Acute cellulitis and erysipelas in adults: Treatment

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INTRODUCTION

Patients with skin and soft tissue infection may present with cellulitis, abscess, and other forms of infection [1-3].

This topic will discuss treatment of cellulitis and erysipelas.

Clinical manifestations and diagnosis of cellulitis and erysipelas are discussed separately. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

Treatment of skin abscess is discussed elsewhere. (See "Skin abscesses in adults: Treatment".)

DIFFERENTIATING CELLULITIS FROM ERYSIPELAS

Effective treatment of cellulitis and erysipelas depends on determining the most likely microorganism causing the infection. Beta-hemolytic streptococci cause most erysipelas infections and most cellulitis infections, but cellulitis is sometimes caused by *Staphylococcus aureus* and occasionally by a multitude of other organisms.

Examination and clinical features cannot always differentiate erysipelas from cellulitis, so we treat for cellulitis whenever we are uncertain. Both erysipelas and cellulitis manifest as areas of skin erythema, edema, and warmth. On physical examination, classic erysipelas presents as a bright red patch of skin with a clearly demarcated raised border (picture 1 and picture 2).

Cellulitis involves deeper layers of the skin, so it classically presents with indistinct borders that are not raised (picture 3 and picture 4).

Details regarding the clinical presentation and diagnosis of erysipelas and cellulitis are found elsewhere. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Cellulitis and erysipelas'.)

DETERMINING THE SITE OF CARE

Cellulitis and erysipelas can both cause rapidly progressive and severe illness. Initial assessment of these infections should focus on determining the severity of illness and whether hospitalization is indicated.

Hospitalization is indicated for most individuals who warrant parenteral antibiotics and for all patients who are suspected to have high-risk "red-flag" conditions.

"Red-flag" conditions that warrant hospitalization — Red-flag conditions warrant immediate hospitalization, and some require urgent surgical intervention. Findings that increase suspicion for these conditions include severe sepsis or septic shock, rapidly progressive infection, or pain out of proportion to exam findings. Because of high morbidity and mortality, such conditions should be considered as part of the initial assessment of every individual with skin and soft tissue infection. Diagnosis and management of these conditions are discussed elsewhere.

- **Toxic shock syndrome** – (See "Invasive group A streptococcal infection and toxic shock syndrome: Epidemiology, clinical manifestations, and diagnosis" and "Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention" and "Staphylococcal toxic shock syndrome".)

- **Necrotizing soft tissue infection (eg, necrotizing fasciitis)** – (See "Necrotizing soft tissue infections".)

- **Joint involvement (with or without prosthesis)** – (See "Septic arthritis in adults" and "Prosthetic joint infection: Epidemiology, microbiology, clinical manifestations, and diagnosis" and "Prosthetic joint infection: Treatment".)

- **Involvement of vascular graft** – (See "Overview of the evaluation and management of surgical site infection", section on 'Deep infection associated with implanted materials'.)

- **Pyomyositis** – (See "Primary pyomyositis".)

- **Clostridial myonecrosis (gas gangrene)** – (See "Clostridial myonecrosis".)
- **Deep venous thrombosis (DVT)** - (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity".)
- **Compartment syndrome** – (See "Acute compartment syndrome of the extremities" and "Pathophysiology, classification, and causes of acute extremity compartment syndrome".)

Indications for parenteral therapy — The decision to initiate parenteral therapy is typically based on the extent and severity of infection and patient comorbidities. Patients who meet criteria for parenteral therapy are usually admitted to the hospital to ensure prompt administration and close observation.

For individuals with cellulitis or erysipelas without red-flag conditions, we suggest initial treatment with parenteral antibiotics in the following circumstances:

- Systemic signs of toxicity such as fever >100.5°F/38°C, hypotension, or sustained tachycardia (refractory hypotension should prompt consideration of toxic shock syndrome).
- Rapid progression of erythema (eg, doubling of the affected area within 24 hours; in particular, expansion over a few hours with severe pain should prompt consideration of necrotizing fasciitis).
- Extensive erythema.
- High-risk neutropenia [4]. Patients with neutropenia are classified as low- or high-risk based on scoring mechanisms that consider the anticipated duration of neutropenia, comorbidities, and severity of illness; such scoring systems are discussed separately. (See "Overview of neutropenic fever syndromes", section on 'Risk of serious complications'.)
- Inability to tolerate or absorb oral therapy

For patients with lymphangitis accompanying cellulitis, some UpToDate contributors would administer parenteral antibiotics because they believe that lymphangitis may be indicative of imminent bacteremia; there are minimal published data to support or refute this notion.

For immunocompromised patients with low-risk neutropenia or a non-neutropenic form of immunocompromise, we have a lower threshold for admission for IV antibiotics than we do for immunocompetent patients. Ultimately, clinical judgment is necessary and should consider the

severity of infection, type of underlying immunocompromise, and ability for close follow-up in the outpatient setting.

ACUTE CELLULITIS

The pillars of cellulitis treatment are antibiotic therapy and management of exacerbating conditions, including the point of entry of infection. (See 'Considerations prior to selecting antibiotics' below and 'Adjunctive treatments' below.)

Considerations prior to selecting antibiotics — At the time of presentation, selection of empiric antibiotic therapy is based on determining the most likely pathogen. In most cases, the causative pathogen is never identified. If a pathogen is identified, antibiotics should be narrowed to target the pathogen.

Factors that should be considered when choosing antibiotics for acute cellulitis include the severity and location of the cellulitis and whether coverage for methicillin-resistant *S. aureus* (MRSA) or atypical organisms is necessary. These issues are discussed in the sections that follow.

Pathogens to always cover — Empiric antibiotics for cellulitis should always cover beta-hemolytic streptococci and methicillin-sensitive *S. aureus* (MSSA), which are the two most common pathogens of cellulitis [1-3]. Further details regarding the microbiology of cellulitis are discussed elsewhere (table 1). (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Cellulitis and erysipelas'.)

Indications for MRSA coverage — Empiric coverage for MRSA is indicated for patients with severe sepsis, certain MRSA risk factors, and those who have increased morbidity if suboptimal antibiotics are administered. Conditions that warrant MRSA coverage include the following [2,5]:

- Systemic signs of toxicity (eg, fever >100.5°F/38°C, hypotension, sustained tachycardia)
- Cellulitis with purulent wound drainage
- Known MRSA colonization or infection
- Injection drug use
- High-risk neutropenia

Other risk factors may not be as strongly associated with MRSA infection, so we individualize the decision for MRSA coverage in such cases. For a complete list of risk factors for MRSA, refer to the table (table 2).

Wounds and exposures that warrant specific coverage — A broad range of organisms can cause cellulitis in individuals with wounds, injuries, or certain environmental exposures (table 1). Antibiotic regimens for these conditions are distinct and discussed in detail elsewhere.

- **Wounds and injuries**
  - Diabetic foot ulcers – (See "Clinical manifestations, diagnosis, and management of diabetic infections of the lower extremities", section on 'Management'.)
  - Animal bites – (See "Animal bites (dogs, cats, and other mammals): Evaluation and management", section on 'Management'.)
  - Human bites – (See "Human bites: Evaluation and management", section on 'Infected bites'.)
  - Puncture wounds other than bites – (See "Infectious complications of puncture wounds".)
  - Pressure injury or pressure ulcer – (See "Infectious complications of pressure-induced skin and soft tissue injury".)
  - Surgical wound – (See "Overview of the evaluation and management of surgical site infection".)
- **Environmental exposures**
  - Water exposure – (See "Soft tissue infections following water exposure".)
  - Soil exposure - (See "Infectious complications of puncture wounds".)
  - Travel-related skin infections – (See "Skin lesions in the returning traveler" and "Melioidosis: Epidemiology, clinical manifestations, and diagnosis", section on 'Skin infection'.)

Anatomic site of infection — Cellulitis can occur on any part of the body. Depending on the location of cellulitis, antibiotic selection and other interventions, including surgery, can vary.

- **Cellulitis of the extremities** – The extremities are the most common site of cellulitis. In the absence of a red-flag condition or other indication for broadened antibiotic coverage, treatment focuses on beta-hemolytic streptococci and *S. aureus*. (See '"Red-flag" conditions that warrant hospitalization' above and 'Selecting an antibiotic regimen' below.)

If cellulitis involves the hand, hospitalization is typically recommended along with evaluation by a surgeon. Management of hand infections is discussed in depth elsewhere. (See "Overview of hand infections".)

- **Facial cellulitis** – Facial skin infections are more often due to erysipelas than cellulitis. Treatment of facial cellulitis focuses on beta-hemolytic streptococci and *S. aureus*. (See 'Selecting an antibiotic regimen' below.)

  If the area around the eye is cellulitic, differentiation of preseptal (periorbital) from orbital cellulitis is paramount. Preseptal cellulitis is generally a mild infection of the skin around the eye, whereas orbital cellulitis involves the deeper tissues of the eye and can lead to loss of vision or even loss of life. Rarely, infections involving the medial third of the face (ie, the areas around the eyes and nose) can be complicated by septic cavernous thrombosis, a life-threatening disease. More details regarding diagnosis and management of preseptal and orbital cellulitis, as well as septic cavernous thrombosis, are found elsewhere. (See "Preseptal cellulitis" and "Orbital cellulitis" and "Septic dural sinus thrombosis".)

- **Neck cellulitis** – Cellulitis of the neck is uncommon. When present, consideration should be given to underlying deep neck space infection or submandibular space infection (Ludwig angina), both of which require urgent evaluation and management. Diagnosis and management of deep neck space infections are discussed elsewhere. (See "Deep neck space infections in adults" and "Ludwig angina".)

- **Breast cellulitis** – Breast cellulitis is usually due to beta-hemolytic streptococci or *S. aureus* and is managed similarly to uncomplicated cellulitis, as described below (see 'Selecting an antibiotic regimen' below). Additional considerations regarding the management of breast cellulitis are found elsewhere. (See "Breast cellulitis and other skin disorders of the breast", section on 'Treatment'.)

- **Cellulitis of the abdominal wall** – Most reports of abdominal-wall cellulitis of adults are in individuals with surgical site infection, abdominal-wall mesh infection, or intra-abdominal conditions such as appendicitis or colon cancer. In each of these situations, both surgical intervention and antibiotic therapy are usually necessary for management [6-17]. Management of these conditions is discussed elsewhere. (See "Overview of the evaluation and management of surgical site infection" and "Wound infection following repair of abdominal wall hernia".)

