

Cellulitis

Cellulitis is an acute skin and soft tissue infection (SSTI). It involves the deeper dermal and subcutaneous layers, which, when infected, are typically painful, red, warm and swollen. If left untreated, the infection can spread to other areas. An infection usually follows a break in the skin, which could be due to a fissure, cut, laceration, puncture wound or bite. Since bacteria can enter even a very small opening, it is not uncommon for patients to be unaware of a specific causative injury.

Incidence and Impact

Since cellulitis is not a reportable disease, it is difficult to determine an exact incidence. However, it is widely reported that cellulitis and other SSTIs are among the most common infections treated in hospitals. With the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA), the incidence of ambulatory care visits, emergency room visits, and hospitalizations for SSTIs is significant and rising.^{1,2} The literature estimates the incidence as between 2 and 3 cases per 100 persons, or about two cases per 1,000 patient-years.³ At one large institution, hospitalizations for SSTIs are now more common than those for community-acquired pneumonia.⁴

Causative Organisms

The microbiologic cause of cellulitis depends in part on host factors and on the nature of the injury to the

skin. By far, group A streptococci — *Streptococcus pyogenes* and *Staphylococcus aureus* — are the most common causative organisms of cellulitis in patients with normal immune systems. Empiric treatment is generally directed toward these pathogens. Importantly, initial therapy must also consider coverage of methicillin-resistant *Staphylococcus aureus*, as this is an ever-increasing cause of community-acquired cellulitis.⁵ It is also important for the clinician to consider all risk factors and the cause of the injury. For example, non-group A streptococci are a common cause of cellulitis in patients with lymphatic obstruction, or who have had a venectomy for coronary artery bypass graft. Cellulitis may result from specific pathogens such as *Pasturella multocida* after a dog or cat bite. Infection from a pathogen such as *Erysipelothrix rhusiopathiae* may result after injury by a saltwater fish or the handling of meat or poultry; infection from *Aeromonas hydrophila* (a gram-negative rod) may result from exposure to fresh water.

Patients who are immunocompromised, such as transplant recipients, oncology patients and the elderly, may develop cellulitis due to infection with other organisms, including gram-negative bacilli (such as *Pseudomonas*, *Proteus*, *Serratia*, *Enterobacter*, and *Citrobacter*), anaerobes, other opportunistic pathogens (such as *Helicobacter cinaedi* and *Fusarium* species), mycobacteria,

and fungi (such as *Cryptococcus*), although fungal infections are rare. *Pneumococcus* may cause a particularly malignant form of cellulitis, typically in an immunocompromised host, and is frequently associated with tissue necrosis, pus, and sepsis.

Risk Factors

The body's normal response to any site of pathogen invasion is inflammation. White blood cells, lymphocytes, and other cells flow to the site to destroy the bacteria. Risk factors for cellulitis, then, include various disease states that limit the flow of blood to the site. These can include: diabetes; collagen vascular diseases; atherosclerosis as well as impaired circulation secondary to arterial insufficiency; venous stasis; and lymphadenectomy following tumor excision, such as mastectomy or venectomy. Additional risk factors are listed in Table 1. Of note, although varicella is a viral illness, a secondary bacterial cellulitis can develop around the viral lesions, which mandates aggressive antibiotic treatment to prevent gangrene.

Table 1

Risk Factors of Cellulitis

- Immunodeficiency
- Varicella
- Other systemic illness
- Chronic steroid use
- IV drug use
- Skin disorders

High-risk Cellulitis

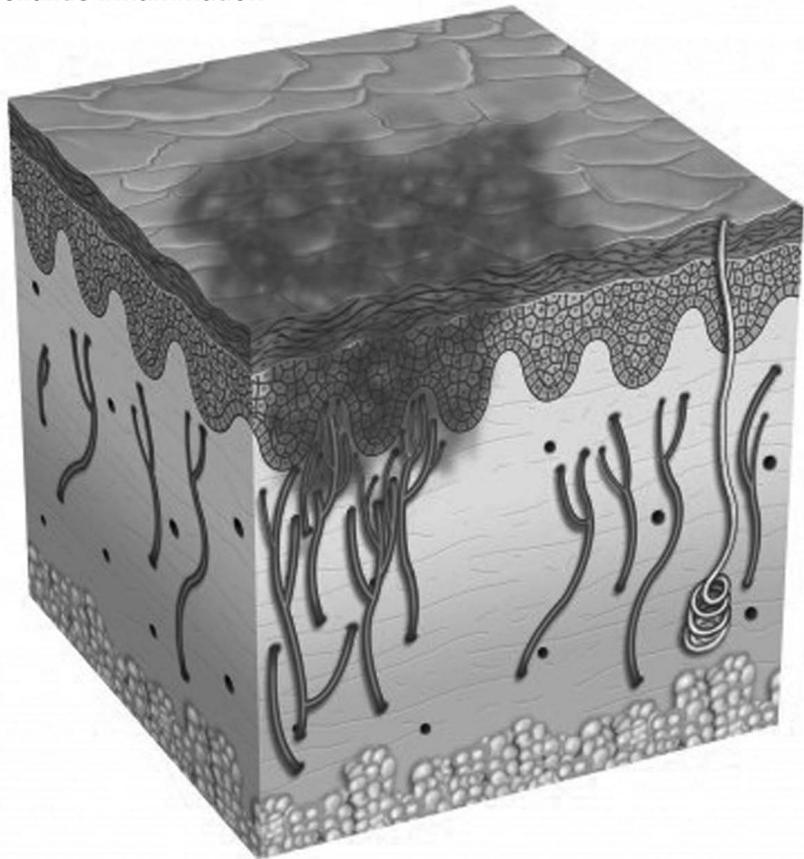
High-risk cellulitis includes facial, periorbital and orbital infection, as well as cellulitis from animal or human bites.

