Abbreviations

Bid	Twice daily (Every 12 hours)
CA-MRSA	Community Acquired Methicillin-resistant Staphylococcus aureus
cSSTIs	Complicated Skin and soft-tissue Infections
CT	Computed Tomography
GAS	Group A Streptococci
HIV	Human immunodeficiency virus
IV	Intravenous administration
IM	Intramuscular administration
MRI	Magnetic Resonance Imaging
MRSA	Methicillin-resistant Staphylococcus aureus
MSSA	Methicillin-sensitive Staphylococcus aureus
NSTIs	Necrotizing Skin and soft-tissue infections
PO	Per oral
SIRS	Systemic Inflammatory Response Syndrome
SMX-TMP	Sulfamethoxazole/ trimethoprim
SSIs	Surgical Site Infections
SSTIs	Skin and soft-tissue Infections
WHO	World Health Organization

Introduction

Skin and soft-tissue infections (SSTIs) encompass a variety of pathological conditions that involve the skin and underlying subcutaneous tissue, fascia, or muscle (Figure 1), ranging from simple superficial infections to severe necrotizing infections. [1]

Damage to the skin can lead to infections of the deeper layers beneath the epidermis.[1] When such damage occurs, both endogenous pathogens (i.e. that naturally reside in the body) and exogenous pathogens (i.e. that enter the body from the environment) can penetrate the epidermis and spread to deeper structures through the lymphatic system.[1],[2] Depending on the depth of the infection, different clinical diseases can occur: impetigo and erysipelas (infections of the upper layer of the skin) and cellulitis (infection of the deep dermis and subcutaneous tissue) (Figure 1).[2]

Most SSTIs are caused by aerobic Gram-positive cocci, specifically S. aureus, and streptococci. [1] Both are responsible for most simple community-acquired SSTIs.[2] Strains of S. aureus and group A streptococci (GAS) can produce a variety of toxins that may both potentiate their virulence and affect the soft tissues and allow invasion of the dermis.[1] S. aureus infections were associated with younger age, carbuncle and furuncle. [1] MRSA infections were associated with extreme age (older age and age <5 years), carbuncle and furuncle, cellulitis, and abscess. [1]

Beta-hemolytic streptococcus was found to cause nearly three-fourths of cases of diffuse cellulitis. [3] S. aureus, P. aeruginosa, Enterococcus, and Escherichia coli are the predominant organisms isolated from hospitalized patients with SSTIs. MRSA infections can lead to ischemia and overlying skin necrosis.[3] Lymphatic and hematogenous dissemination cause septicemia and spread to other organs (e.g., lung, bone, heart valves). Diabetic lower limb infections, severe hospital-acquired infections, necrotizing infections, and head and hand infections pose higher risks of mortality and functional disability.[3]

Bacterial skin infections occur worldwide and can affect all age groups; erysipelas is more frequent in children and elderly patients. Cellulitis, the most common skin infection, accounted for 0.04% (4 in 10,000) of the overall burden of all diseases combined in 2013.[2] In 2017, the Global Burden of Disease study reported 43 million new cases of cellulitis worldwide. Diabetes, peripheral arterial disease, HIV infection and other causes of immunosuppression are risk factors for severe skin infections. [2]

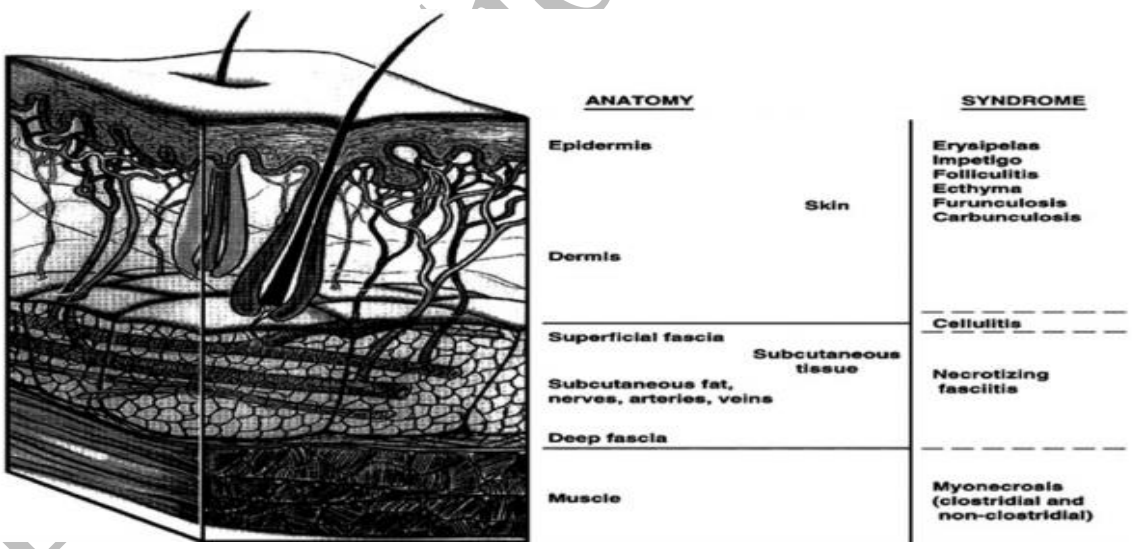


Figure 1: layers of the skin highlighting the various types of SSTIs

Adopted from: Duane, Therese M., et al. "Surgical Infection Society 2020 updated guidelines on the management of complicated skin and soft tissue infections." *Surgical infections* 22.4 (2021): 383-399.

Classification of SSTIs

SSTIs are classified as:

1. Simple or complicated as follows:

Table 1: Simple and complicated SSTIs

Simple infections (uncomplicated)	**Complicated infections** (necrotizing or non-necrotizing)
• The skin and underlying superficial soft tissues. (3) • Common simple SSTIs include cellulitis, erysipelas, impetigo, ecthyma, folliculitis, furuncles, carbuncles, simple abscesses, and trauma related infections. (1), (3) • Respond well to outpatient management. • Management typically involves antibiotics or surgical incision to drain abscess alone. (1)	• Extending into and involving the underlying deep tissues. (1), (3) • Include major deep abscesses, infected decubitus ulcers, necrotizing fasciitis, Fournier`s gangrene, infected burn and infections from human or animal bites, perianal infections, diabetic foot infections, infections in patients with significant comorbidities, and infections from resistant pathogens. (1), (3) • Might be necrotizing or non-necrotizing. (3) • These infections may present with features of systemic inflammatory response syndrome or sepsis, and, occasionally, ischemic necrosis. (3) • Requiring antibiotics ,and significant surgical intervention with drainage and debridement. (1)

2. Purulent or non-purulent (mild, moderate, or severe) (4)
   - Purulent: furuncle, carbuncle, and abscess.
   - Non-purulent: cellulitis, erysipelas, and necrotizing infections.
3. According to the anatomical tissue layers involved (1)
   - Superficial infections such as erysipelas, impetigo, folliculitis, furuncles, and carbuncles are located at the epidermal and dermal layers, while cellulitis is located in the dermis and subcutaneous tissue.
   - Deep infections that extend below the subcutaneous tissue may involve fascial planes or muscular compartments, presenting as complex abscesses, fasciitis, or myonecrosis.
4. According to the severity of local and systemic signs and the presence or absence of comorbid conditions. In this classification system, SSTIs are divided into four classes as follows: (1), (3)

Table 2: SSTIs classification according to the severity of local and systemic signs and the presence or absence of comorbid conditions.