  Few reports of idiopathic abdominal-wall cellulitis exist, but the infection is probably more common than the medical literature suggests. In a case series of 260 patients with cellulitis and morbid obesity between 1998 and 2003, 24 (9 percent) had idiopathic

abdominal-wall cellulitis [18]. Of those 24 patients, 17 (71 percent) had a remote history of healed abdominal surgery, 10 (42 percent) had diabetes mellitus, 7 (29 percent) experienced recurrences, and 3 (13 percent) underwent surgical debridement and/or panniculectomy. Eleven (46 percent) had an underlying dermatologic condition of the abdominal wall, most commonly lymphedema and/or intertrigo.

No studies have evaluated treatment of idiopathic abdominal-wall cellulitis. We use the same approach as for cellulitis in general. (See 'Selecting an antibiotic regimen' below.)

We suggest treating underlying dermatologic and other contributing conditions, such as intertrigo, while the patient is receiving antimicrobial therapy.

- **Cellulitis of the perineum or genitalia** – Skin infections of the perineum and genitals can be due to cellulitis, folliculitis, or other etiologies. Of most concern is Fournier gangrene, a polymicrobial necrotizing fasciitis of the perineum that can involve the lower abdominal wall, the penis and scrotum in men, and the labia in women. Fournier gangrene is a medical and surgical emergency with a high fatality rate. Details regarding diagnosis and management of Fournier gangrene are found elsewhere. (See "Necrotizing soft tissue infections".)

Selecting an antibiotic regimen — The first step when selecting an initial antibiotic regimen for cellulitis is to determine whether providing coverage beyond beta-hemolytic streptococci and *S. aureus* is necessary. Certain conditions, exposures, or anatomic sites often require broader antibiotic coverage than standard regimens, and antibiotic selection for those conditions is discussed elsewhere (table 1). (See '"Red-flag" conditions that warrant hospitalization' above and 'Considerations prior to selecting antibiotics' above.)

For most patients with cellulitis who don't have features that warrant specific management, our approach depends on the severity of illness, patient's immune status, and risk for MRSA, as outlined below and in the algorithm (algorithm 1).

In general, our antibiotic recommendations match those of expert guidelines [2].

Patients with severe sepsis — In the setting of severe sepsis, rapid administration of empiric broad-spectrum antibiotics is indicated because delay or lack of adequate coverage increases mortality [19,20]. Of note, patients with septic shock, manifest by refractory hypotension, may have toxic shock syndrome or another red-flag condition and should be managed accordingly, as discussed elsewhere. (See '"Red-flag" conditions that warrant hospitalization' above.)

- **Initial therapy** – We suggest the following antibiotic regimen for patients with severe sepsis (algorithm 1):

  - Intravenous vancomycin (see table for dosing (table 3))

    PLUS

    Cefepime 2 g intravenously (IV) every eight hours

  Other regimens may be more appropriate in certain situations:

  - For patients who are known or suspected of having an infection due to an organism with an extended-spectrum beta-lactamase (ESBL), we suggest using an empiric carbapenem (eg, meropenem 1 g IV every eight hours) in conjunction with vancomycin.

  - For patients with reported beta-lactam allergies, empiric antibiotic selection depends on the type and severity of the reaction (algorithm 2). Patients with mild, non-immunoglobulin (Ig)E-mediated reactions to penicillins (eg, maculopapular rash) can usually safely receive cephalosporins; carbapenems are typically safe in patients who cannot take penicillins or cephalosporins (see "Choice of antibiotics in penicillin-allergic hospitalized patients"). For patients who cannot take any beta-lactam agent, we suggest intravenous vancomycin (table 3) paired with either levofloxacin (750 mg IV once daily) or aztreonam (2 g IV every eight hours; dosing up to 2 g every six hours may be reasonable for weight >120 kg). Note that individuals with a history of life-threatening or anaphylactic reaction to ceftazidime should not be given aztreonam, but levofloxacin is generally safe.

- **Oral step-down therapy** – Once clinical improvement and resolution of sepsis occur, it is generally appropriate to transition to an oral regimen. If a pathogen is identified during the course of therapy, antibiotics should be narrowed to coverage specific for that pathogen.

  If a pathogen is not identified, stable patients who are not immunocompromised can generally be transitioned to one of the narrower oral agents described below. (See 'Immunocompetent patients without severe sepsis' below.)

The rationale for using a spectrum that covers pathogens in addition to streptococci and *S. aureus* is the risk of poor outcomes with a narrower spectrum of empiric therapy in severely ill patients if other pathogens are involved.

Immunocompetent patients without severe sepsis — We typically divide this group of patients into those who warrant MRSA coverage and those who do not (algorithm 1). Indications for MRSA coverage are described above. (See 'Indications for MRSA coverage' above.)

Without an indication for MRSA coverage — For most patients, antibiotic regimens that cover beta-hemolytic streptococci and MSSA are effective, and coverage for MRSA is not necessary [2,5,21,22]. We suggest one of the following regimens (algorithm 1):

- **Oral antibiotic regimens** – Many patients with cellulitis of the lower extremity can be managed with oral antibiotics in the outpatient setting [23]. For such patients, we suggest one of the following regimens:

  - Dicloxacillin 500 mg orally every six hours
  - Flucloxacillin 500 to 1000 mg orally every six hours (not available in the United States)
  - Cephalexin 500 mg orally every six hours
  - Cefadroxil 500 mg orally every 12 hours or 1 g orally once daily

- **Parenteral antibiotic regimens** – Parenteral antibiotics are recommended for higher risk patients (see 'Indications for parenteral therapy' above). For such patients, we suggest one of the following regimens:

  - Cefazolin 1 to 2 g IV every eight hours
  - Nafcillin 1 to 2 g IV every four hours
  - Oxacillin 1 to 2 g IV every four hours
  - Flucloxacillin 2 g IV every six hours (not available in the United States)

  For cefazolin, nafcillin, and oxacillin, we usually favor the higher dosages listed above (ie, 2 g) for treatment of these infections.

  Once there is evidence of clinical improvement, parenteral antibiotics should be switched to one of the oral regimens listed above [24].

Studies suggest that most patients with cellulitis do not need MRSA coverage:

- A randomized trial of adults with nonpurulent cellulitis in five emergency departments in the United States noted similar clinical cure rates among those treated with cephalexin plus TMP-SMX and those treated with cephalexin plus placebo [21]. In the per-protocol analysis, 182 (84 percent) of 218 individuals in the cephalexin plus TMP-SMX group achieved cure versus 165 (86 percent) of 193 in the cephalexin group (difference -2 percent; 95% CI, -9.7 to 5.7 percent). The modified intention-to-treat analysis suggested a

possible trend favoring the cephalexin plus TMP-SMX group, but those results are difficult to interpret due to a large number of patients in both groups who did not complete the full course of therapy.

- Another randomized trial of 153 patients with cellulitis without abscess noted comparable cure rates among those treated with cephalexin and TMP-SMX (85 percent) and those treated with cephalexin and placebo (82 percent; difference 2.7 percent, 95% CI -9.3 to 15 percent) [22].

With an indication for MRSA coverage — MRSA coverage is indicated if certain conditions are present (see 'Indications for MRSA coverage' above). We suggest one of the following regimens (algorithm 1):

- **Oral antibiotic regimens** – For many patients, treatment in the outpatient setting with oral antibiotics is effective [23]. We suggest one of the following regimens:

  - TMP-SMX (one to two double-strength tablets orally twice daily; for patients who weigh more than 70 kg and have normal renal function, we favor two double-strength tablets twice daily).

  - Amoxicillin (875 mg orally twice daily) plus doxycycline (100 mg orally twice daily).

  TMP-SMX has activity against both *Streptococcus* and *S. aureus*, including MRSA. Doxycycline provides coverage for *S. aureus*, including MRSA; amoxicillin is added to it for streptococcal coverage. Cellulitis cure rates with TMP-SMX range from 78 to 83 percent [25,26], and support for doxycycline is based on observational data, as discussed elsewhere. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections", section on 'Oral antibiotic therapy'.)

  Linezolid (600 mg orally every 12 hours) is acceptable if the above agents cannot be used. Meta-analyses, systematic reviews, and randomized trials suggest that linezolid has at least equivalent outcomes for skin and soft tissue infections (including MRSA infections) when compared with intravenous vancomycin [27-30]. The analyses also found elevated rates of nausea, vomiting, and thrombocytopenia when linezolid was administered; we suggest weekly complete blood counts for patients receiving linezolid for longer than two weeks. Linezolid is discussed in more detail elsewhere. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections", section on 'Linezolid and tedizolid'.)

Clindamycin (450 mg orally every eight hours) may have activity against both *Streptococcus* and *S. aureus* and is an alternative if no other options exist; we avoid its use due to risk for *Clostridioides difficile* infection and the possibility of streptococcal and staphylococcal resistance. Local rates of resistance to clindamycin should be considered before prescribing, as described below. (See 'Alternatives for serious beta-lactam allergy' below.)

- **Parenteral antibiotic regimen** – For patients who meet criteria for parenteral antibiotics, we suggest the following regimen (see 'Indications for parenteral therapy' above):

  - Intravenous vancomycin (see table for dosing (table 3))

  - Daptomycin 4 to 6 mg/kg IV every 24 hours (alternative)

  Vancomycin is the preferred option because of extensive experience with this agent. When daptomycin is used, we usually favor the higher dose (ie, 6 mg/kg). For patients who cannot take vancomycin or daptomycin, alternative agents can be used and are listed in the table (table 4), and their efficacy is discussed elsewhere. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections".)

  Once there is evidence of clinical improvement, parenteral antibiotics should be switched to one of the oral regimens listed above.

Alternatives for serious beta-lactam allergy — Although many patients have reported beta-lactam allergies, most do not have allergies that would prohibit the use of beta-lactams. In particular, many with penicillin allergies can still take a cephalosporin (algorithm 2). Evaluation and management of reported penicillin allergies are discussed in detail elsewhere. (See "Choice of antibiotics in penicillin-allergic hospitalized patients" and "Allergy evaluation for immediate penicillin allergy: Skin test-based diagnostic strategies and cross-reactivity with other beta-lactam antibiotics".)

For immunocompetent patients without severe sepsis who have serious allergies that preclude use of beta-lactams, we suggest one of the following regimens (algorithm 1):

- **Oral antibiotic regimen** – If no indication for parenteral antibiotics is present, we suggest either of the following:

  - TMP-SMX (one to two double-strength tablets orally twice daily).

  - Linezolid (600 mg orally every 12 hours). More detail regarding this agent is discussed above. (See 'With an indication for MRSA coverage' above.)