Because of its proximity to the eyes and brain, facial cellulitis is particularly high-risk. Facial cellulitis can progress to orbital cellulitis and its associated potential complications such as blindness and meningitis. In adults, facial cellulitis normally appears after an episode of pharyngitis with fever. Patients present with progressive anterior neck swelling, tenderness, erythema, and dysphagia. Children under 5 years of age are most susceptible to facial cellulitis. The most common causative organism in patients between 6 months and 3 years of age is *Haemophilus influenzae*, likely resulting from local mouth trauma or otitis media.

Another high-risk infection site is around the eyes. It may be preseptal (periorbital) or postseptal (orbital) cellulitis, depending on where the infection is occurring. The orbital septum is the seal that circles the globe of the eye and separates the mucous membranes of the lids and the sclera from the deeper attachments of the eye muscles. It is an important anatomical landmark because it determines the direction of venous drainage. In the preseptal region, the veins drain directly back to the body circulation through facial veins. In the postseptal region, the veins drain into the intracranial cavity. Periorbital/preseptal cellulitis, the more common infection, is limited to the eyelids, external to the orbital septum. Sinusitis, upper respiratory infections, and eye trauma may predispose to preseptal cellulitis, with staphylococci and streptococci being the most common causative pathogens in adults, and *H. influenzae* the most common in children.

Orbital/postseptal cellulitis is an infection of tissues behind the

Cellulitis Inflammation



orbital septum. Rarely seen, it is typically caused by extension of sinusitis or periorbital cellulitis and is more likely to be seen in children than adults. The infection may be complicated by persistent blindness, limitation of eye movement, diplopia, and abscess formation. It has been reported that as many as 11% of cases of orbital cellulitis result in loss of vision.⁶ Postseptal cellulitis is an ocular emergency and requires prompt diagnosis, hospitalization, and aggressive management including IV anti-infectives. Given that the primary cause of orbital cellulitis is *Streptococcus pneumoniae* and other streptococci, *Staphylococcus aureus*, and *Haemophilus influenzae*, intravenous antibiotics with coverage for those pathogens should be started. Since MRSA in orbital cellulitis is also rising, empiric therapy should include coverage for MRSA. The antibiotic regimen empirically chosen may be adjusted depending on the results of a

culture and sensitivity (if available) and response to therapy. Surgery may be required to drain infected sinuses or abscesses.

Diagnosis

The diagnosis of cellulitis is based primarily on history and clinical presentation, differentiating between simple, complex, and high-risk cellulitis. It is important to identify the cause of a break in the skin, what the potential pathogenic exposure is, and what comorbidities or other risk factors exist. For example, did the patient have a recent traumatic event? Recent surgery? Prior surgery involving lymph node dissection? Coronary artery bypass? Does the patient have a history of IV drug abuse? What is the patient's work environment? Was the patient recently in a river, lake, or ocean? Unfortunately, blood cultures or cultures of needle aspiration rarely identify causative organisms.

Inflammation with erythema, warmth, edema, and pain are the fundamental basics of the clinical diagnosis of cellulitis. *Simple cellulitis* typically presents with a slow onset of localized symptoms, indicating a limited amount of tissue involvement, and non-palpable margins.