Class	Description
1	• Patients with SSTI, but no signs or symptoms of systemic toxicity or co-morbidities • Amenable to outpatient management with topical or oral antimicrobials.

2	• Patients are either systemically unwell with stable co-morbidities OR • Systemically well, but with comorbidity (e.g., diabetes, obesity) that may complicate or delay resolution.
3	• Patient appears toxic and unwell (fever, tachycardia, tachypnoea, and/or hypotension) • Inpatient management with parenteral antibiotics is required.
4	• Infection with signs of potentially fatal systemic sepsis (mental status changes, tachycardia, tachypnea, and hypotension). • Patients have sepsis syndrome and life-threatening infection, for example, necrotizing fasciitis. • Management involve urgent inpatient care (possibly in critical care), parenteral antibiotics & surgery if indicated.

5. SSTIs are divided into three main groups: surgical site infections (SSIs), non-necrotizing SSTIs, and necrotizing SSTIs (NSTIs). [1]

a) SSIs are post-operative infections, and they are framed into a separate group because of their multifaceted aspects.
SSIs are classified into two subgroups: (a) incisional and (b) organ and organ/space
- The incisional SSIs are divided into superficial (skin and subcutaneous tissue) and deep (deep soft-tissue muscle and fascia). [1]
- Organ and organ/space infections are not considered truly soft-tissue infections. [1]

b) Non-necrotizing SSTIs, including erysipelas, impetigo, folliculitis, simple abscess, and a complex abscess, may be treated by antibiotics or drainage alone. [1]

c) NSTIs require surgical intervention, including drainage and debridement of necrotic tissue in addition to antibiotic therapy. [1]

N.B., the necrotizing or non-necrotizing character of the infection, the anatomical extension, the characteristics of the infection (purulent or not purulent), and the clinical condition of the patient should always be assessed independently to classify patients with SSTIs. [1]

Classification of NSTIs [1]

1- According to anatomical location: Fournier gangrene
2- According to the depth of infection:
   a) Dermal and subcutaneous: Necrotizing cellulitis
   b) Fascial: Necrotizing Fasciitis
   c) Muscular components: Necrotizing myositis
3- Microbiologically: (mentioned in table 6)

Risk Factors for Skin and Soft Tissue Infections

Table 3: General Risk Factors for Skin and Soft Tissue Infections

Host-related	Exposure related	Health care related
Age (children, older adults)	Alcohol abuse	Prolonged hospitalization
Asplenia	Military personnel	Long-term care facility
Cardiopulmonary disease	Sports participation (contact	Dialysis (peritoneal, hemodialysis)
Debility or Poor nutrition	Water exposure (e.g., ocean, hot tubs)	Long-term intravascular access
Diabetes mellitus	Trauma (including surgery)	Health care professional
Peripheral arteriovenous insufficiency	Human or animal bites	Subcutaneous or intravenous drug use
Hepatorenal disease		
Obesity		
Peripheral neuropathy		
Immunocompromise (e.g., human immunodeficiency virus infection, chemotherapy, antiretroviral therapy, disease-modifying antirheumatic drugs)		

Adopted from:

- Ramakrishnan K, Salinas RC, Higuita NI. Skin and soft tissue infections. American family physician. 2015 Sep 15;92(6):474-83.
- Bechar J, Sepehripour S, Hardwicke J. Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature. The Annals of The Royal College of Surgeons of England. 2017 May;99(5):341-6

Table 4: Risk Factors Associated with MRSA SSTI

Risk Factors Associated with MRSA SSTI (including CA-MRSA)

- Ethnicity (African Americans, Hispanic compared with Caucasian); recent travel (in Africa, Latin America or Southeast Asia)
- Socioeconomic lower quintile, poor hygienic conditions, overcrowded housing, incarceration
- Previous antibiotic therapy; recent (last three previous months)
- History of MRSA: Previous colonization or S. aureus infection
- Exposure: hospitalization in the previous 12 months, ICU admission, residence of long-term care facility, household contacts
- Previous minor or major surgery
- Intensive procedures and other instrumental techniques (e.g. image or radiological studies, central vascular catheters, implantable device)
- Contact activities, such as daycare young children, contact sports activities, military service, contact with farm animals, insect bite injuries

- Presence of underlying comorbidities: diabetes mellitus, peripheral vascular disease, cardiovascular disease, chronic wounds on extremities (often open), chronic renal disease, dialysis dependence, intravenous drug use,
  preexisting skin lesions (burns, eczematous dermatitis, etc.).
- Purulent cellulitis
- Hereditary (primary or congenital immunodeficiencies) or iatrogenic neutrophil disorder; immunosuppression.

Risk factor for hospital-acquired MRSA

- Diabetes mellitus
- Long-term care
- Long-term intravascular access
- Prolonged hospitalization
- Dialysis (peritoneal, hemodialysis)

Adopted from:
- Ramakrishnan K, Salinas RC, Higuita NI. Skin and soft tissue infections. American family physician. 2015 Sep 15;92(6):474-83.
- Bechar J, Sepehripour S, Hardwicke J. Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature. The Annals of The Royal College of Surgeons of England. 2017 May;99(5):341-6

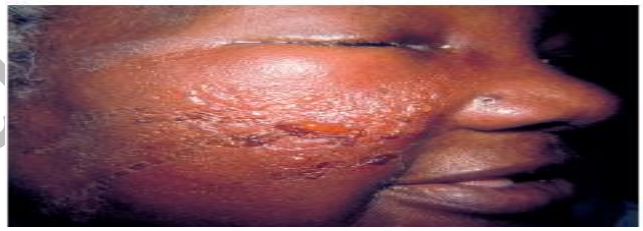
Table 5: Predisposing factors to necrotizing fasciitis
Alcohol abuse
Poor nutrition
Sports participation
Trauma (including surgery)
Diabetes mellitus

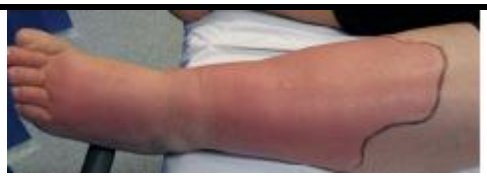
Adopted from:
Ramakrishnan K, Salinas RC, Higuita NI. Skin and soft tissue infections. American family physician. 2015 Sep 15;92(6):474-83.