An alternative is clindamycin (450 mg orally every eight hours), but we generally avoid it due to risk *of C. difficile* infection and the possibility of streptococcal and staphylococcal resistance [25,31]. Local rates of resistance to clindamycin should be considered before prescribing. Data from the United States Centers for Disease Control and Prevention (CDC) found that 22 percent of group A *Streptococcus* isolates and 47 percent of MRSA isolates were resistant to clindamycin in 2017 [32,33]. In Australia in 2019, clindamycin resistance was reported in 7 percent of group A *Streptococcus* and 30 percent of MRSA isolates [34].

Data suggest that TMP-SMX and clindamycin are equally effective for management of cellulitis. In one randomized trial of outpatients with cellulitis, 110 (81 percent) of 136 individuals who received clindamycin achieved cure versus 110 (76 percent) of 144 who received TMP-SMX (difference -4.5 percent; 95% CI, -15.1 to 6.1 percent) [25].

We do not recommend macrolides, such as azithromycin, due to high resistance rates among beta-hemolytic streptococci [2,32,35]. The CDC reported that 23 percent of group A streptococci were resistant to macrolides in 2017 [32].

- **Parenteral antibiotic regimen** – For patients with an indication for parenteral therapy, we suggest intravenous vancomycin (table 3). (See 'Indications for parenteral therapy' above.)

  For patients who cannot take vancomycin, alternative parenteral agents can be used and are listed in the table (table 4).

  Once there is evidence of clinical improvement, parenteral antibiotics should be switched to one of the oral regimens listed above.

Immunocompromised patients without severe sepsis — Patients who have certain immunocompromising conditions are at risk for a wide range of pathogens. However, there is a spectrum of immunocompromising conditions, and some do not substantially increase risk. Ultimately, choosing an antibiotic regimen for immunocompromised patients should depend on the type of underlying immunocompromise, severity of infection, and ability for close follow-up in the outpatient setting.

- **Patients with high-risk neutropenia** – We hospitalize these patients for prompt administration of intravenous broad-spectrum antibiotics that cover gram-negative pathogens (including *Pseudomonas* spp) in addition to streptococci and *S. aureus*. Our preferred regimen is vancomycin plus cefepime (table 5). (See "Treatment of neutropenic fever syndromes in adults with hematologic malignancies and hematopoietic cell transplant recipients (high-risk patients)", section on 'Initial regimen'.)

- **Patients with immunocompromise other than high-risk neutropenia** – In our experience, many patients in this group can be treated with IV or oral therapy using the same regimens as the immunocompetent population. (See 'Immunocompetent patients without severe sepsis' above and 'Indications for parenteral therapy' above.)

  Some immunocompromising conditions can be associated with specific pathogens (table 1). For example, patients with cirrhosis can develop cellulitis from enteric gram-negative bacilli (eg, *Klebsiella* spp), so some experts select a regimen that covers those organisms (eg, amoxicillin-clavulanate). As another example, patients with low-risk neutropenia are at risk for pseudomonal infection, so many experts administer combination therapy (eg, amoxicillin-clavulanate plus ciprofloxacin).

  Ultimately, the decision to broaden coverage beyond beta-hemolytic streptococci and *S. aureus* is nuanced and requires clinical judgment.

Duration of antibiotic therapy — The duration of therapy should be individualized depending on clinical response. In general, five to six days of therapy is appropriate for patients with uncomplicated cellulitis whose infection has improved [2,36,37]. Extension of antibiotic therapy (up to 14 days) may be warranted in the setting of severe infection, slow response to therapy, or immunocompromise.

The above suggested duration is supported by a meta-analysis of eight randomized controlled trials totaling almost 1500 adults with cellulitis that found no difference in response rates between short (five to six days) and longer courses of antibiotics (relative risk [RR] 0.99, 95% CI 0.96-1.03) [23]. The only trial that assessed outcome beyond 30 days was a trial of 151 individuals hospitalized with nonpurulent cellulitis who were randomized to treatment with a 6-day or 12-day course of flucloxacillin [38]. Cure rates were similar between the groups (74 versus 67 percent); relapse rates after 90 days were higher in the 6-day group (6 versus 24 percent), but most relapses in the 6-day group were in patients with a history of at least one prior episode of cellulitis.

Adjunctive treatments — When treating cellulitis of the lower extremities, management of exacerbating conditions and any points of entry for microorganisms is paramount.

Elevation and edema management — Edema, a common manifestation of cellulitis, can impair antibiotic penetration into infected tissue and prevent resolution of infection. For lower extremity cellulitis, elevation of the affected limb hastens improvement by allowing gravity drainage of edema and inflammatory substances [2]. To optimize the effect of gravity, we instruct patients to elevate the heel of the foot above the knee and the knee above the hip.

Lymphedema and venous insufficiency are commonly associated with lower extremity cellulitis, especially in individuals who are obese. In addition to elevation, compression therapy can be used to treat both lymphedema and venous insufficiency. While compression therapy has been shown to be effective for preventing recurrences of cellulitis in individuals with lymphedema, the efficacy of compression therapy during acute cellulitis is uncertain, and clinical practice varies, including among UpToDate contributors. Traditionally, compression therapy was felt to be contraindicated during episodes of acute cellulitis for fear of compromising vascular function, although no data support this contraindication. Limited data suggest that individualized compression therapy applied by specialized lymphedema physiotherapists may not be harmful and does not compromise microcirculation in patients with active cellulitis [39,40]. Compression therapy should be avoided in individuals with known or suspected arterial insufficiency. Details regarding the management of lymphedema and venous insufficiency are found elsewhere. (See "Lower extremity lymphedema" and "Clinical staging and conservative management of peripheral lymphedema" and "Overview of lower extremity chronic venous disease" and "Compression therapy for the treatment of chronic venous insufficiency".)

Skin management — Treatment of skin conditions and the point of microorganism entry can expedite resolution of cellulitis.

The point of entry of microorganisms should be identified and managed at the time of diagnosis of cellulitis. Common points of entry include intertrigo in the toe webs of the feet, tinea pedis, onychomycosis, and lower extremity ulcers. Details regarding diagnosis and management of these issues are found elsewhere. (See "Intertrigo" and "Dermatophyte (tinea) infections", section on 'Tinea pedis' and "Onychomycosis: Management" and "Approach to the differential diagnosis of leg ulcers".)

As cellulitis evolves, skin can begin to weep, blister, flake, or crack. Dermatologists and wound care specialists can provide assistance with management of these conditions. More details regarding the cutaneous progression of cellulitis are found below. (See 'Monitoring response to therapy' below.)

Numerous underlying skin conditions are risk factors for the development of cellulitis including atopic dermatitis (eczema) and psoriasis. Such conditions should be optimally managed in conjunction with standard cellulitis treatment. Details regarding skin conditions that predispose to cellulitis are discussed elsewhere. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Epidemiology'.)

Interventions that are not recommended — We do not recommend the following therapies. These recommendations generally match those of expert guidelines [2].

- **Anti-inflammatory medications** – We suggest not using nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids when there is concern for moderate to severe cellulitis. These drugs can mask signs and symptoms of inflammation in patients with necrotizing soft tissue infection, and their use may be associated with delay in diagnosis.

  For patients with mild infection, anti-inflammatory medications may reduce symptoms of pain. While some data suggest that use of NSAIDs or corticosteroids may hasten healing among patients with cellulitis or erysipelas, these results are inconclusive and are limited by small sample size [41-43]. (See "Necrotizing soft tissue infections".)

- **Topical antibiotics** – Although topical antibiotics are effective for some skin infections (eg, impetigo, folliculitis), topical antibiotics are unlikely to be effective for cellulitis or erysipelas due to involvement of the layers of skin below the epidermis.

- **Hyperbaric oxygen therapy** – For cellulitis, hyperbaric oxygen therapy has not been shown to be effective [2]. Further information on hyperbaric oxygen therapy is found elsewhere. (See "Hyperbaric oxygen therapy".)

TREATMENT OF ERYSIPELAS

Management of erysipelas primarily consists of antibiotic therapy along with the adjunctive therapies described above. (See 'Adjunctive treatments' above.)

Oral antibiotics for erysipelas — Most cases of erysipelas can be managed with oral antibiotics in the outpatient setting. For patients with unambiguous erysipelas who do not meet criteria for parenteral antibiotics, empiric oral antibiotics active against beta-hemolytic streptococci should be administered (see 'Indications for parenteral therapy' above). We suggest one of the following regimens:

- Penicillin V potassium 500 mg orally every six hours
- Amoxicillin 875 mg orally every 12 hours
- Cephalexin 500 mg orally every six hours
- Cefadroxil 500 mg orally every 12 hours or 1 g orally once daily

For patients with serious beta-lactam allergies that preclude use of the above regimens, oral options are the same as those listed above for cellulitis. (See 'Alternatives for serious beta-lactam allergy' above.)

Parenteral antibiotics for erysipelas — We suggest antibiotics that cover beta-hemolytic streptococci and *S. aureus* for patients with erysipelas who have an indication for parenteral

therapy (see 'Indications for parenteral therapy' above). Differentiating erysipelas from cellulitis is not always straightforward, so we believe that adding staphylococcal coverage is prudent in individuals who are ill enough to warrant parenteral therapy.

For such patients, appropriate regimens include those described in the above discussion about antibiotic therapy for cellulitis.

If a microbiologic diagnosis of beta-hemolytic *Streptococcus* is subsequently established (eg, by a positive blood culture), then we recommend switching to parenteral aqueous crystalline penicillin G (2 to 4 million units intravenously [IV] every four to six hours).

For patients in whom outpatient parenteral antibiotic is desired, ceftriaxone (1 to 2 g IV once daily) is an alternative that allows for convenient once-daily outpatient administration.

Once there is evidence of clinical improvement, parenteral antibiotics should be switched to oral antibiotics that cover streptococci. Appropriate oral antibiotics for erysipelas are described above. (See 'Oral antibiotics for erysipelas' above.)

Duration of antibiotic therapy — In general, the duration of therapy for erysipelas is analogous to the duration used for cellulitis. (See 'Duration of antibiotic therapy' above.)

MONITORING RESPONSE TO THERAPY

Patients with cellulitis or erysipelas typically have symptomatic improvement within 24 to 48 hours of beginning antimicrobial therapy, although visible improvement of skin manifestations can take 72 hours or longer [44,45]. In some cases, we monitor patients remotely by having patients send daily pictures of their infection to our clinic; we advise patients to take photographs from the same angle and in the same environment, with particular attention to lighting.

It is useful to document the baseline appearance of the physical findings at the start of antibiotic therapy. We obtain a baseline digital photograph to help monitor progress. Some experts outline the area of infection with an indelible marker at the time of treatment initiation to allow objective monitoring of progress. Other do not outline the infection because patients sometimes experience unnecessary anxiety if the infection appears to extend beyond the line as the infection dissipates. In the early stages of treatment, erythema may expand beyond the initial margins of infection as the infection dissipates. Deepening of erythema may be observed due to destruction of pathogens that can enhance local inflammation. These findings should not be mistaken for therapeutic failure. Clues that the infection is improving include reductions

in fever, pain, brightness or intensity of erythema, peripheral white blood cell count, and other signs of infection.