In addition to the aforementioned signs and symptoms, more complex presentations of cellulitis can include lymphangitis (associated red streaking visible in the skin proximal to the area of cellulitis, which indicates spread through the lymphatic system), regional lymphadenopathy, and fever and chills. The presence of purplish vesicles or blisters (bullae) suggests infection with *Streptococcus pneumoniae*. Blood tests such as a white blood cell count, sedimentation rate, and C-reactive protein are often performed. A CT scan, MRI or x-ray may be ordered to rule out underlying fasciitis or osteomyelitis. An x-ray may also be used to rule out crepitus. An ultrasound may be ordered not only to assess the degree of suppuration,

but also as a guide when a needle aspiration is performed.

Treatment

Initiating timely, appropriate antibiotic therapy is critical to supporting positive outcomes. Early and effective treatment reduces mortality, hospital length of stay, and inpatient costs.⁷ Guidelines for selecting a specific anti-infective have been published by the Infectious Diseases Society of America and pertain to the:

- Depth of infection (e.g., lymphadenitis, marked edema, and/or crepitus)
- Proximity to vital tissues or organs (e.g., facial or periorbital cellulitis)
- Source of injury (e.g., high-risk animal or human bites)
- Presence of comorbidities (e.g., wound infection or diabetes)
- Presence of systemic toxicity (e.g., nausea, vomiting, fever, chills, hypotension, or rapidly progressing symptoms)

- Culture results (commonly unobtainable)^{8,9}

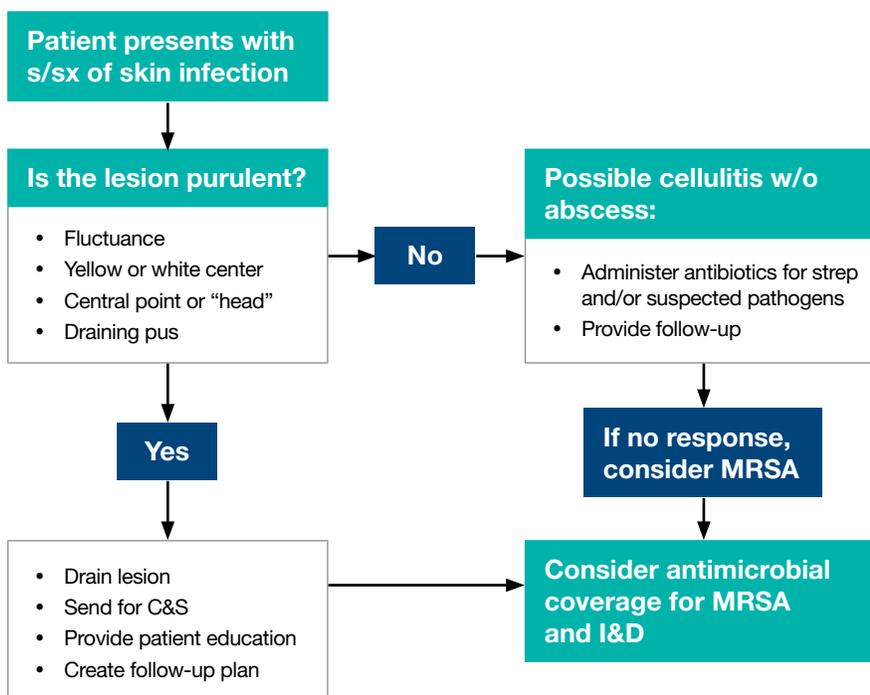
Generally, when the infection involves soft-tissue structures that are anatomically deeper, has a close proximity to a vital organ, and/or is exhibiting symptoms of systemic toxicity, parenteral anti-infective therapy will likely be required.

Patients with a mild or simple cellulitis can typically be treated as outpatients with oral antibiotics for about seven days. Some clinicians will choose an initial IV antibiotic dose with a switch to an oral agent. No matter what the initial route, it is important to reevaluate the patient within 24 to 48 hours. If there is no sign of improvement, hospital admission may be necessary.

Patients with high-risk conditions are often initially treated with IV antibiotics and potentially transitioned to oral administration when adequate clinical response is achieved. Site-of-care options must include home infusion in lieu of hospitalization if the patient is clinically stable and otherwise an appropriate candidate for home infusion. Hospitalization is necessary for patients who:

- Are not responding to therapy,
- Have rapidly progressive infections,
- Are hemodynamically unstable,
- Raise clinical suspicion of sepsis,
- Are dehydrated,
- Are non-compliant, or
- Require surgical intervention.

Sample Algorithm for Cellulitis Care



Related Skin Conditions

Erysipelas

Erysipelas is a generally benign skin infection most commonly caused by group A beta-hemolytic streptococci. The infection is more superficial than cellulitis, involving the dermis and lymphatics. Erysipelas is characterized by

intense erythema, induration, and a sharply demarcated border, which further differentiates it from cellulitis. Patients with erysipelas also present with what is termed an orange peel, or “peau d’orange,” appearance at the site of infection. The skin puckers due to the significant amount of dermal edema that lifts the skin while hair follicles or sweat glands hold it down.