Bacteriology and Clinical Features of Skin and Soft Tissue Infections

Table 6: Bacteriology and Clinical Features of SSTIs (ordered alphabetically)

Infection	Microbiology	Clinical features and definitions
Abscess (1),(3),(4)	• Often polymicrobial. (3) • Staphylococcus aureus, Streptococcus, and anaerobes.(3)	• **Abscess**: collection of pus with surrounding granulation; painful, tender swelling with induration and often with central fluctuant red nodule; possible overlying skin necrosis; signs or symptoms of infection. (3), (4) • **Cutaneous abscesses**: collections of pus within the dermis and deeper tissues. (1) • **Simple abscess**: induration and erythema should be limited only to a defined area of the abscess and should not extend beyond its borders of the abscess. (1) Additionally, simple abscesses should not have extension into deeper tissues or multiloculated extension.(1)

		• **Complex abscess:** common sites of origin of complex abscesses may be perineal or perianal, perirectal. [1]
Bites (human, animal) [3]	Polymicrobial (Bacteroides, Bartonella henselae, Capnocytophaga canimorsus, Eikenella corrodens, Pasteurella multocida (the most common in human bites), Peptostreptococcus, S. aureus, Streptobacillus moniliformis)	• Cat bites become infected more often than dog or human bites. • Infection sets in 8 to 12 hours after animal bites. • Human bites may transmit herpes, hepatitis, or HIV. • May involve tendons, tendon sheaths, bone, and joints.
Erysipelas, cellulitis [1], [3], (4),(5)	• The pathogens involved are streptococci, S. aureus and Haemophilus influenzae (children) • Erysipelas is commonly caused by Streptococcus spp., usually S. pyogenes. S. aureus rarely causes erysipelas. • Cellulitis associated with abscesses is usually caused by S. aureus. • In contrast, typical (non-purulent) cellulitis is most commonly caused by both streptococcal species and S. aureus. • MRSA is an unusual cause of typical cellulitis	**Erysipelas:** • Acute onset of a red skin lesion. • The lesion is usually painful. • Fever (≥ 38.0 °C) and other signs of systemic infection (e.g. tachycardia, leukocytosis) may be present. • Usually over face, ears, or lower legs. • Distinctly raised inflamed skin.  **Cellulitis** • Acute bacterial infection primarily of the dermal lymphatics and the subcutaneous tissue (the deeper layer of subcutaneous tissue). • It typically presents with local signs of inflammation, such as warmth, erythema, pain, lymphangitis, and frequently systemic upset impact with fever and raised white blood cell count. • The condition can occur anywhere on the body but predominantly affects the skin of the lower part of the legs and feet or the face. • It can be developed in areas of skin breakdown, such as cuts, ulcers, or insect bites

	• In neutropenic and immunocompromised patients, Gram-negative bacteria should be considered	 **Recurrent cellulitis** • For adults who have had treatment in hospital, or under specialist advice, for at least 2 separate episodes of cellulitis or erysipelas in the previous 12 months or over a six-month period. Or patients who have 3–4 episodes of cellulitis per year despite attempts to treat or control predisposing factors. (5) **<u>Erysipelas is distinguished clinically from cellulitis by the following two features (1):</u>** • In erysipelas the lesions are raised above the level of the surrounding skin. • Erysipelas is characterized by a clear line of demarcation between involved and uninvolved tissue.
Erysipeloid (3)		• It is a zoonosis acquired by handling fish, marine animals, swine, or poultry. • One day to 7 days after exposure, a red maculopapular lesion develops, usually on fingers or hands. • Erythema spreads centrifugally, with central clearing. • A blue ring with a peripheral red halo may appear, giving the lesion a target appearance.
Folliculitis(3)	Candida, dermatophytes, Pseudomonas aeruginosa, S. aureus.	• Folliculitis is the name given to a group of skin conditions in which there are inflamed hair follicles. • It presents as tender erythematous papules or pustules, sometimes associated with underlying swelling. • Lesions may be painful or painless. • Tends to occur in areas with increased sweating. • Associated with acne or steroid use.
Furuncle, carbuncle (deep folliculitis) (1), (5),(6)	S. aureus	**Furuncle (boils)** • Furuncles can occur anywhere on hairy skin. • Unlike folliculitis, which is a superficial inflammation confined to the dermis, a furuncle extends deeper into the dermis and subcutaneous tissue. Furuncle appear as a painful inflammatory nodule with overlying pustules through which hair emerges.

		Carbuncle • It is a coalescence of several inflamed follicles into a single inflammatory mass with purulent drainage from multiple follicles. • Carbuncles develop most commonly on the back of the neck, especially in individuals with diabetes. • These are typically larger and deeper than furuncles.
Fournier gangrene (1),(3) (4), (5)	Polymicrobial	• It is a severe type of NSTI involving the genital area (the scrotum and penis or vulva) and/or perineum. • It is considered as cellulitis at the mentioned areas, and signs or symptoms of infection(*) followed by suppuration and necrosis of overlying skin. • The average age at onset is 50–60 years.
Gas gangrene (1), (3) **Clostridial myonecrosis**	• C. perfringens causes 80–90%, of gas gangrene cases. Other species can cause infection, including C. novyi, C. septicum, C. histolyticum, C. bifermentans, C. fallax, and C. sordellii.	• It is type III NSTI. • The infection involves deeper tissue such as a muscle which can lead to a rapidly spreading infection along tissue planes, and patients often present with sepsis. • The fulminant clinical and histological features of an infection with clostridia are mediated by potent bacterial exotoxins, making clostridial myonecrosis the most rapidly spreading and lethal infection in humans. • Clostridial infections usually arise in traumatized tissues. However, it can also arise spontaneously. • Severe pain at injury site followed by skin changes (e.g., pale, bronze, purplish red), tenderness, induration, blistering, and tissue crepitus, diaphoresis, fever, hypotension, and tachycardia.
Impetigo (non-bullous, bullous) (2),(3)	Beta-hemolytic streptococci and S. aureus.	• Common in infants and children; affects skin of nose, mouth, or limbs. • Impetigo begins as erythematous papules that rapidly evolve into vesicles and pustules that rupture, with the dried discharge forming honey-colored crusts on an erythematous base • Bullous impetigo can extend to form vesicopustules. • Bullous lesions may rupture, creating crusted, erythematous erosions, often surrounded by a collar of the roof's remnants. • Vesicles may enlarge (bullae); may spread to lymph nodes, bone, joints, or lung. • Minority of cases: vesicles evolve to form larger bullae (bullous form).

		• Most cases: papules progressing to vesicles and pustules that break to form crusts (non-bullous form). • **Rare complication of impetigo:** post-streptococcal glomerulonephritis**, septicemia, scarlet fever and psoriasis**
Necrotizing STIs (NSTIs) (1),(3)	**Type 1 (polymicrobial)** • Anaerobes (e.g. Bacteroides spp., Clostridium perfringens, Peptostreptococcus spp. or mouth anaerobes when head/neck involved) • Enterobacterales • Pseudomonas spp. • Streptococcus spp. • Staphylococcus aureus (including MRSA) •It is associated with surgical procedures involving the bowel or penetrating abdominal trauma, with infections developed in damaged skin, such as decubitus ulcer or animal bites, with infections at the site of injection in injection drug users, or with a perianal, prostate or vulvovaginal abscess. •Type I infection may be often associated with gas in the tissue and thus is difficult to distinguish from gas gangrene.	• NSTIs are life-threatening, invasive, soft-tissue infections with a necrotizing component involving any or all layers of the soft-tissue compartment, from the superficial dermis and subcutaneous tissue to the deeper fascia and muscle. • Toxin production, cytokine activation, micro thrombosis and ischemia, tissue dysfunction and death, and in turn, greater dissemination of infection is central to the rapidly progressive necrosis seen in NSTIs and differentiates it from that of the other SSTIs. **Necrotizing fasciitis** (2), (3) • Life-threatening necrotizing infection of the deep soft tissues affecting the muscular fascia- the fascia is the connective tissue surrounding the muscle- caused mostly by bacteria and characterized by acute/fulminant necrosis with tissue destruction and systemic signs of toxicity. • It affects subcutaneous tissue; usually affects genitalia, perineum, or lower extremities; severe, constant pain; signs or symptoms of infection*; overlying redness and cutaneous anesthesia; edema and induration of apparently uninvolved tissues; skin crepitus; progression despite antibiotics. • Classification based on: a) Causative pathogen b) Presence or absence of gas in tissues, for example, presence of gas is common in polymicrobial infections Involved site (leg, head and neck, perineum (Fournier gangrene))