As cellulitis evolves, skin can begin to weep, blister, flake, or crack. None of these findings are necessarily indications of worsening infection. As discussed elsewhere, wound care specialists or dermatologists can help to manage these conditions. (See 'Skin management' above.)

Residual skin inflammation is a common finding after completion of effective therapy [38,44]. In a study of 216 patients hospitalized for cellulitis, more than half had residual inflammation at the end of therapy [45]. Per telephone consultation done approximately two weeks after completion of therapy, approximately 40 percent still had residual inflammation and 16 percent had deterioration or required readmission.

REFRACTORY INFECTION

Significant progression of erythema or persistence of systemic symptoms after 24 to 48 hours should prompt a search for possible reasons for treatment failure. Evaluation should consider multiple possibilities:

- **Red-flag condition** – Any time cellulitis progresses rapidly or clinical symptoms, especially pain, seem to be out of proportion to physical exam, red-flag conditions should be considered. A low threshold for surgical consultation to evaluate for these conditions is prudent. A list of red-flag conditions is provided above. (See '"Red-flag" conditions that warrant hospitalization' above.)

- **Inadequate dosing or tissue penetration of antibiotics** – Conditions at the site of infection, such as edema or peripheral artery disease, can markedly reduce the ability of antibiotics to penetrate into soft tissue. To optimize tissue penetration of the antibiotics, management of these conditions is paramount. (See 'Adjunctive treatments' above.)

  In patients failing oral antibiotics, switching from oral to intravenous antibiotics can markedly increase antibiotic delivery to the site of infection. This is especially the case for antibiotics with poor bioavailability (such as some beta-lactam agents) or for patients whose ability to absorb oral medications is uncertain.

  In select situations, using higher antibiotic dosages may be beneficial. Obesity can increase drug clearance from circulation and thereby limit the amount of antibiotic that reaches the site of infection [46]. Moreover, certain bacteria, such as *Pseudomonas* spp,

require higher antibiotic dosages to achieve bacterial killing. Consultation with a pharmacist may be helpful in these cases.

- **Abscess** – As cellulitis responds to antibiotic therapy, sometimes the infection can coalesce to form an abscess below the surface. Abscess should be suspected when focal tender fluctuance is found on exam, and ultrasound can aid in detection. If present, surgical consultation for incision and drainage is recommended. Detailed discussion of skin abscess management is found elsewhere. (See "Skin abscesses in adults: Treatment".)

- **Diagnosis other than cellulitis or erysipelas** – Failure to respond to appropriate therapy should prompt consideration that the initial diagnosis of cellulitis is incorrect. Cellulitis is often confused with other infectious and noninfectious illnesses, and misdiagnosis is perhaps the most common cause of lack of response to therapy [47,48]. The differential diagnosis of cellulitis and erysipelas is broad and is discussed in detail elsewhere. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Cellulitis and erysipelas'.)

- **Resistant pathogen** – Re-evaluating for the possibility of resistant microorganisms and reviewing past culture data can help guide antibiotic change. Methicillin-resistant *S. aureus* (MRSA) or other organisms associated with certain conditions or environmental exposures should be considered. (See 'Considerations prior to selecting antibiotics' above.)

  In immunocompromised individuals, cellulitis can be due to a multitude of organisms including atypical bacteria, fungi, viruses, and parasites. If these individuals fail to respond to broad-spectrum antibiotic therapy, a dermatologic evaluation and skin biopsy can be beneficial. Nodular or ulcerative lesions should be biopsied early during the clinical course in highly immunocompromised individuals, especially for those who are septic or have rapidly progressive illness. Further discussion of skin infection in neutropenic individuals is found elsewhere. (See "Diagnostic approach to the adult cancer patient with neutropenic fever", section on 'Skin and mucous membranes'.)

- **Inadequate adherence** – A repeat course of antimicrobial therapy and further instruction regarding elevation and other adjunctive therapies may be appropriate for patients with inadequate adherence to the treatment plan.

RECURRENT INFECTION

Recurrent erysipelas and cellulitis are not uncommon occurrences. Recurrences have been reported to occur in 14 percent of cellulitis cases within one year and up to 45 percent of cases

within three years, usually in the same location [3,49,50]. In one review of over 400,000 admissions for cellulitis, the readmission rate was 10 percent and most readmissions were due to recurrent cellulitis [51].

Management of recurrent infection — During the active stage of infection, management of recurrent episodes is the same as the approach for initial episodes (see 'Acute cellulitis' above). For individuals who have frequent or severe recurrences, prefilled prescriptions for treatment doses of antibiotics can be provided so that patients can self-initiate antibiotic therapy at the onset of symptoms while seeking immediate medical attention.

Prevention of recurrences — Potential tools for prevention of recurrent cellulitis include alleviation of predisposing conditions (such as use of compression therapy for management of edema), antibiotic prophylaxis, and *S. aureus* decolonization. These are discussed below.

Alleviation of predisposing conditions — Predisposing conditions should be identified and treated, if possible [3]. Examples of modifiable predisposing conditions include the following:

- Edema. Elevation of the affected area and diuretic therapy can help to alleviate edema. Compression therapy has been shown in studies to be highly effective for lymphedema and venous insufficiency and is discussed in detail below. (See 'Compression therapy' below.)
- Foot infections including intertrigo in the toe webs of the feet, tinea pedis, and onychomycosis. (See "Intertrigo" and "Dermatophyte (tinea) infections" and "Onychomycosis: Management".)
- Lower extremity ulcers. (See "Approach to the differential diagnosis of leg ulcers".)
- Chronic skin conditions, such as eczema and psoriasis. (See "Treatment of atopic dermatitis (eczema)" and "Treatment of psoriasis in adults".)
- Obesity. (See "Obesity in adults: Overview of management".)
- Immunosuppression.

Compression therapy — For patients with recurrent episodes of cellulitis in the setting of chronic lower extremity venous insufficiency or lymphedema, compression therapy is an essential component of management that has been shown to be effective in reducing episodes of recurrent cellulitis [52].

In a randomized trial involving 84 patients with chronic lower extremity edema and ≥2 prior episodes of cellulitis, daily use of compression therapy reduced the rate of recurrent cellulitis compared with no compression therapy (15 versus 40 percent, respectively, at a median follow-up of six months; hazard ratio [HR] 0.23, 95% CI 0.09-0.59) [52]. The compression therapy was provided by specialized lymphedema physiotherapists and usually consisted of prescription knee-high stockings that included the foot and were worn throughout the day. The compression therapy was provided only when no active cellulitis was present, and no adverse events related to compression therapy were observed. Of note, the trial was stopped early for benefit, which tends to overestimate treatment efficacy.

Additional details regarding compression therapy in patients with chronic venous insufficiency and lymphedema are provided separately. (See "Lower extremity lymphedema" and "Clinical staging and conservative management of peripheral lymphedema" and "Compression therapy for the treatment of chronic venous insufficiency".)

Antibiotic prophylaxis for selected patients — For patients who optimize predisposing conditions but still develop recurrent cellulitis in the same anatomic site, we suggest suppressive antibiotic therapy [2]. Although infrequent, there are scenarios (eg, complicated bacteremia in patients with a prosthetic device) when initiation of suppressive therapy after an initial bout of cellulitis may be warranted; consultation of clinicians with experience in these cases is suggested.

For suppressive therapy, we suggest one of the following antibiotic regimens:

- For patients with known or presumed beta-hemolytic streptococcal infection [53-55]:
  - Penicillin V (250 to 500 mg orally twice daily)
  - Penicillin G benzathine intramuscular (IM) injections (1.2 to 2.4 million units IM every four weeks; shorten interval to every two weeks if longer interval is not effective)
- For patients with known or presumed staphylococcal infection:
  - Cefadroxil (500 mg orally twice daily)
  - Cephalexin (500 mg orally four times daily)
  - Trimethoprim-sulfamethoxazole (TMP-SMX; one double-strength tablet orally twice daily)

Cefadroxil and cephalexin have no activity against methicillin-resistant *S. aureus* (MRSA) and should only be used if recurrent methicillin-sensitive *S. aureus* (MSSA) infection is suspected.

For patients with reported beta-lactam allergies, we suggest referral to an allergist. If beta-lactam allergy is confirmed and TMP-SMX is not an option, we try doxycycline (100 mg orally twice daily). We avoid clindamycin (150 mg orally once daily) unless there are no other options due to risk of *C. difficile* infection [56].

Other than penicillin and clindamycin, minimal data exist to support the options listed above as suppressive agents. The optimal dosing for these antibiotics when used as prophylaxis is unknown and may be lower than the suggested doses. Titration to lower dosages over time may allow determination of the best dose for individual patients.

Serologic testing for beta-hemolytic streptococci may be a useful diagnostic tool to help guide the choice of suppressive antibiotic therapy. Such tests include the anti-streptolysin-O reaction and the anti-deoxyribonuclease B test (anti-DNAse B). Further information regarding serologic testing for beta-hemolytic streptococci is found elsewhere. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Diagnosis'.)

Support for suppressive antibiotic therapy for prevention of recurrent cellulitis comes from multiple trials:

- In a randomized trial that included 274 patients with two or more episodes of lower extremity cellulitis, penicillin (250 mg orally twice daily) nearly halved the risk of recurrence during 12 months of prophylaxis (HR 0.55, 95% CI 0.35 to 0.86), but the protective effect diminished rapidly after the prophylaxis period ended [53]. A lower likelihood of response was observed among patients with a body mass index ≥33 kg/m^2, multiple previous episodes of cellulitis, or lower extremity edema.

- Two separate meta-analyses of five trials totalling over 500 patients with recurrent cellulitis concluded that prophylactic antibiotics substantially reduce the risk of subsequent cellulitis (relative risk [RR] 0.46, 95% CI 0.26-0.79, and RR 0.31, 95% CI 0.13 to 0.72, respectively) [57,58]. Findings from two of the included studies also demonstrated that antibiotic prophylaxis is cost-effective [55,59].

In the trials and meta-analyses, no significant differences in adverse effects were found between the groups that received antibiotics and those that did not.

Suppressive therapy may be continued for several months to years with interval assessments for efficacy and tolerance. Patients in whom recurrent cellulitis occurs while on suppressive therapy should undergo re-evaluation of predisposing conditions and antimicrobial agents. (See 'Prevention of recurrences' above.)