Symptoms include an abrupt onset of fever and chills, with an ensuing painful rash and irregular erythema in one to two days. Patients often present with more systemic manifestations of infection as well, such as muscle and joint pain, nausea, and headache. Diagnosis is typically made by clinical exam, although an attempt may be made to collect a blood culture.

Because of the potential for rapid progression, prompt treatment with antibiotics is essential. Intravenous antibiotics effective against group A beta-hemolytic streptococci and staphylococci are usually indicated in all but the mildest of cases. Patients may be able to be transitioned to oral antibiotics once their symptoms improve and they are clinically stable.

Necrotizing Fasciitis

While rare, necrotizing fasciitis (NF) is a particularly fulminant SSTI, with infection involving the dermal, fascial, and subcutaneous layers of the skin. NF can be caused by a number of aerobic or anaerobic microorganisms. This infection can spread rapidly along fascial planes, causing necrosis of fascia, overlying skin, and vasculature, and quickly leading to septic shock. With a reported mortality rate of >23%, early detection and aggressive treatment is paramount.¹⁰ Unfortunately, NF is difficult to diagnose, with definitive diagnosis only possible with surgical intervention.

While the risk factors for developing NF are similar to those for cellulitis, it is important to note that NF also strikes young, previously healthy individuals.

NF most commonly occurs on the extremities, abdomen and perineum, and its initial presentation is similar to that of cellulitis. Early clinical clues to suspect NF include edema disproportionate to the erythema, pain out of proportion to other clinical findings, gas in the subcutaneous tissues as seen on x-ray, clinical crepitus, and the presence of skin vesicles or bullae. NF typically does not present with lymphangitis or lymphadenitis.

The patient with suspected NF should be treated aggressively to reduce morbidity and mortality. Treatment includes intravenous antibiotics with coverage for aerobic and anaerobic bacteria. Surgical debridement to remove all infected tissue is essential, and repeat debridements are often necessary. Most debridement sites are left open to heal by secondary intention, resulting in significant disfigurement. ♦

Do not use the information in this article to diagnose or treat a health problem or disease without consulting a qualified physician. Patients should consult their physician before starting any course of treatment or supplementation, particularly if they are currently under medical care, and should never disregard medical advice or delay in seeking it because of something set forth in this publication.

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Self-Assessment Quiz: Cellulitis

LEARNING GOAL

To understand the clinical complexities of and treatment options for cellulitis.

LEARNING OBJECTIVES

At the end of this program, the reader will be able to:

1. List risk factors for cellulitis.
2. Identify clinical findings for simple, complex, and high-risk cellulitis.
3. Describe treatment options for cellulitis and related skin conditions.

SELF-ASSESSMENT QUESTIONS

In the Quiz Answers section on the next page, fill in the correct answer for each question. To obtain two (2.0) contact hours toward CE credit, the passing score is 100%. Return your Self-Assessment Quiz to Coram via email or fax. See the next page for details on how to return to your quiz. Please allow approximately seven days to process your test and receive your certificate upon achieving a passing score.

1. Cellulitis and other infections of the skin and soft tissue are among the most common infections treated in hospitals.
 - a. True
 - b. False
2. The most common causative organism(s) of cellulitis in patients with normal immune systems is (are):
 - a. Group A streptococci
 - b. Staphylococcus aureus
 - c. B
 - d. A and B
3. Empiric therapy for cellulitis must also consider coverage for methicillin-resistant *Staphylococcus aureus*.
 - a. True
 - b. False
4. Likelihood of specific causative organisms is impacted by the site or nature of the injury.
 - a. True
 - b. False
5. Risk factors for cellulitis include:
 - a. Diabetes
 - b. Venous stasis
 - c. Lymphadenectomy
 - d. IV drug abuse
 - e. A, C and D
 - f. All of the above
6. Facial cellulitis is not considered high-risk.
 - a. True
 - b. False
7. Orbital cellulitis is more common in adults than children.
 - a. True
 - b. False
8. Orbital cellulitis is an ocular emergency.
 - a. True
 - b. False
9. Initiating timely, appropriate antibiotic therapy is critical in the treatment of cellulitis.
 - a. True
 - b. False
10. Home infusion is an option for many patients with cellulitis.
 - a. True
 - b. False

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Cellulitis

QUIZ ANSWERS

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1. (a) (b)
2. (a) (b) (c) (d)
3. (a) (b)
4. (a) (b)
5. (a) (b) (c) (d) (e) (f)
6. (a) (b)
7. (a) (b)
8. (a) (b)
9. (a) (b)
10. (a) (b)

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