	Type 2 (mono-microbial) • The most common pathogens are anaerobic streptococci and S. aureus. Staphylococci and streptococci can occur simultaneously. •Most infections are community-acquired and present in the limbs, with approximately two-thirds of cases in the lower extremities. • Vibrio vulnificus and Aeromonas hydrophilia are the most common Gram-negative bacteria causing type II NSTIs. **Type 3 (gas gangrene)** • Gas gangrene (clostridial myonecrosis) N.B., NSTIs may also be caused by mycotic species, occasionally in immunocompromised patients.	
Pyomyositis (2)	• Staphylococcus aureus (>90%, including MRSA) Some strains can produce the Panton-Valentine leukocidin, a toxin that can cause a more severe disease.	• An infection of a skeletal muscle caused by bacteria usually accompanied by abscess formation. • Symptoms include pain, swelling and fever. • Most common in tropical climates & increased in immunocompromised hosts.

	• Streptococcus spp. (mostly Streptococcus pyogenes). • Escherichia coli (sometimes, especially in oncology patients)	
Pressure ulcer, also known as bedsores, decubitus ulcers and pressure injuries.[1],[7]	• Exposed to Gram-negative and Gram-positive bacterial contamination from fecal material.[1] • Shallow ulcer (superficial): mostly S. epidermidis • Deep ulcer: mixed infections (S. aureus, S. pyogenes or P. aeruginosa with E. coli, enterococci or P. vulgaris) • Lesions appear grayish white when infected by S. epidermidis, yellowish green when infected by *S.* aureus and greenish blue with a sweet–sour odor when infected by *P.* aeruginosa. Mixed infection with anaerobic bacteria causes a brownish color and a foul odor.	• They are localized areas of tissue necrosis developing when soft tissue is compressed between a bony prominence and an external surface for a prolonged period of time. • They are an important problem in critically ill patients, older adults, and in persons with spinal cord injury and are one of the most common types of complex wound. • Pressure ulcers can offer an ideal environment for microbial colonization.
*—Signs and symptoms of infection include fever, tachycardia, diaphoresis, fatigue, anorexia, nausea, and vomiting. Mental status changes and hypotension suggest worsening sepsis and hemodynamic compromise		

Diagnosis Remarks

Table 8: Diagnosis remarks of simple and complicated SSTIs

	Simple SSTIs	Complicated SSTIs
Clinical presentation [3], [5]	• Local signs:Erythema, warmth, edema, and pain over the affected site. [3] • Systemic features of infection may follow, their intensity reflecting the magnitude of infection. [3] • The lower extremities are most commonly involved. [3] • Induration is characteristic of more superficial infections such as erysipelas and cellulitis. [3]	• The diagnosis of fasciitis may not be apparent upon first seeing the patient. [5] • The most important diagnostic feature of necrotizing fasciitis is the appearance of the subcutaneous tissues or fascial planes at operation. [5] • Overlying cutaneous inflammation may resemble cellulitis. However, features that suggest involvement of deeper tissues include: [5] 1. Severe pain that seems disproportional to the clinical findings. 2. Failure to respond to initial antibiotic therapy. 3. The hard, wooden feel of the subcutaneous tissue, extending beyond the area of apparent skin involvement. 4. Systemic toxicity, often with altered mental status. 5. Edema or tenderness extending beyond the cutaneous erythema. 6. Crepitus, indicating gas in the tissues. 7. Bullous lesions. 8. Skin necrosis or ecchymoses.
	• The diagnosis of SSTIs is predominantly clinical. [3] • A complete blood count, C-reactive protein level, and liver and kidney function tests should be ordered for patients with severe infections, and for those with comorbidities causing organ dysfunction. [3]	
Culture [1], [3]	**Blood culture is useful in simple SSTIs only in the following conditions:** [3] • Severe infections or signs of systemic involvement. • Older or immunocompromised patients • Patients requiring surgery.	• Blood culture and wound culture. • Tissue biopsies, which are the preferred diagnostic test for necrotizing SSTIs, are ideally taken from the advancing margin of the wound, from the depth of bite wounds, and after debridement of necrotizing infections and traumatic wounds [3]. • Sterile aspiration of infected tissue is another recommended sampling method, preferably before commencing antibiotic therapy [3].

	Wound cultures are useful in simple SSTIs in the following conditions: Immunocompromised patients and those with significant cellulitis; lymphangitis; sepsis; systemic signs of inflammation; recurrent, persistent, or large abscesses; don`t respond to first line. • Gram stain and culture of pus from carbuncles and abscesses are recommended, but treatment without these studies is reasonable in typical cases [5]	• Pyomyositis: cultures of blood and abscess material should be obtained [5]
Imaging	➢ Imaging studies are not indicated for simple SSTIs, and surgery should not be delayed in suspected severe cases while awaiting imaging. ➢ ➢ Plain radiography, ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI) may show soft tissue edema or fascial thickening, fluid collections, or soft tissue air [3].	➢ MRI is highly sensitive for necrotizing fasciitis, and also it is the recommended imaging modality for establishing the diagnosis of pyomyositis [3],[5]. ➢ Extensive involvement of the deep intermuscular fascia, fascial thickening (more than 3 mm), and partial or complete absence of signal enhancement of the thickened fasciae on post gadolinium images suggest necrotizing fasciitis. ➢ CT scan and ultrasound studies are also useful especially in pyomyositis [5].
➢ Adding ultrasonography to clinical examination in children and adolescents with clinically suspected SSTI increases the accuracy of diagnosing. [3]		

Table 9: Classification and Risk Indicator Score of some SSTIs

Stages of Pressure Ulcer

Stage I
- Nonblanchable erythema
- Skin intact

Stage II
- Possible blister formation
- Partial-thickness skin damage (partial skin loss)

Stage III
- Subcutaneous fat exposed
- Full-thickness skin loss

Stage IV

- Exposed muscles, bones, tendons, or vital organs
- Skin, subcutaneous and possibly more tissue loss

Unstageable

- Entire wound base covered by slough and/or eschar
- Full-thickness skin loss

Deep tissue injury

- Unknown level of tissue injured below skin
- Hidden from observer by intact skin appears as a bruise from above.
- Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear.

Adopted from:
1. Norman G, Dumville JC, Moore ZE, et al. Antibiotics and antiseptics for pressure ulcers. Cochrane Database of Systematic Reviews. 2016(4).
2. BoykoTatiana V, LongakerMichael T, YangGeorge P. Review of the current management of pressure ulcers. Advances in wound care. 2018 Feb 1.

Risk Indicator for Necrotizing Fasciitis

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) [10]

- An LRINEC of six or greater confers a higher risk of necrotizing fasciitis [10]
- With a score of 8 or higher, there is a 75% risk of an NSTI [1]
- Scores <6 were low risk — but not no risk — for necrotizing soft tissue infections [11]
- The LRINEC score has poor diagnostic accuracy for NSTI, and a low score does not rule out the diagnosis [1].
- If high suspicion for necrotizing fasciitis through clinical history and physical exam, do not calculate a LRINEC score, and go straight to operative debridement [11].