S. aureus decolonization — For patients with suspected recurrent *S. aureus* infection, we suggest an attempt at *S. aureus* decolonization. Detailed discussion of *S. aureus* decolonization is found elsewhere. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Prevention and control", section on 'Decolonization' and "Methicillin-resistant *Staphylococcus aureus* (MRSA) in children: Prevention and control".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Skin and soft tissue infections".)

SUMMARY AND RECOMMENDATIONS

- **Overview** – Patients with skin and soft tissue infection may present with cellulitis, erysipelas, or abscess. This topic addresses management of cellulitis and erysipelas in adults. The management of skin abscess is discussed separately. (See "Skin abscesses in adults: Treatment".)

- **Identify conditions treated differently than cellulitis** (algorithm 1)

  - **"Red-flag" conditions** – These warrant immediate hospitalization and often surgery. Examples include (table 6):
    - Toxic shock syndrome
    - Necrotizing soft tissue infection (eg, necrotizing fasciitis, including Fournier's gangrene)
    - Clostridial myonecrosis
    - Pyomyositis
    - Deep venous thrombosis (DVT)
    - Compartment syndrome

    (See '"Red-flag" conditions that warrant hospitalization' above.)

  - **Specific exposures and anatomic sites –** Some exposures or anatomic sites may require distinct antibiotic coverage, surgical intervention, or specific radiographic imaging:

    - Involvement of the hand, periorbital space, or neck

- Location over a joint (native or prosthetic), vascular graft, or other foreign body
- Infection of a diabetic foot ulcer, pressure ulcer, animal or human bite, puncture wound, or surgical wound
- Infection following exposure to water, soil, or recent travel

(See 'Wounds and exposures that warrant specific coverage' above and 'Anatomic site of infection' above.)

- **Antibiotic selection for cellulitis in immunocompetent patients without severe sepsis**

  - **Determine risk for MRSA or adverse outcomes** – Antibiotic selection depends on the risk for methicillin-resistant *S. aureus* (MRSA) or adverse outcomes. Features that increase those risks in this population include (see 'Indications for MRSA coverage' above):

    - Systemic toxicity (eg, fever, tachycardia)
    - Purulent wound drainage
    - Known MRSA colonization or infection
    - Injection drug use
    - Immunocompromise

  - **Antibiotic regimens**

    For immunocompetent patients with one of the above features, we suggest a regimen that covers beta-hemolytic streptococci, methicillin-sensitive *S. aureus* (MSSA), and MRSA (algorithm 1) (**Grade 2C**) (see 'With an indication for MRSA coverage' above):

    - Oral – Trimethoprim-sulfamethoxazole, amoxicillin plus doxycycline, or linezolid
    - Intravenous (IV) – Vancomycin
    - Other risk factors (table 2) may not be as strongly associated with MRSA infection so we individualize the decision for MRSA coverage in such cases.

    For immunocompetent patients without the above features, we suggest a narrower regimen with coverage for beta-hemolytic streptococci and MSSA (algorithm 1) (**Grade 2C**). (See 'Without an indication for MRSA coverage' above.)

    - Oral – Dicloxacillin, flucloxacillin, cephalexin, or cefadroxil
    - IV – Cefazolin, nafcillin, oxacillin, or flucloxacillin

    Intravenous therapy is warranted for patients with systemic toxicity (eg, fever, tachycardia), rapidly progressive or extensive erythema, or inability to absorb oral

therapy. (See 'Indications for parenteral therapy' above.)

- **Antibiotic regimens for cellulitis in patients with severe sepsis or an immunocompromising condition**

  - For patients with severe sepsis (eg, evidence of tissue hypoperfusion or organ dysfunction) or high-risk neutropenia (table 5), we suggest initial therapy with vancomycin plus cefepime (**Grade 2C**). This regimen provides broad coverage against MRSA, methicillin-sensitive *S. aureus* (MSSA), beta-hemolytic streptococci, and gram-negative organisms for patients at highest risk for poor outcomes. (See 'Patients with severe sepsis' above.)

  - For patients with other immunocompromising conditions (and without severe sepsis), we often use the same regimens as for immunocompetent patients. The decision to cover additional pathogens associated with specific conditions should be individualized (table 1). (See 'Immunocompromised patients without severe sepsis' above.)

- **Antibiotic regimens for erysipelas** – For patients with unambiguous erysipelas (eg, bright red erythema with distinct raised borders), we suggest antibiotics that primarily target streptococci (**Grade 2C**).

  Oral options include penicillin V potassium, amoxicillin, cephalexin, and cefadroxil. Parenteral options include cefazolin, nafcillin, and flucloxacillin. (See 'Treatment of erysipelas' above.)

- **Duration of antibiotic therapy** – We suggest five to six days of therapy rather than longer durations (**Grade 2C**). However, extended regimens (ie, up to 14 days) may be appropriate for severe or slowly responding cellulitis. Parenteral antibiotics should be switched to an oral option once clinical improvement has occurred. (See 'Duration of antibiotic therapy' above.)

- **Adjunctive therapy** – We instruct patients with cellulitis of the limb to elevate it to allow drainage of edema and hasten improvement.

  Areas of skin breakdown are potential points of entry that should be identified and managed. Common points of entry include intertrigo in the toe webs, tinea pedis, onychomycosis, lower extremity ulcers, atopic dermatitis, and psoriasis. (See 'Adjunctive treatments' above.)

- **Expected response** – Symptomatic improvement typically occurs within 24 to 48 hours, although visible improvement of skin manifestations can take 72 hours or longer. (See

'Monitoring response to therapy' above.)

- **Refractory infection** – Significant progression of erythema or continued systemic symptoms should prompt a search for possible reasons for treatment failure. Considerations include deeper infection, inadequate antibiotic penetration (eg, due to edema), or incorrect diagnosis. (See 'Refractory infection' above.)

- **Recurrent infection** – During the active stage of infection, management of recurrent episodes is the same as the approach for initial episodes.

  There are multiple tools to prevent recurrences (see 'Recurrent infection' above):

  - **Treating points of entry** (eg, intertrigo, chronic skin conditions). (See 'Alleviation of predisposing conditions' above.)

  - **Managing predisposing conditions** – For patients with lymphedema or venous insufficiency, we suggest compression therapy (**Grade 2B**). (See 'Compression therapy' above.)

  - **Antibiotic prophylaxis for select patients** – For patients who optimize predisposing conditions but still have recurrent cellulitis in the same anatomic site, we suggest prophylactic antibiotics (**Grade 2B**). For most patients, our preferred regimen is penicillin V (250 to 500 mg orally twice daily). (See 'Antibiotic prophylaxis for selected patients' above.)

  - ***S. aureus* decolonization** – For patients with suspected recurrent *S. aureus* infection, some experts attempt decolonization. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Prevention and control", section on 'Decolonization' and "Methicillin-resistant *Staphylococcus aureus* (MRSA) in children: Prevention and control".)

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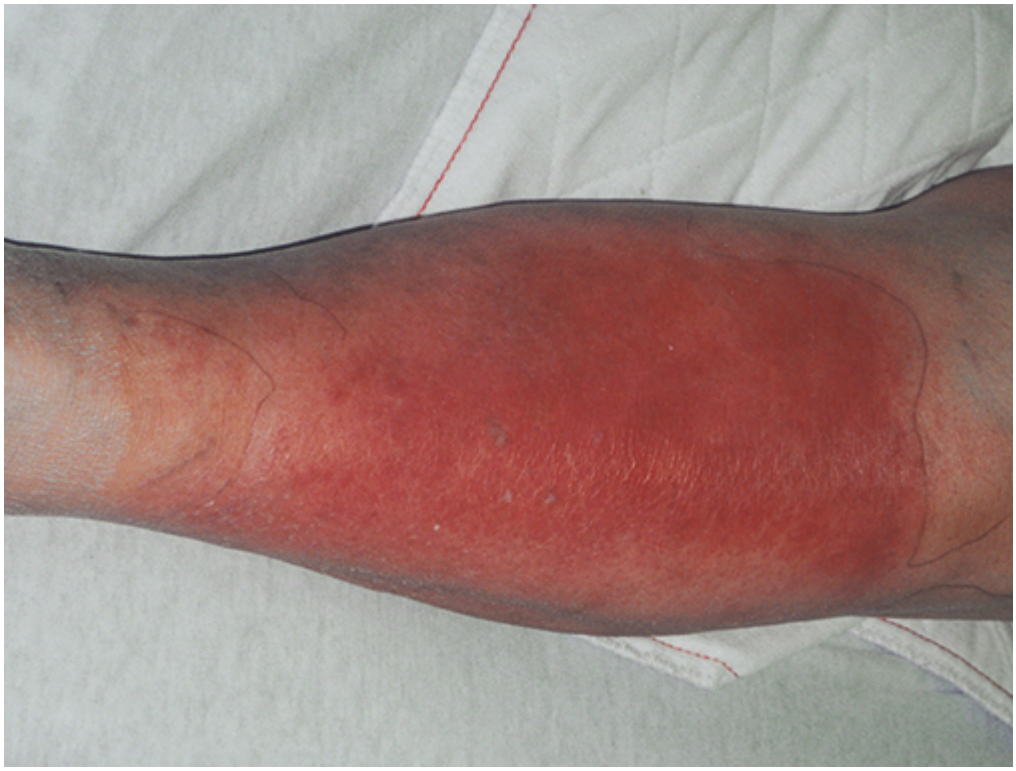
Topic 110530 Version 40.0

GRAPHICS

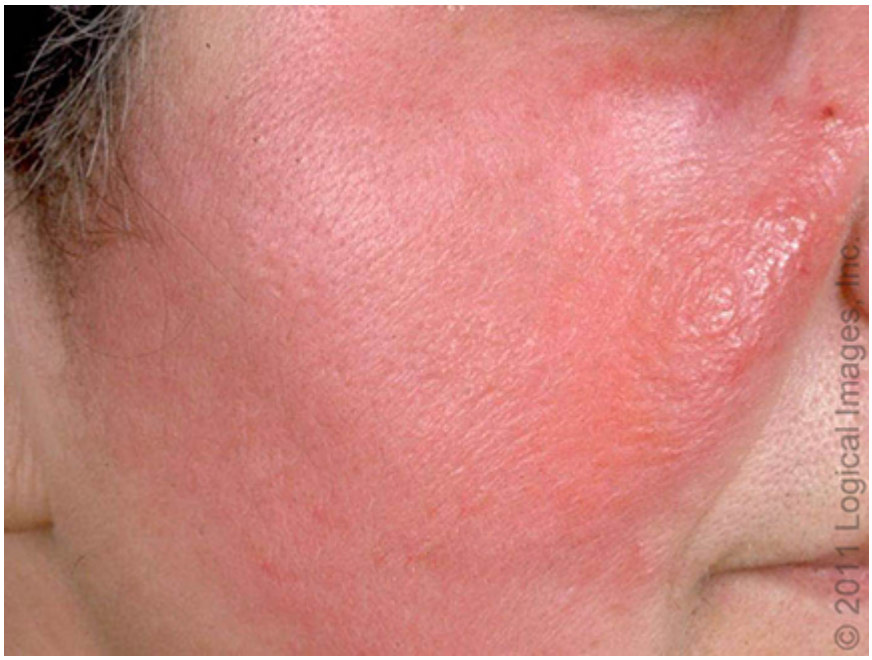
Erysipelas of the leg



Erysipelas of the lower leg. The rash is intensely red, sharply demarcated, swollen, and indurated.

