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Cellulitis

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Updated: May 7, 2010

Introduction

Background

The term "cellulitis" is commonly used to indicate an uncomplicated nonnecrotizing inflammation of the dermis and hypodermis related to acute infection that does not involve the fascia or muscles, and that is characterized by localized pain, swelling, tenderness, erythema, and warmth.^[1]

Pathophysiology

Cellulitis usually follows a break in the skin, such as a fissure, cut, laceration, insect bite, or puncture wound. Facial cellulitis of odontogenic origin may also occur. Patients with toe web intertrigo and/or tinea pedis and those with lymphatic obstruction, venous insufficiency, pressure ulcers, and obesity are particularly vulnerable to recurrent episodes of cellulitis. [2,3,4,5] Organisms on the skin and its appendages gain entrance to the dermis and multiply to cause cellulitis.

The vast majority of cases are caused by *Streptococcus pyogenes* or *Staphylococcus aureus*. Occasionally, cellulitis may be caused by the emergence of subjacent osteomyelitis. Cellulitis may rarely result from the metastatic seeding of an organism from a distant focus of infection, especially in immunocompromised individuals. This is particularly common in cellulitis due to *Streptococcus pneumoniae* and marine vibrios. *Neisseria meningitidis*, *Pseudomonas aeruginosa*, *Brucella* species, and *Legionella* species have also been reported as rare causes of cellulitis resulting from hematogenous spread.^[6]

Frequency

United States

Because cellulitis is not a reportable disease, the exact prevalence is uncertain; however, it is a relatively common infection. A 2006 study found an incidence rate of 24.6 cases per 1000 person-years.^[7]In a large epidemiological hospital-based study on skin, soft tissue, bone, and joint infections, 37.3% patients were identified as having cellulitis.^[8]More recently, an increasing trend has been registered.^[9]

International

Cellulitis has been found to account for approximately 3% of emergency medical consultations at one United Kingdom district general hospital.

Mortality/Morbidity

Cellulitis generally is a localized infection. Most patients treated appropriately recover completely. Mortality is rare (5%) but may occur in neglected cases or when cellulitis is due to highly virulent organisms (eg, *P aeruginosa*). Factors associated with an increased risk of death are the presence of concurrent illness (eg,

congestive heart failure, morbid obesity, hypoalbuminemia, diabetes, renal insufficiency, chronic liver disease, peripheral arterial disease, venous stasis, immune deficiency, cancer) or complications (eg, shock). [10,11]

Race

No racial predilection has been noted.

Sex

No predilection for either sex is usually reported, although a higher incidence among males has been reported in some studies. [7,12]

Age

No age predilection is usually described; however, studies found a higher incidence of cellulitis in general among individuals older than 45 years. [3,7,12] Moreover, cellulitis at certain anatomic sites may show a predilection for persons in certain age groups.

- Facial cellulitis is more common in children younger than 3 years.
- Perianal cellulitis is predominantly a disease of children. [13]

Clinical

History

The incubation period is somewhat organism dependent. Postoperative cellulitis at the surgical site due to group A beta-hemolytic streptococci may develop rather rapidly. On the other hand, cellulitis due to staphylococci usually is delayed in onset.

Patients report local pain and swelling at the site of cellulitis. Fever is common, and chills may be noted, particularly if suppuration has occurred. Malaise may be present.

The patient may report a history of trauma to the site. Severe bacterial cellulitis may occur as a postsurgical complication (eg, following hip replacement [14] or intravenous catheters insertion), after invasive cosmetic procedures (eg, liposuction or injection of nonbiodegradable fillers [15]), or secondary to lymphatic occlusion following either radical mastectomy [16,17] or conservative breast surgery [18]; impaired lymphatic drainage and edema are also considered predisposing factors to leg cellulitis following saphenous vein resection for coronary artery bypass. [19] Cellulitis has also rarely been reported as a possible postprocedural complication of radiation therapy. [20] However, cellulitis may just develop after a subtle disruption of the epithelial barrier or a trivial injury to the skin (eg, scratch, abrasion, animal bite, intravenous or subcutaneous drug injection, body piercing). [21,22,23,11]

Physical

The following images show the clinical appearance of cellulitis:



Cellulitis involving the hand.



Cellulitis involving the lower extremity.



Cellulitis involving the abdominal wall.