Table 10: Laboratory Risk Indicator for Necrotizing Fasciitis [3], [11]

Laboratory value	score
C-reactive protein	
< 15 mg per dL	0
≥ 15 mg per dL	4
Creatinine	
≤ 1.6 mg per dL	0
> 1.6 mg per dL	2
Glucose	
≤ 180 mg per dL	0
> 180 mg per dL	1
Hemoglobin	
> 13.5 g per dL	0
11 to 13.5 g per dL	1
< 11 g per dL	2
Sodium	
≥ 135 mEq per L	0

< 135 mEq per L	2
Total white blood cells < 15,000 per mm^3 15,000 to 25,000 per mm^3 > 25,000 per mm3	 0 1 2

Management of Skin and Soft Tissue Infections in a Hospital Facility

Table 11: Management of SSTIs at Hospital Facility (In patient)

	Management Strategy	Empiric Antibiotic Regimens	Duration
Abscess	• **Empiric broad-spectrum antibiotic therapy with coverage of Gram-positive, Gram-negative, and anaerobic bacteria should be considered (in addition to drainage with incision, culture sensitivity) in the following conditions** [1]. - Moderate: patients with purulent infection with systemic signs of infection e.g., presence of systemic inflammatory response syndrome (SIRS), such as temperature >38°C or 24 breaths per minute, tachycardia >90 beats per minute, or white blood cell count >12 000 or < 400 cells/ µL. [5] - Associated with extensive cellulitis. [3] - Abscess that occurs in children and older adults or in those who have significant comorbid illness. [3] • **An antibiotic active against MRSA is needed in the following conditions:** [5] - Severe abscess: patients who have failed incision and drainage, and oral antibiotic OR have markedly impaired host defenses	**Moderate** • Sulfamethoxazole/ trimethoprim (SMX-TMP). [4], [5] OR • Doxycycline. [4], [5] **Severe** • Vancomycin. [5] OR One of the following: • Linezolid [5] • Daptomycin [5] • Ceftaroline. [1] **Perianal and perirectal abscesses** [1] • Ceftriaxone OR • Cefotaxime. COMBINED WITH • Metronidazole OR (single agent of:) • Piperacillin/tazobactam **A) If beta-lactam allergy:** • Ciprofloxacin COMBINED WITH • Metronidazole **B) If risk for CA-MRSA or who do not respond to first-line therapy or worsen after 48 hours, add one of following intravenous antibiotics:** • Vancomycin. [1] OR	It is recommended that the duration of treatment for most bacterial SSTIs should be for 7–14 days. [5] **Perianal and perirectal abscesses** • Antibiotic therapy for 5 days in selected patients. • It may be extended up to 7–10 days if lack of symptom resolution at 5 days. [1]

	(Immunocompromised patients). [3], [5] OR Those with SIRS and hypotension. [5] **Perianal and perirectal abscesses** • Perianal and perirectal abscesses are typically well-circumscribed and respond to incision and drainage.	• Linezolid. [1]	
Burn wounds [1]	• Topical antimicrobial agents should be used in conjunction with appropriate basic wound care. • Early initiation of dressings and effective topical antimicrobial therapy. • Daily inspection of the wounds by a qualified surgeon. • Early excision of all full thickness and deep partial thickness burns. • systemic antimicrobials are typically reserved for septic patients or those with invasive burn wound infections. • Graft and coverage options.	• Ceftriaxone or cefotaxime COMBINED WITH • Metronidazole OR (single agent of:) • Piperacillin/tazobactam **If risk for CA-MRSA or who do not respond to first-line therapy** • Vancomycin OR • Linezolid **If risk for MDR G-** Carbapenems +/− aminoglycoside	
Cellulitis and Erysipelas	• Hospitalization is recommended in the following conditions: [3],[5] - There is concern for a deeper or necrotizing infection - Patients with poor adherence to therapy	**Erysipelas or cellulitis (non-purulent), moderate infection** [1], [5] • Cefazolin OR • Amoxicillin-clavulanate. OR • Ceftriaxone. **Erysipelas or cellulitis (non-purulent), moderate at risk for**	• The recommended duration of antibiotic therapy for hospitalized patients is 7-14 days.[3] • A longer course length (up to 14 days in total) may be needed based on

	- Infection in a severely immunocompromised patient - Failed outpatient treatment (moderate or severe) - Unstable comorbid illnesses - Signs of systemic sepsis - If surgical intervention under anesthesia. • N.B., Purulent cellulitis: Incision and drainage are recommended as primary management for abscesses with associated cellulitis. In these cases, antibiotics are generally suggested. (1) • Systemic antibiotics are indicated in the following conditions: - Moderate infection: typical cellulitis/erysipelas with systemic signs of infection. (5) - Severe infection: patients who have failed oral antibiotic treatment or those with systemic signs of infection, or those who are immunocompromised, or those with clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction. (5)	**CA-MRSA** including critically ill and immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line, add one of following intravenous antibiotics: (1), (4) • Vancomycin OR • Linezolid **Purulent cellulitis** One of the following intravenous antibiotics: (1) • Vancomycin OR • Linezolid **In patients at risk for Gram-negative infection and MRSA (polymicrobial) or severe infection (erysipelas/cellulitis purulent or non-purulent):** patients who do not respond to first line therapy or those with systemic signs of infection, or those who are immunocompromised, or those with clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction: • Vancomycin (1), (5) + • Piperacillin/Tazobactam (1), (5) • If monomicrobial: (5) *Streptococcus Pyogenes* or *Clostridial sp.*:	clinical assessment. However, skin may take some time to return to normal, and full resolution of symptoms at 5 to 7 days is not expected. (12) • Intravenous antibiotics should be continued until the clinical picture improves, the patient can tolerate oral intake, and drainage or debridement is completed. (3)

		• Penicillin + • Clindamycin *Vibrio vulnificus*: • Doxycycline + • Ceftazidime *Aeromonas hydrophila*: • Doxycycline + • Ciprofloxacin	
Necrotizing fasciitis	• Treatment of necrotizing fasciitis involves early recognition and surgical consultation for debridement of necrotic tissue combined with empiric high-dose intravenous broad-spectrum antibiotics [3], [5]. • The antibiotic spectrum can be narrowed once the infecting microbes are identified and susceptibility testing results are available [3]. • Patients may require repeated surgery until debridement and drainage are complete and healing has commenced [3],[5] • It should include agents effective against both aerobes, including MRSA, and anaerobes. [5],[4] • Empiric coverage against fungi should be started in high-risk patients [1].	• Vancomycin [4], [5], [13], [14] OR • Linezolid [4], [5] COMBINED WITH (one of the following) • Piperacillin/tazobactam [5], [14] • Meropenem • Imipenem/cilastatin [5], [14] • Ceftriaxone [5] COMBINED WITH (Metronidazole [5] • For the treatment of necrotizing fasciitis, some experts prefer the addition of a bacteriostatic that inhibits toxin production such as one of the following: - Clindamycin (would be added to vancomycin, not replace vancomycin) [2], [14] • If monomicrobial: [5] *Streptococcus Pyogenes* or *Clostridial sp.*: • Penicillin + • Clindamycin *Vibrio vulnificus*:	• Antimicrobial therapy should be administered until further debridement is no longer necessary, the patient has improved clinically, and fever has been absent for 48–72 hours [5]. • The recommended duration of antibiotic therapy for hospitalized patients 7-14 days extending to 6 weeks if joint is involved [3] • Intravenous antibiotics should be continued until the clinical picture improves, the patient can tolerate oral intake, and drainage or debridement is completed [3].