Graphic 82542 Version 3.0

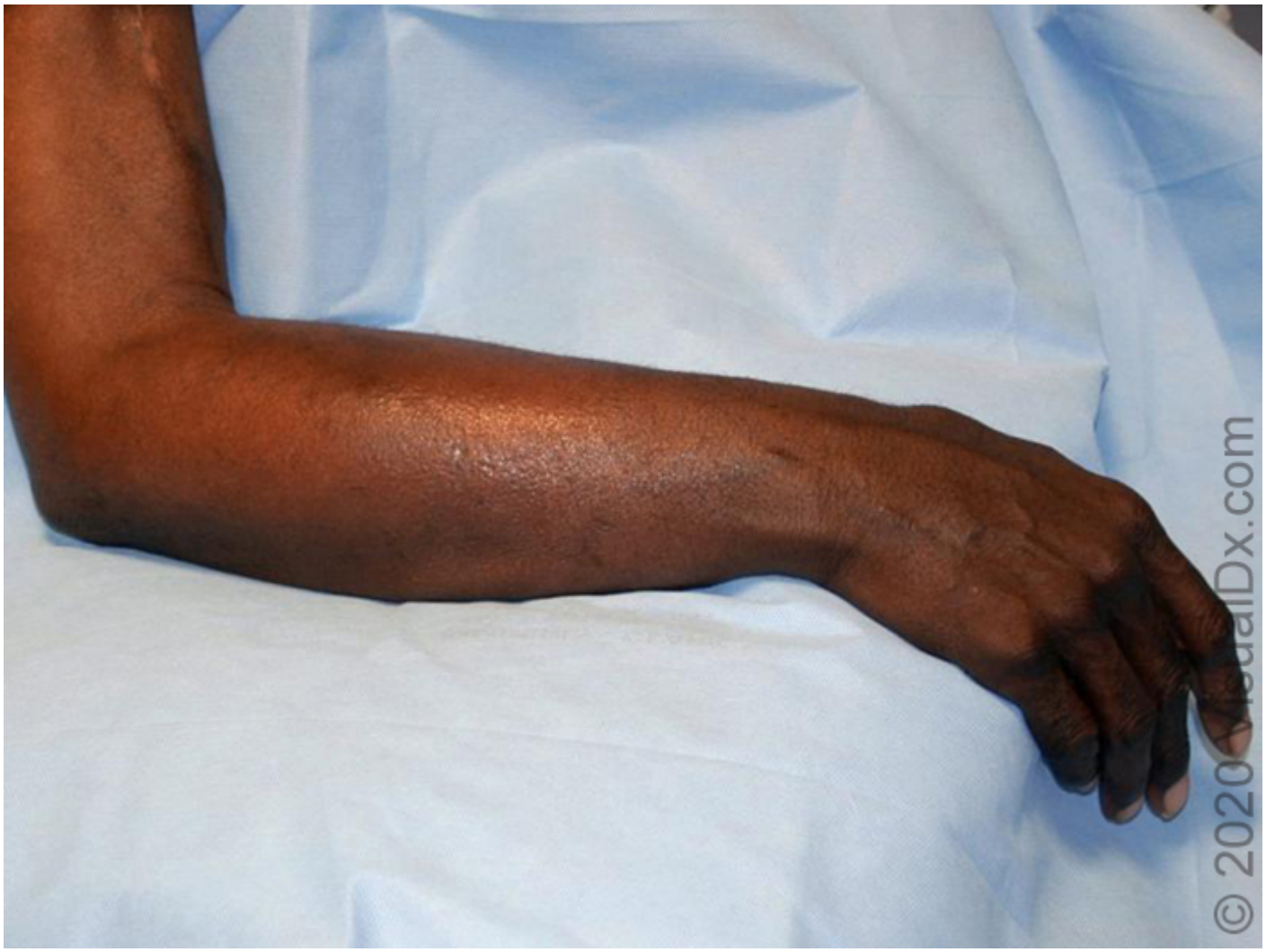
Erysipelas



Erysipelas lesions are raised above the level of surrounding skin, and there is a clear line of demarcation between involved and uninvolved tissue.

Graphic 67112 Version 6.0

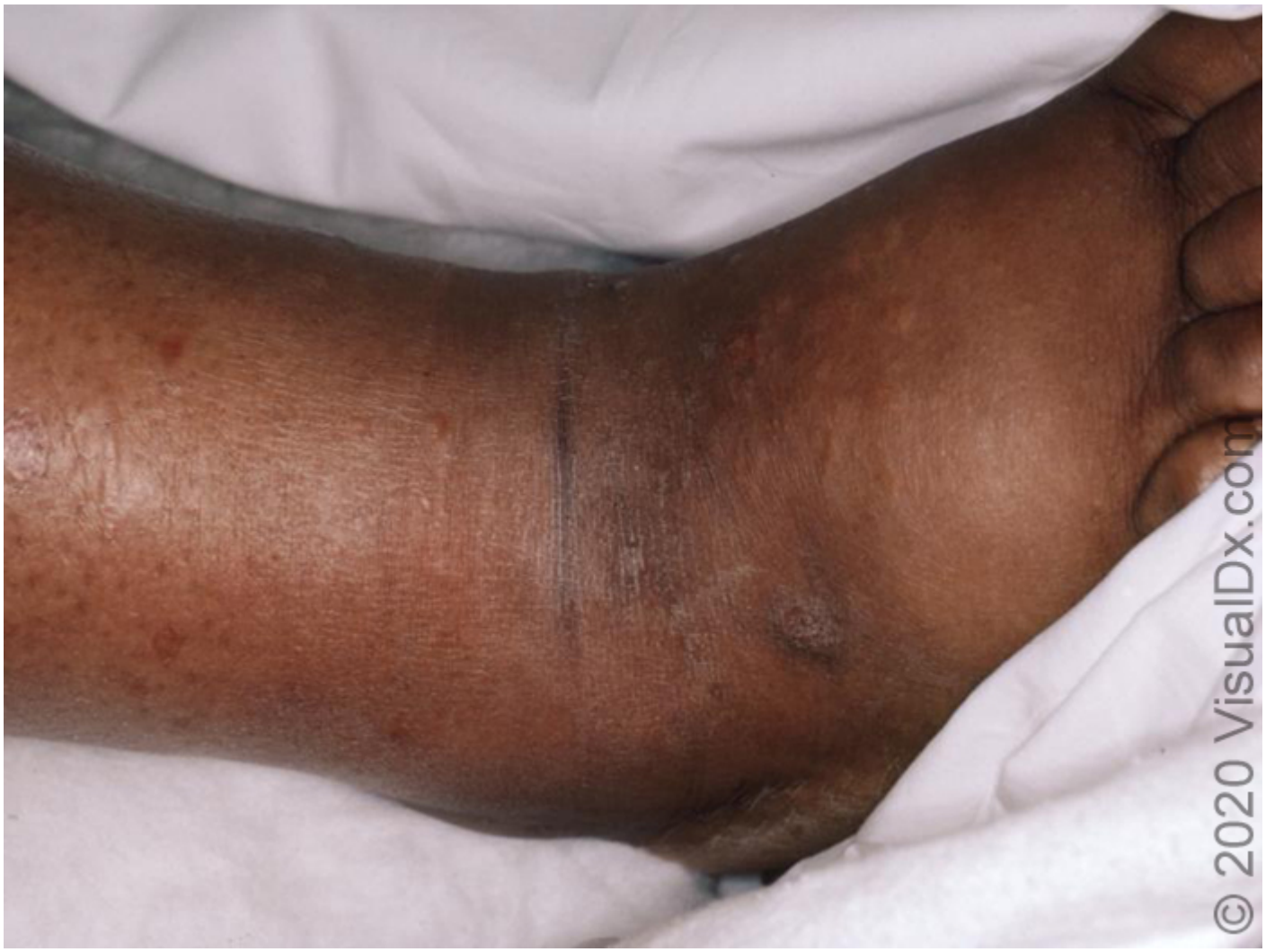
Cellulitis with erythema and edema



An extensive edematous and erythematous plaque on the arm.

Graphic 128910 Version 1.0

Cellulitis of the ankle



Edema and erythema around the ankle and on the dorsal foot.

Graphic 128906 Version 1.0

Microbiology of acute cellulitis

Exposure	Pathogen
Most common pathogens (regardless of exposure)	▪ Group A *Streptococcus* (ie, *Streptococcus pyogenes*) ▪ Non-group A, beta-hemolytic streptococci (groups B, C, G, and F) ▪ *Staphylococcus aureus* (*S. aureus*)
Cirrhosis	▪ Gram-negative bacilli: • *Klebsiella* spp • *Escherichia coli* • *Vibrio vulnificus* and *Vibrio parahaemolyticus** • *Aeromonas* spp*
Splenic or humoral immune dysfunction	▪ Encapsulated bacteria: • *Streptococcus pneumoniae* • *Haemophilus influenzae*
Neutropenia	▪ *Pseudomonas aeruginosa* and other Gram-negative bacilli ▪ *Clostridium* spp ▪ Invasive fungal infections
Fresh water (lakes, rivers)	▪ *Aeromonas hydrophila* ▪ *Plesiomonas shigelloides* ▪ *Edwardsiella tarda* ▪ *Pseudomonas aeruginosa* ▪ *Shewanella* spp
Salt water	▪ *Vibrio vulnificus* and *Vibrio parahaemolyticus* ▪ *Erysipelothrix rhusiopathiae*
Shellfish ingestion, especially oysters	▪ *Vibrio vulnificus* and *Vibrio parahaemolyticus*
Animal bite	▪ *Pasteurella multocida* ▪ *Capnocytophaga canimorsus* ▪ Anaerobic bacteria
Human bite	▪ *Eikenella corrodens* ▪ Anaerobic bacteria ▪ Viridans streptococci
Traumatic wound contaminated by soil	▪ *Clostridium* spp ▪ *Pseudomonas aeruginosa* and other Gram-negative bacilli ▪ Fungi (eg, mucormycosis)

Nail puncture through sneakers	▪ *Pseudomonas aeruginosa*
Recent travel	▪ Depends on the location of travel

* In patients with cirrhosis, *Vibrio* spp are only isolated following salt-water or raw shellfish exposure; *Aeromonas* spp cause infections following fresh-water exposure.