Involved sites are red, hot, swollen, and tender. Unlike erysipelas, the borders are not elevated or sharply demarcated. Lymphangitis, regional lymphadenopathy, or both may be present. Malaise, chills, fever, and toxicity may occur. In severe cases, patients may develop hypotension. Local suppuration may follow if therapy is delayed. Overlying skin may develop areas of necrosis. The most commonly involved site is the leg. [7,24]

Perianal cellulitis due to group A streptococci is usually observed among children with perianal fissures. It is characterized by perianal erythema and pruritus, purulent secretions, painful defecation, and bleeding in the stools.^[13]

Pneumococcal facial cellulitis occurs primarily in young children who are at risk for pneumococcal bacteremia. [25,26] Pneumococcal facial cellulitis may also manifest in adults as 2 distinctive clinical syndromes:

- Extremity involvement in individuals with diabetes mellitus or substance abuse
- Head, neck, and upper torso involvement in individuals with systemic lupus erythematosus, nephrotic syndrome, or hematologic disorders

Causes

In immunocompetent adults, cellulitis is usually due to *S pyogenes* and, occasionally, *S aureus*. [6,10,27,28,29] Isolation of methicillin-resistant *S aureus* (MRSA) is steadily increasing, especially among intravenous drug

users, HIV infected patients, prisoners, athletes, military trainees, and male homosexuals. [5,30]Bacterial strains may also show multiple resistance to other standard antibiotic treatments, including erythromycin.

In children, the most common cause of cellulitis is *S aureus*. Other causes include *S pyogenes* (perianal cellulitis), *Haemophilus influenzae*, and *S pneumoniae*.

Recurrent staphylococcal cellulitis may occur in patients with nasal carriage of staphylococci and those with Job syndrome. *S aureus* is also the leading cause of soft tissue infections in persons who abuse injection drugs.^[31]

Recurrent cellulitis due to streptococci may be observed in patients with chronic lymphedema (eg, from lymph node dissection, irradiation, Milroy disease, elephantiasis). [27,32,11] Streptococcal infections are also common in injection drug users. [33] Non-group A streptococci (ie, groups B, C, and G) are commonly implicated in cellulitis in patients with lymphatic obstruction or venectomy for coronary artery bypass graft. [19,34]

S pneumoniae is an uncommon cause of cellulitis in adults. [26,35,36] Pneumococcal cellulitis may occur from bacteremia. In a review of pneumococcal skin infection in adults, all such patients had an underlying chronic illness or were immunocompromised by drug or alcohol abuse. [37] Pneumococcal facial cellulitis occurs primarily in young children at risk for pneumococcal bacteremia. [25,38]

Patients who are immunocompromised with granulocytopenia, such as renal transplant recipients, may develop cellulitis due to infection with other organisms, including gram-negative bacilli (eg, *Pseudomonas, Proteus, Serratia, Enterobacter, Citrobacter*), anaerobes, other opportunistic pathogens (eg, *Helicobacter cinaedi, Fusarium* species), mycobacteria, and fungi (eg, *Cryptococcus*). [28,39,40,41,42,43,44,45,46,47] Preseptal cellulitis caused by dermatophytes is rarely observed, mostly in the pediatric age group. [48] Persistent cellulitis due to *Cryptococcus neoformans* infection has also been reported in a patient receiving renal dialysis. [49] *Escherichia coli* may be responsible for cellulitis in patients with nephrotic syndrome. [50]

Cellulitis from unusual bacterial species, including *Enterococcus faecalis*, Enterobacteriaceae, and *Bacteroides* and *Clostridium* species, may be observed following subcutaneous injections of illegal drugs. [51] If *Clostridium* species or other anaerobes (*Bacteroides*, *Peptostreptococcus*, *Peptococcus*, *Prevotella*) cause the infection, crepitant cellulitis is often observed clinically. [6]

Other uncommon causes of cellulitis include *Neisseria meningitidis; Mycobacterium avium-intracellulare; Mycobacterium marinum* following fish-tank or brackish water exposure; *Pasteurella multocida,* following animal bites; *Aeromonas hydrophilia,* following contact with fresh water^[52]; *Streptococcus iniae,* a fish pathogen causing infections in aquaculture farms; and *Chromobacterium violaceum* and *Vibrio vulnificus,* following contact with seawater. Cellulitis from marine vibrios in hepatopathic patients may also follow ingestion of contaminated raw oysters. [53,54,55,56,57,58,59,60,61]

Acinetobacter baumannii is an emerging multidrug-resistant pathogen that causes hospital-acquired soft tissue infections, including cellulitis, following gunshot wounds or use of invasive devices. [62] H influenzae has become a rare cause of buccal cellulitis in children after the introduction of the H influenzae type B vaccine. [63,64]

Differential Diagnoses

Angioedema, Acquired Nocardiosis

Erysipelas Pyoderma Gangrenosum

Erysipeloid Scleredema

Human Bites Thrombophlebitis

Impetigo Vibrio Vulnificus Infection

Insect Bites Wells Syndrome (Eosinophilic Cellulitis)