		• Doxycycline + • Ceftriaxone or cefotaxime *Aeromonas hydrophila*: • Doxycycline + • Ciprofloxacin • Note: empiric treatment for necrotizing fasciitis based on some other references, use one of the following: (2) - Piperacillin-tazobactam + clindamycin - Ceftriaxone and metronidazole - If MRSA suspected, consider adding vancomycin	• Most patients with necrotizing fasciitis should return to the operating room 24–36 hours after the first debridement and daily thereafter until the surgical team finds no further need for debridement. • Although discrete pus is usually absent, these wounds can discharge large amounts of tissue fluid, and aggressive fluid administration is a necessary adjunct (5)
Pyomyositis (5)	• Early drainage of purulent material should be performed. • Repeated imaging studies should be performed in the patient with persistent bacteremia to identify undrained foci of infection. • Antibiotics should be administered intravenously initially, but once the patient is clinically improved, oral antibiotics are appropriate for patients in whom bacteremia cleared promptly and there is no evidence of endocarditis or metastatic abscess.	**Initial empirical therapy:** Vancomycin An agent active against enteric gram-negative bacilli e.g., Piperacillin/tazobactam should be added for infection in immunocompromised patients or following open trauma to the muscles. Cefazolin Recommended for treatment of pyomyositis caused by MSSA.	• 2 to 3 weeks of therapy is recommended. (2),(5)
Pressure ulcers (1), (7)	• Standard care for adults with pressure ulcers includes a correct prevention and management.	• If there are signs of systemic infection, a second-generation cephalosporin antibiotic should be selected until the results of	

	• Prevention of pressure ulcer formation is directed at alleviating the risk factors for the individual patient, and is primarily focused on minimizing episodes of prolonged pressure either by placing appropriate padding at pressure points or by frequent patient repositioning. • Debridement of devitalized tissue and biofilm and abscess drainage are necessary in the treatment of pressure ulcers • Systemic antibiotics should be administered only when there are systemic signs of serious infection, spreading cellulitis (deep skin infection) or underlying osteomyelitis.	bacterial culture become available. • Once the causative bacteria are identified, it is important to select agents with limited spectrum based on antibiogram results of antibiotic sensitivity testing. • If antibiotics are not effective, their use should not be continued aimlessly, but rather the causative microorganisms and their foci (e.g. is there an abscess below the ulcer, is there sepsis) should be reevaluated. • If an MRSA infection is suspected, the drug should be promptly changed to an anti-MRSA drug. [7] **Topical agents which should be used as local treatments for controlling infection:** Silver sulfadiazine, iodine ointment. [7]	
N.B.,In some patients, cutaneous inflammation and systemic features worsen after initiating therapy, probably because sudden destruction of the pathogens releases potent enzymes that increase local inflammation.[5]			

Management of Skin and Soft Tissue Infections in Primary Health Care and Outpatients

Table 12: Management of SSTIs at Primary Health Care and Outpatient

	Management Strategy	Empiric Antibiotic Regimens	Duration of Antibiotic Regimen
Abscess (1), (3), (5)	**Antibiotic therapy (in addition to incision, drainage, culture sensitivity), should be prescribed for:** - Abscesses greater than 5 cm. (1) - in an area difficult to drain (e.g., face, hand, and genitalia). (1), (3) - If there is lack of response to incision and drainage alone. (1) - If there are multiple localizations. (1) - Patients with immunosuppression. N.B., Incision and drainage of superficial abscesses rarely causes bacteremia, and thus prophylactic antibiotics are not recommended. (5)	One of the following: • Amoxicillin-clavulanate. (1) • Cephalexin. (1) **If risk for CA-MRSA** including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to first line therapy: Add One of the following: • Doxycycline. (1) • SMX-TMP. (1) **In patients with beta-lactam allergy:** • Clindamycin. (1) **Perianal and perirectal abscesses** (1) a) Outpatient therapy or step-down: • Amoxicillin/clavulanate b) Outpatients with beta-lactam allergy • Ciprofloxacin COMBINED WITH • Metronidazole c) Outpatients at risk for CA-MRSA or who do not respond to first-line therapy or worsen after 48 hours add one of following oral antibiotics: One of the following: • Doxycycline. (1) • SMX-TMP. (1)	**Simple abscess** • Antibiotic therapy for 5 days in selected patients. • It may be extended up to 7–10 days if lack of symptom resolution at 5 days. (1) **Recurrent abscess**: • Systemic antibiotic for 5-10 days. • Decolonization for 5 days

		Recurrent Skin Abscesses [5] Course of an antibiotic active against the pathogen isolated. Consider a decolonization regimen of intranasal mupirocin, and daily chlorhexidine washes.	
Bites (human & animal) (1), (3), (5), (15)	Antimicrobial therapy should be used for: - Moderate to severe injuries, especially to the hand or face. - Injuries that may have penetrated or in proximity to the bone or joint capsule. - Associated crush injury. - Associated edema (either preexisting or subsequent) of the affected area. - Immunocompromised hosts. - A splenic. - Advanced liver disease • Irrigation of the wound and debridement of necrotic tissue is needed. • Primary wound closure is not recommended for bite wounds, with the exception of those to the face, which should be managed with copious irrigation, cautious debridement, and preemptive antibiotics. [5] • A patient who has sustained a bite should always confirm that their tetanus booster is up to date. • Tetanus toxoid should be administered to patients without toxoid vaccination within 10 years. • Postexposure prophylaxis for rabies may be indicated;	One of the following: • Amoxicillin/clavulanate. [3], [15] • Cefazolin • Cephalexin • Clindamycin • Doxycycline (oral or intravenous) • SMX-TMP **Cat scratch disease** • Azithromycin	• Antibiotic therapy for 5 days. • Therapy may be extended up to 7–10 days if lack of symptom resolution at 5 days. [1] • **Cat scratch disease:** 5 days [5]

	consultation is recommended to determine if vaccination should be initiated.		
Burn wounds (1)		**a) <u>Outpatient therapy or step-down</u>** Amoxicillin/clavulanate b) <u>Outpatients with beta-lactam allergy</u> Ciprofloxacin COMBINED WITH Metronidazole c) <u>Risk for CA-MRSA or who do not respond to first-line therapy</u>: One of the following: Doxycycline. (1) SMX-TMP. (1)	
Carbuncle, Furuncle, and Folliculitis	• Incision and drainage are the recommended treatment for carbuncles, and large furuncles. (5) • Furuncles often rupture and drain spontaneously or following treatment with moist heat. (5) • Excision of carbuncle with primary split-thickness skin grafting is an alternative treatment modality. (1) • The antibiotics against staph (in adjunct to incision and drainage) should be used in moderate infection in the following conditions: systemic inflammatory response syndrome (SIRS), such as temperature >38°C or 24 breaths per minute, tachycardia >90 beats per minute, or white	**<u>Folliculitis</u>** Topical antibiotics (e.g., mupirocin, retapamulin). (3) **<u>Furuncle, carbuncle</u>** <u>Moderate:</u> One of the following: • Doxycycline. (4), (5) • SMX-TMP. (4), (5) <u>Severe:</u> One of the following: • Vancomycin. (5) OR • Linezolid. (5)	