Graphic 143607 Version 1.0

Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in adults

Health care exposures during the prior 12 months:
▪ Recent hospitalization
▪ Residence in a long-term care facility
▪ Recent surgery
▪ Hemodialysis
Patient-specific risk factors:
▪ Known MRSA colonization or past infection with MRSA
▪ Recent close contact with a person colonized or infected with MRSA
▪ HIV infection
▪ Injection drug use
▪ Homelessness
▪ Men who have sex with men
▪ Antibiotic use within prior 6 months
Environmental exposures associated with outbreaks of MRSA skin abscesses*:
▪ Incarceration or working as prison guard
▪ Military service
▪ Attending schools or living in communities with high colonization rates
▪ Living in crowded conditions
▪ Attending or working in childcare centers
▪ Playing contact sports or sharing sporting equipment
▪ Sharing needles, razors, or other sharp objects

This list of risk factors is based on observational studies performed in different regions of the world. MRSA risk factors for individual countries may vary depending on local MRSA epidemiology.

MRSA: methicillin-resistant *Staphylococcus aureus*.

* These exposures are generally not associated with other types of MRSA infections, including cellulitis without abscess.

Graphic 53504 Version 14.0

Antibiotic selection for cellulitis in immunocompetent adults (no abscess present)

This algorithm is intended for immunocompetent adults with cellulitis. Treatment of erysipelas and skin abscess is discussed elsewhere, as is treatment of cellulitis in immunocompromised patients. Refer to UpToDate content for details.

ESBL: extended-spectrum beta-lactamase; IDU: intravenous drug use; IV: intravenous; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*.

* Patients with cellulitis and sustained refractory hypotension (ie, septic shock) are typically treated as toxic shock syndrome if no other red-flag conditions or causes of shock are identified. Refer to UpToDate content on toxic shock syndrome.

¶ For patients with severe sepsis who cannot take any beta-lactam agents, we suggest IV vancomycin plus either levofloxacin (750 mg IV once daily) or aztreonam (2 g IV every 8 hours; dosing up to 2 g every six hours may be reasonable for weight >120 kg).

Δ If a causative organism is identified, narrow antibiotics to target the pathogen as appropriate.

◇ For patients with lymphangitis, some UpToDate contributors would require additional criteria to warrant parenteral antibiotics.

§ Other risk factors may not be as strongly associated with MRSA infection, so we individualize the decision for MRSA coverage in such cases. A complete list of MRSA risk factors can be found in UpToDate content.

¥ Five to six days of antibiotic therapy is generally adequate; extension up to 14 days may be warranted for severe infection or slow clinical response.

‡ The majority of patients with reported beta-lactam allergies can take a cephalosporin (refer to UpToDate content for details).

† We generally avoid clindamycin, if possible, due to risk of *Clostridium difficile* infection and the possibility of streptococcal and staphylococcal resistance (refer to UpToDate content for details).

** For further details about vancomycin dosing, refer to UpToDate content.

Graphic 139109 Version 7.0

Approach to vancomycin dosing for adults with normal kidney function*

Loading dose (for patients with known or suspected severe *Staphylococcus aureus* infection)¶	Load 20 to 35 mg/kg (based on actual body weight, rounded to the nearest 250 mg increment; not to exceed 3000 mg). Within this range, we use a highe dose for critically ill patients; we use a lower dose for patients who are obese and/or are receiving vancomycin via continuous infusion.
Initial maintenance dose and interval	Typically 15 to 20 mg/kg every 8 to 12 hours for most patients (based on actual body weight, rounded to the nearest 250 mg increment). In general, the approach to establishing the vancomycin dose/interval is guided by a nomogram.Δ
Subsequent dose and interval adjustments	Based on AUC-guided (preferred for severe infection)[1] or trough-guided serum concentration monitoring.◇

AUC: area under the 24-hour time-concentration curve.

* Refer to the UpToDate topic on vancomycin dosing for management of patients with abnormal kidney function.

¶ For patients with known or suspected severe *S. aureus* infection, we suggest administration of a loading dose to reduce the likelihood of suboptimal initial vancomycin exposure. Severe *S. aureus* infections include (but are not limited to) bacteremia, endocarditis, osteomyelitis, prosthetic joint infection, pneumonia warranting hospitalization, infection involving the central nervous system, or infection causing critical illness.

Δ If possible, the nomogram should be developed and validated at the institution where it is used to best reflect the regional patient population. Refer to the UpToDate topic on vancomycin dosing for sample nomogram.

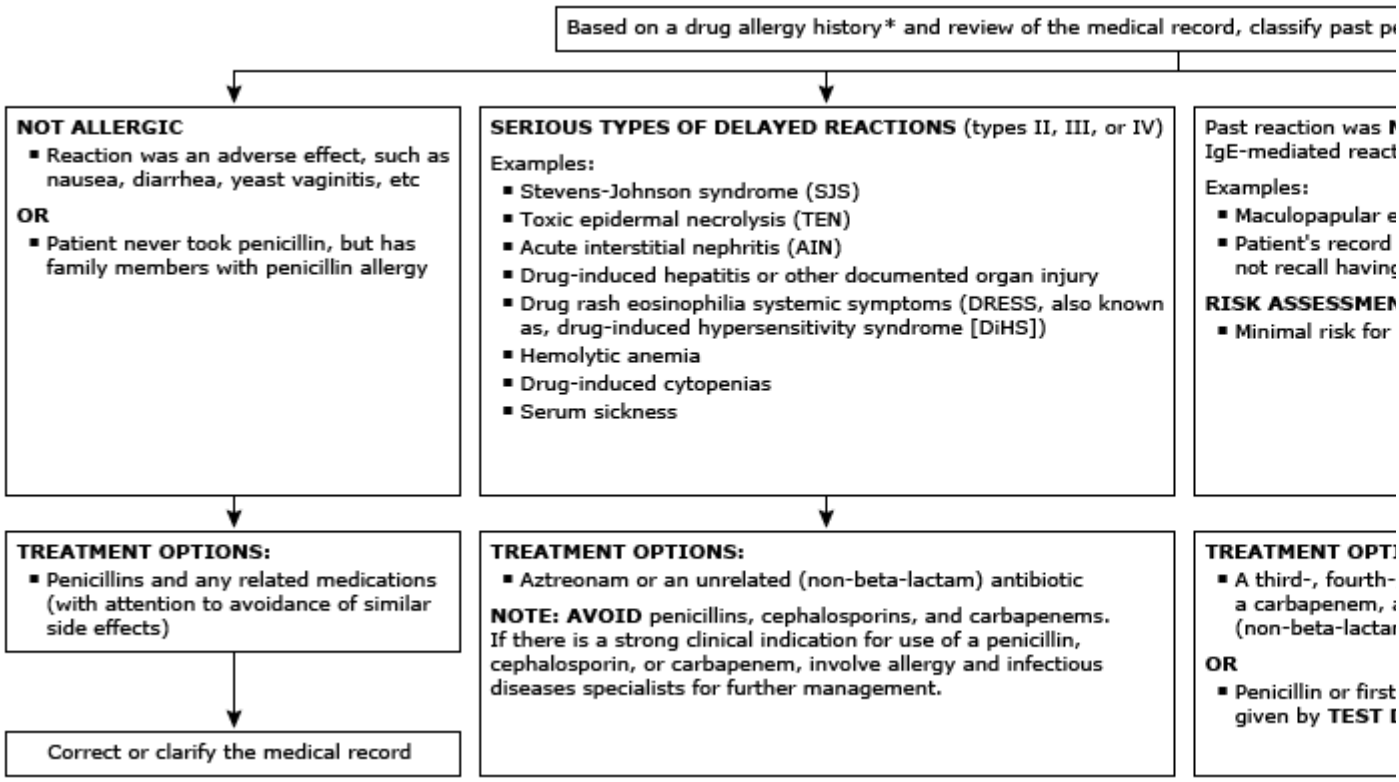
◇ Refer to the UpToDate topic on vancomycin dosing for discussion of AUC-guided and trough-guided vancomycin dosing. For patients with nonsevere infection who receive vancomycin for <3 days (in the setting of stable kidney function and absence of other risk factors for altered vancomycin kinetics), vancomycin concentration monitoring is often omitted; the value of such monitoring prior to achieving steady state (usually around treatment day 2 to 3) is uncertain.

Reference:

1. *Rybak MJ, Le J, Lodise TP, et al. Therapeutic Monitoring of Vancomycin for Serious Methicillin-Resistant Staphylococcus Aureus Infections: A Revised Consensus Guideline and Review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2020; 77:835.*

Graphic 128911 Version 5.0

Approach to the patient with a past penicillin reaction who requires antibiotics



This algorithm is intended for use in conjunction with the UpToDate content on choice of antibiotics in penicillin-allergic hospitalized patients. It is oriented toward hospitalized patients but also applies to outpatients if test dose procedures can be performed in an appropriately monitored setting with the staff and equipment needed to manage allergic reactions, including anaphylaxis.

IgE: immunoglobulin E.

* Ask the following:

1. What exactly were the symptoms?
    - Raised, red, itchy spots with each lesion lasting less than 24 hours (hives/urticaria)?
    - Swelling of the mouth, eyes, lips, or tongue (angioedema)?
    - Blisters or ulcers involving the lips, mouth, eyes, urethra, vagina, or peeling skin (seen in SJS, TEN, other severe type IV reactions)?
    - Respiratory or hemodynamic changes (anaphylaxis)?
    - Joint pains (seen in serum sickness)?
    - Did the reaction involve organs like the kidneys, lungs, or liver (seen in DRESS, other severe type IV reactions)?
2. What was the timing of the reaction after taking penicillin: Minutes, hours, or days later? Was it after the first dose or after multiple doses?
3. How long ago did the reaction happen? (After 10 years of avoidance, only 20% of patients with IgE-mediated penicillin allergy will still be allergic).
4. How was the reaction treated? Was there a need for urgent care or was adrenaline/epinephrine administered?

5. Has the patient tolerated similar medications, such as ampicillin, amoxicillin, or cephalexin since the penicillin reaction?

¶ Isolated mild hives, without other symptoms of an IgE-mediated reaction, can often occur in the setting of an infection. Patients with this history, especially if it occurred in childhood or >10 years ago, may also be considered to be at minimal risk for a recurrent serious reaction.