	blood cell count >12 000 or <400 cells/µL. [5] • An antibiotic active against MRSA is recommended for patients with severe infection: who have failed initial antibiotic treatment or have markedly impaired host defenses or in patients with SIRS and hypotension. [5]		
Cellulitis and Erysipelas	• Outpatient therapy is recommended for patients who do not have SIRS, altered mental status, or hemodynamic instability (mild nonpurulent) [1],[5] • Incision and drainage needed in purulent cellulitis. • Typical cases of mild cellulitis without systemic signs of infection should receive an antimicrobial agent that is active against streptococci. [5] • For cellulitis with systemic signs of infection (moderate nonpurulent), systemic antibiotics are indicated [5] **Recurrent cellulitis:** [5] • Identify and treat predisposing conditions such as edema, obesity, eczema, venous insufficiency, and toe web abnormalities.	Erysipelas or cellulitis outpatient therapy or step down or mild infection: typical cellulitis/ erysipelas (non-purulent or purulent) One of the following: • Amoxicillin/clavulanate, [1], [2] • Cephalexin [1], [2], [4], [5] • Clindamycin [5] If penicillin allergy: [12] • Doxycycline Moderate: [4], [5] • Cefazolin • Clindamycin OR • Ceftriaxone • Cefuroxime Outpatients at risk for CA-MRSA a) Non- purulent cellulitis / erysipelas: including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line therapy. [1]	• Antibiotic therapy for 5 days, therapy may be extended up to 7-10 days if lack of symptom resolution at 5 days. [1],[3],[5] • In medically stable patients with cellulitis, patients who fail outpatient oral therapy can be treated with 3 days of outpatient IV therapy and conversion to oral therapy for an additional 7 days [4] **Recurrent Cellulitis** The antibiotics should be continued so long as the predisposing factors persist. [5]

		b) <u>Purulent cellulitis / erysipelas</u> in a region or a population with a high prevalence of CA-MRSA, where > 10% of clinical S. aureus isolates are MRSA isolates. For (a) or (b), **add** one of the following oral antibiotics: • Doxycycline. [1] • SMX-TMP. [1] **<u>Recurrent cellulitis:</u>** • Administration of prophylactic antibiotics, such as oral penicillin for 4–52 weeks, or intramuscular benzathine penicillin every 2–4 weeks.	
Erysipeloid [5]		• Amoxicillin **For those intolerants to penicillin:** Cephalosporins, clindamycin, or fluoroquinolones. [5]	7–10 days. Untreated erysipeloid resolves over about 3–4 weeks, but treatment probably hastens healing and may reduce systemic complicaptions
Impetigo [2], [5]	• Bullous and non-bullous impetigo can be treated with oral or topical antimicrobials. • Oral therapy is recommended for patients with numerous lesions or in outbreaks affecting several people to help decrease transmission of infection. Treatment for ecthyma should be an oral antimicrobials.[5]	• Localized non-bullous impetigo: Topical treatment is preferred over an oral antibiotic, whenever possible. For example, mupirocin 2% ointment. [2] • For impetigo requiring oral antibiotics or ecthyma: • Amoxicillin/clavulanate. [2] • Cephalexin [2], [5] • Clindamycin [2] When MRSA is suspected or confirmed: One of the following: Doxycycline. [5] SMX-TMP. [5] Clindamycin [5]	• Ointments of mupirocin or retapamulin twice daily for 5 days. Oral therapy for ecthyma or impetigo should be a7-day.

Management of Wound Infections

- Adjunctive systemic antimicrobial therapy is not routinely indicated, but in conjunction with incision and drainage may be beneficial for surgical site infections if there is a significant systemic response in the following conditions: erythema and induration extending >5 cm from the wound edge, temperature >38.5°C, heart rate >110 beats/minute, or white blood cell (WBC) count >12 000/µL.[5]
- A brief course of systemic antimicrobial therapy is indicated in patients with wound infections following clean operations on the trunk, head and neck, or extremities that also have systemic signs of infection. [5]
- A first-generation cephalosporin or an antistaphylococcal penicillin for MSSA, or vancomycin, linezolid, daptomycin where risk factors for MRSA are high (nasal colonization, prior MRSA infection, recent hospitalization, recent antibiotics), is recommended. [5]
- Agents active against gram-negative bacteria and anaerobes, such as a cephalosporin or fluoroquinolone in combination with metronidazole, are recommended for infections following operations on the axilla, gastrointestinal tract, perineum, or female genital tract. [5]

Table 13: Management of Incisional Wound Infections

Incisional Wound Infections	Empiric Antibiotic Regimens
Surgery of Intestinal or Genitourinary Tract	One of the following regimens: Regimen 1: • Ceftriaxone COMBINED WITH • Metronidazole Regimen 2: • Ampicillin-sulbactam COMBINED WITH • Gentamicin Regimen 3: One of the following: • Piperacillin-tazobactam • Imipenem-cilastatin • Meropenem
Surgery of trunk or extremity away from axilla or perineum	One of the following: • Cefazolin • Cephalexin • SMX-TMP
Surgery of axilla or perineum	Metronidazole COMBINED WITH one of the following: Ciprofloxacin, Levofloxacin Ceftriaxone May also need to cover for MRSA with Vancomycin

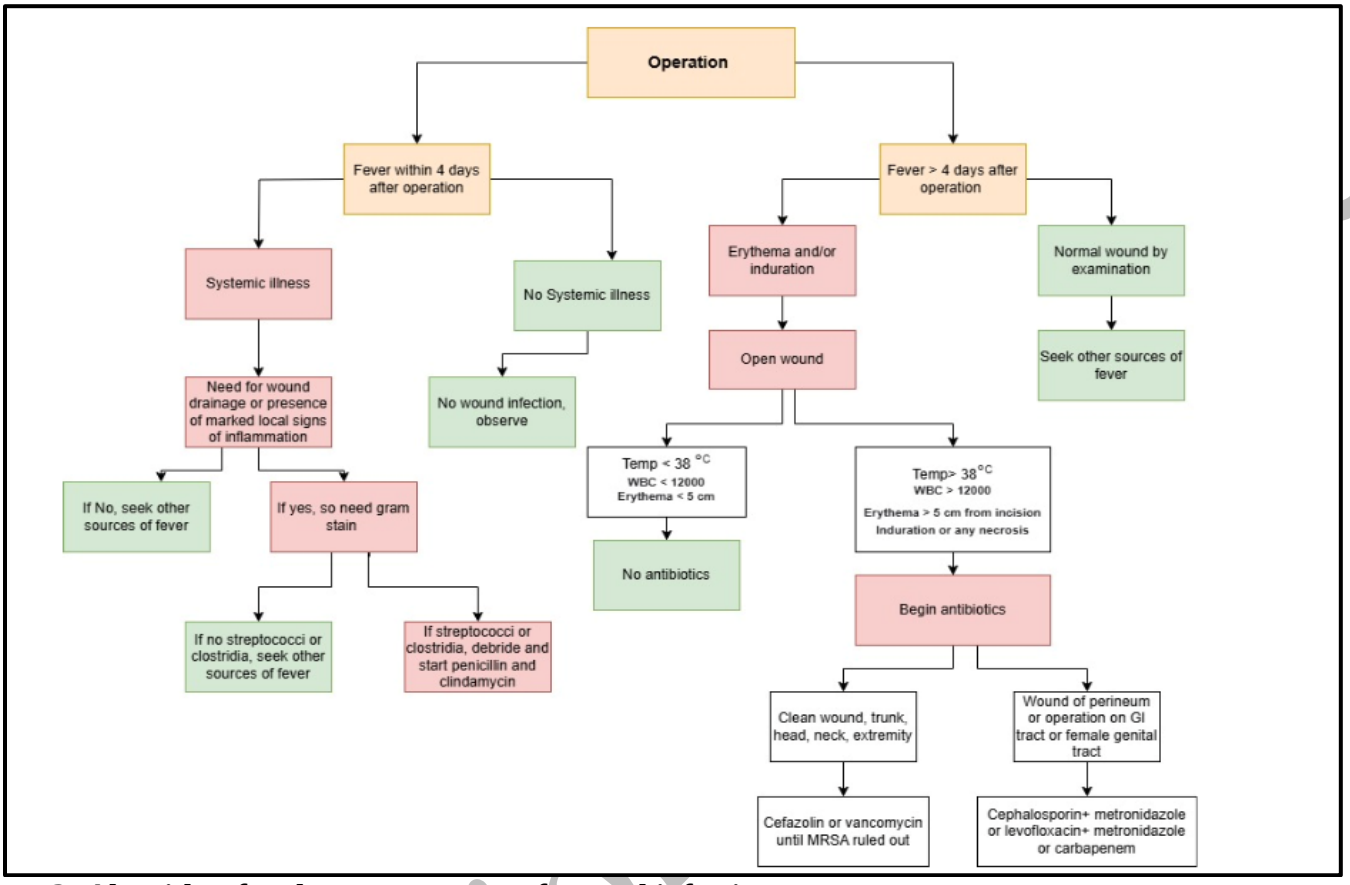


Figure 3: Algorithm for the management of wound infection.

Adopted from: Stevens DL, Bisno AL. et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clinical infectious diseases. 2014 Jul 15;59(2):e10-52.

Appendix 1: Antibiotics used for SSTI treatment (special considerations) [1]

Clindamycin	➢ Has been used to treat community acquired (CA-MRSA). ➢ Like penicillin, clindamycin has activity against group A and B streptococci and S. aureus. ➢ It has no activity against Gram-negative bacteria. ➢ Clindamycin resistance is now very common. ➢ Bacteriostatic. ➢ It inhibits toxin production. Its use is at high risk for the development of Clostridioides difficile infection
TMP-SMX **Doxycycline**	➢ Effective against CA-MRSA. ➢ They have no activity against group A and B streptococci.
Vancomycin	Used for: ➢ Complicated Gram-positive infections. ➢ Treatment of infections caused by MRSA.
Linezolid	➢ It has been considered an agent of choice in complicated SSTIs. ➢ It has the advantages to be a lipophilic drug with possibility of early intravenous-to- oral switch with the oral preparation having very high bioavailability ➢ It inhibits toxin production.
Daptomycin	➢ Has proven efficacy in patients with gram positive complicated SSTIs, including those caused by MRSA. ➢ Achieves very good concentrations in the skin and soft tissues. ➢ has a rapid bactericidal effect
Ceftaroline	➢ Advanced-generation broad-spectrum cephalosporin which has in vitro activity against both MSSA and MRSA. ➢ It has been found to be similar efficacy compared to vancomycin plus aztreonam for the treatment of cSSTI.

If coverage for both streptococci and MRSA is desired for oral therapy, one of the following options are needed:

- Clindamycin, linezolid or tedizolid alone or
- The combination of (TMP-SMX or doxycycline) with (a beta-lactam agent (e.g., amoxicillin, cephalexin) or azithromycin in the case of beta-lactam allergy). [1]

Appendix 2: Dosage of Antibiotics in Skin and Soft Tissue Infections in Adults

Antibiotics	Dosage
Amoxicillin/ clavulanate	875/125 mg bid po [5] or 1 g/ 8 hrs [1]
Cefazolin	250 to 500 mg IV or IM every 8 hours (500 to 1,500 mg IV or IM every 6 to 8 hours for moderate to severe infections)[3] .

Cefotaxime	2 g IV every 6 hours [3] or 1 gm /12 for mild infection or 1 to 2 g every 8 hours[15]
Ceftaroline	600 mg IV every 12 hours. [3]
Ceftriaxone	1 to 2 g IV every 24 hours. [3] , 1 gm /12 hr (bite)
Cephalexin	500 mg orally 4 times per day [3] Cellulitis (nonpurulent)/erysipelas, mild: Oral: 500 mg 4 times daily. [15] Cellulitis, long-term suppression of recurrent infection: 500 mg two to four times daily. [15] Impetigo or ecthyma Oral: 250 to 500 mg 4 times daily.[15]
Cefuroxime	750 mg to 1.5 g three or four times a day IV. [12] Initial therapy for mild infection or step-down therapy after parenteral treatment 500 mg twice daily). [15]
Clindamycin	300–400 mg 4 times per day po. [3], [5] 150 to 450 mg orally 4 times per day (300 to 450 mg orally 4 times per day.[3] 300 mg 4 times daily or 450 mg 3 times daily. [15] MRSA: 600-900 mg every 8 h IV or 300 mg 4 times daily or 450 mg 3 times. [5] 150mg once in long term suppression of recurrent cellulitis. [5]
Doxycycline	100 mg orally or IV 2 times per day. [3],[15]
Daptomycin	4-6 mg per kg IV once daily. [3],[15]
Fluoroquinolones	Ciprofloxacin: 750 mg orally 2 times per day (500mg/8 hrs for abscess) or 400 mg IV 2 times per day.[1],[3] Moxifloxacin, 400 mg orally or IV per day.[3]
Imipenem/cilastatin	1 g IV every 6 to 8 hours. [3] Non-necrotizing infection: IV: 500 mg every 6 hours.[15]
Linezolid	600 mg IV or orally every 12 hours
Metronidazole	500 mg IV/oral every 8 hours. [3] 500 mg IV /6 hours (Necrotizing infection). [15]
Mupirocin	2% ointment applied 3 times per day. [3]
Meropenem	1 g IV every 8 hours
Penicillin plus clindamycin (for Streptococcus Pyogenes or Clostridial sp)	2 to 4 million units of penicillin IV every 6 hours plus 600 to 900 mg clindamycin IV every 8 hours. [3]
Piperacillin/ tazobactam	3.375 g every 6 hours **or** 4.5 g every 8 hours. [15]
Retapamulin	1% ointment applied twice daily. [3], [5]
Tigecycline	100 mg IV followed by 50 mg IV every 12 hours. [3], [5]
SMX-TMP	1 or 2 double-strength tablets 2 times per day. [3], [5]
Vancomycin	15-20 mg per kg IV every 12 hours. [3], [5], [15]

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