Δ This algorithm is intended for use in conjunction with additional UpToDate content. For a description of how to safely perform a TEST DOSE PROCEDURE, refer to the UpToDate topic on choice of antibiotics in penicillin-allergic hospitalized patients.

◇ Consult allergist to perform skin testing. If skin testing is not possible, patient may still be able to receive penicillins or first- or second-generation cephalosporins using a desensitization (also known as tolerance induction) procedure. Refer to the UpToDate topic on rapid drug desensitization for immediate hypersensitivity reactions.

Original figure modified for this publication. Blumenthal KG, Shenoy ES, Varughese CA, et al. Impact of a clinical guideline for prescribing antibiotics to inpatients reporting penicillin or cephalosporin allergy. Ann Allergy Asthma Immunol 2015; 115:294.

Graphic 112936 Version 5.0

Parenteral antimicrobial therapy for treatment of skin and soft tissue infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) in adults

Drug	Adult dose
Antibiotics of choice*	
Vancomycin¶	15 to 20 mg/kg/dose every 8 to 12 hours
Daptomycin△	4 to 6 mg/kg IV once daily
Alternative agents	
Short-acting agents with parenteral or oral dosing	
Linezolid	600 mg IV (or orally) twice daily
Tedizolid	200 mg IV (or orally) once daily
Delafloxacin	300 mg IV twice daily (or 450 mg orally twice daily)
Omadacycline◇	100 mg IV once daily (or 300 mg orally once daily)
Short-acting agent with parenteral dosing§	
Ceftaroline	600 mg IV every 12 hours
Telavancin	10 mg/kg once daily
Long-acting agents with parenteral dosing	
Dalbavancin	Single-dose regimen: 1500 mg once Two-dose regimen: Initial dose 1000 mg, followed by 500 mg dose one week later
Oritavancin	1200 mg IV as a single dose

MRSA: methicillin-resistant *S. aureus*; IV: intravenously; AUC: area under the 24-hour time-concentration curve.

* In areas outside the United States where teicoplanin is available, some use it as the drug of choice for initial therapy of gram-positive pathogens, while others favor its use for patients with intolerance to vancomycin.

¶ For severely ill patients, a vancomycin loading dose (20 to 35 mg/kg) is appropriate[1]; within this range, we use a higher dose for critically ill patients. The loading dose is based on actual body weight, rounded to the nearest 250 mg increment and not exceeding 3000 mg. The initial maintenance dose and interval are determined by nomogram (typically 15 to 20 mg/kg every 8 to 12 hours for most patients with normal renal function). Subsequent dose and interval adjustments are based on AUC-guided or trough-guided serum concentration monitoring. Refer to the UpToDate topic on vancomycin dosing for sample nomogram and discussion of vancomycin monitoring.

Δ Dosing of daptomycin for treatment of skin and soft tissue infection is 4 to 6 mg/kg IV once daily; dosing for treatment of bacteremia is at least 6 mg/kg IV once daily. (Refer to the UpToDate topic on treatment of MRSA bacteremia for further discussion.)

◇ A loading dose may be used: 200 mg IV over 60 minutes OR 100 mg IV over 30 minutes twice.

§ Ceftobiprole has broad-spectrum activity against gram-positive and gram-negative organisms and is available in some countries outside the United States.

Data from: Lui C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis 2011; 52:285.

Reference:

1. *Rybak MJ, Le J, Lodise TP, et al. Therapeutic Monitoring of Vancomycin for Serious Methicillin-Resistant Staphylococcus Aureus Infections: A Revised Consensus Guideline and Review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2020; 77:835.*

Graphic 110072 Version 11.0

Patients with chemotherapy-induced neutropenic fever who are at high risk fo serious complications

Patients with **any** of the following characteristics are considered to be at high risk for serious complications during episodes of neutropenic fever:
Receipt of cytotoxic therapy sufficiently myelosuppressive to result in anticipated severe neutropenia (ANC <500 cells/mcL) for >7 days*
MASCC risk index score <21[Δ]
CISNE score of ≥3[Δ] (in patients with solid tumors)
Presence of any active uncontrolled comorbid medical problems, including, but not limited to: ▪ Signs of severe sepsis or septic shock (eg, hemodynamic instability, mental status changes of new onset, respiratory dysfunction, oliguria) ▪ Oral or gastrointestinal mucositis that interferes with swallowing or causes severe diarrhea ▪ Gastrointestinal symptoms, including abdominal pain, nausea and vomiting, or diarrhea ▪ Intravascular catheter infection, especially catheter tunnel infection ▪ New pulmonary infiltrate or hypoxemia ▪ Underlying chronic lung disease ▪ Complex infection at the time of presentation
Alemtuzumab or CAR-T cell use within the past two months
Uncontrolled or progressive cancer[¶]
Evidence of hepatic insufficiency (defined as aminotransferase levels >5 times normal values) or renal insufficiency (defined as a creatinine clearance of <30 mL/minute)

ANC: absolute neutrophil count; MASCC: Multinational Association for Supportive Care in Cancer; CISNE: Clinical Index of Stable Febrile Neutropenia; CAR: chimeric antigen receptor.

* The authors use an anticipated ANC threshold of <500 cells/microL for >7 days to consider a patient at high risk for serious complications. It should be noted that the Infectious Diseases Society of America and the National Comprehensive Cancer Network guidelines use an ANC threshold of ≤100 cells/microL for >7 days[1,2]. At the time that the patient presents with neutropenic fever, it is not always possible to anticipate whether the patient will have severe neutropenia (<500 cells/microL) for >7 days. Clinical circumstances that are likely to result in severe neutropenia for >7 days put patients at high risk for serious complications; these criteria are most likely to be met following induction chemotherapy for acute leukemia and during the pre-engraftment phase of myeloablative hematopoietic cell transplantation (particularly allogeneic).

¶ Defined as any leukemic patient not in complete remission or a nonleukemic patient with evidence of disease progression after more than two courses of chemotherapy.

Δ Refer to the associated UpToDate topic review for details about the MASCC risk index and the CISNE score.

Data adapted from:

1. *Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2011; 52:e56.*
2. *National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Prevention and treatment of cancer-related infections. Version 1.2018. Available at: http://www.nccn.org (Accessed on August 01, 2018).*
3. *Taplitz RA, Kennedy EB, Bow EJ, et al. Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America clinical practice guideline update. J Clin Oncol 2018; 36:1443.*

Graphic 67027 Version 15.0

Differential diagnosis of acute cellulitis

Etiology	Distinguishing features
Infectious	
Erysipelas	▪ Bright red appearance, most commonly on malar region of face ▪ Borders are raised and distinct
Necrotizing soft tissue infection (eg, necrotizing fasciitis)*	▪ Dusky skin appearance or woody induration ▪ Pain out of proportion to exam; tenderness may extend beyond the area of visible skin inflammation ▪ Rapid progression with severe sepsis or shock ▪ Crepitus and/or bullae in some cases
Toxic shock syndrome*	▪ Sustained hypotension ▪ Signs of organ failure (eg, acute kidney injury, thrombocytopenia)
Clostridial myonecrosis (gas gangrene)*	▪ Rapidly progressive severe muscle pain ▪ Crepitus and/or bullae in some cases
Skin abscess	▪ Tender, erythematous, fluctuant subcutaneous nodule
Pyomyositis*	▪ Localized muscle pain
Vascular graft infection*	▪ Cellulitis overlying a vascular graft ▪ Bloodstream infection
Mycotic aneurysm*	▪ Painful pulsatile mass
Native or prosthetic joint infection*	▪ Erythema overlying a joint ▪ Severe pain with joint manipulation, or inability to bear weight due to pain ▪ Prosthetic joint infection may have less severe pain
Acute osteomyelitis	▪ Erythema, edema, and point tenderness overlying bone
Erythema migrans	▪ Nontender, slowly progressive round or oval erythematous patch ▪ May have central clearing ▪ Patient may recall tick bite
Erythrasma	▪ Brown- or orange-hued erythema ▪ Distinct borders ▪ Located in intertriginous areas
Herpes zoster	▪ Vesicles or crusted lesions in dermatomal pattern

Vascular	
Venous stasis dermatitis	▪ Chronic scaly plaques with acute erythematous exacerbations ▪ Usually bilateral ▪ May be pruritic ▪ Often involves the medial ankle
Lipodermatosclerosis (panniculitis from chronic venous stasis)	▪ Firm, pigmented, painful induration ▪ Often begins on medial ankle ▪ Can be unilateral or bilateral
Lymphedema	▪ Chronic extremity edema ▪ May have pitting or firm induration ▪ Can be unilateral or bilateral
Deep venous thrombosis*	▪ Unilateral extremity edema ▪ Erythema, warmth, tenderness, and rate of progression less impressive compared with cellulitis ▪ May have low-grade fever
Hematoma	▪ Erythematous, orange, or violaceous hue ▪ Often associated with local trauma ▪ May be painful
Allergic or inflammatory	
Contact dermatitis	▪ Pruritic eczematous erythema with edema, vesicles, and distinct border ▪ Located around area of contact with allergen ▪ Patient may recall exposure
Insect bite/sting	▪ Painful or pruritic erythema expanding from site of bite ▪ Examination may reveal bite marks ▪ Some patients may not recall bite
Fixed drug reaction	▪ Round or oval erythematous or violaceous patch or patches ▪ Located on any part of body ▪ Begins 30 minutes to 8 hours after drug administration
Reaction to foreign body implant (eg, metal, mesh, silicone)	▪ Erythema overlying site of known foreign material
Injection site reaction	▪ Erythema expanding from site of injection
Eosinophilic cellulitis (Well syndrome)	▪ Recurrent erythematous patches or plaques ▪ Pruritic and non-tender

Miscellaneous	
Compartment syndrome*	▪ Tense, firm, "wood-like" edema ▪ Pain out of proportion to exam
Panniculitis	▪ Palpable nodules or plaques on deep palpation
Malignancy*	▪ Slowly progressive erythematous patches or plaques ▪ Examples include Inflammatory breast cancer and extramammary Paget disease of the genitalia or perineum
Calciphylaxis	▪ Extremely painful indurated nodules or plaques that progress to necrotic ulcers ▪ Occurs in patients with chronic kidney disease, especially those on hemodialysis
Radiation recall	▪ Painful erythema at site of prior radiation therapy ▪ Triggered by certain chemotherapeutic agents ▪ Occurs minutes to months after drug administration

The differential diagnosis of cellulitis is broad, and this table is not all-inclusive. In cases of presumed refractory cellulitis, consultation with an expert (eg, infectious diseases clinician, dermatologist) may be helpful.

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* These conditions are associated with high morbidity or mortality if not promptly recognized. Surgical intervention is often required.

Graphic 143606 Version 1.0