Myiasis

Necrotizing Fasciitis

Other Problems to Be Considered

Acute gout

Anaerobic myonecrosis

Calciphylaxis

Cutaneous anthrax

Graft versus host disease

Hyperimmunoglobulin D syndrome

Inflammatory carcinoma of the breast^[65]

Cutaneous metastasis from neoplasms (especially adenocarcinoma)

Envenomation by puncture with spines of stone fish (in the South Pacific)

Familial Mediterranean fever

Neutrophilic eccrine hidradenitis

Seal finger secondary to seal bites (in aquarium workers and veterinarians)^[66]

Sweet syndrome^[67]

Tumor necrosis factor receptor-associated syndrome

Other diseases that may sometimes mimic cellulitis include contact dermatitis, [68] drug or foreign body reactions, erythema nodosum, [68] urticaria, lymphedema, lupus erythematosus, sarcoidosis, lymphoma, leukemia, Paget disease, dendritic cell sarcoma, [69] rheumatoid arthritis, and panniculitis. [70]

Workup

Laboratory Studies

A raised white blood cell count is a frequent finding (unless the bone marrow is compromised from chemotherapy, malignancy, or infection), along with an increased body temperature, in up to 42% of patients. The erythrocyte sedimentation rate and C-reactive protein level are also frequently elevated, especially in patients with severe disease requiring prolonged hospitalization.

- Culture and Gram stain of draining material is helpful if blisters or abscesses are present.
- Needle aspiration of the advancing edge of cellulitis may also be stained with Gram stain and cultured. However, the organism can be so cultured in only approximately 30% of patients with cellulitis. [4] Therefore, because the bacterial etiology of cellulitis in usual cases is highly predictable, needle aspiration should be performed only in selected patients and/or in unusual cases. These include diabetic patients, immunocompromised individuals, patients with neutropenia or those not responding to empiric therapy, and patients with a history of animal bites or immersion injury. [5,72,73]
- Blood cultures are positive in only a few patients. [73,74] In one study, blood cultures performed for 553 patients with cellulitis revealed a significant patient-specific microbial strain in only 2%. The low yield from blood cultures has a marginal impact on clinical management, and this testing does not

appear to be cost effective for most patients with cellulitis, unless chills and high fever, which strongly suggest bacteriemia, are present.

- The prevalence of bacteriemia is higher in patients with cellulitis complicating lymphedema. Therefore, blood cultures are advisable in such patients; they are also recommended in patients with cellulitis involving specific anatomic sites, such as the oral and ophthalmic area, and in those with a history of contact with potentially contaminated water.
- If recurrent episodes of cellulitis are suspected to be secondary to tinea pedis, mycologic investigations are advisable.^[76]
- Skin biopsy is unnecessary, unless a nonbacterial etiology is suspected or in immunocompromised individuals.

Imaging Studies

Ultrasonography may be helpful in evaluating suppuration at the site and as an aid in guiding needle aspiration. [77] It can also help rule out deep vein thrombosis mimicking cellulitis. [6]

CT scanning or MRI may be helpful to rule out any underlying fasciitis or osteomyelitis, if suspected.

Procedures

Incision and drainage is recommended in case of blister or abscess formation, both to obtain material for microbiological investigations and hasten recovery.

Histologic Findings

Areas of cellulitis reveal findings of soft tissue inflammation. Leukocyte infiltration, capillary dilatation, and bacterial invasion of tissue are observed.

Treatment

Medical Care

Assessment of the infection and clinical history, taking into account patient comorbidities as well as recent surgery, traumas or burns, travel history, water exposure, and animal or bite exposure, is essential for adequate treatment planning.^[78]

Patients with mild cases of cellulitis may be treated in an outpatient setting. Oral agents with activity against staphylococci and streptococci (eg, dicloxacillin or flucloxacillin, cephalexin, cefuroxime axetil, erythromycin, clindamycin, cotrimoxazole, amoxicillin/clavulanate) are usually effective for the treatment of cellulitis in immunocompetent hosts. [4] Levofloxacin may also represent an alternative, but the prevalence of resistant strains has increased and fluoroquinolones are best reserved for organisms with sensitivity demonstrated by culture. [5,79,80] Sulfa drugs are effective against staphylococci but unreliable against streptococci.

Severely ill patients and those unresponsive to standard oral antibiotic therapy should be treated with intravenous antibiotics in the hospital. This is also recommended in immunosuppressed individuals, in those with facial cellulitis, and in any patients with a clinically significant concurrent condition, including lymphedema and cardiac, hepatic, or renal failure. Additionally, consider hospitalization when laboratory investigations reveal elevated creatinine, creatine phosphokinase, or C-reactive protein and/or low serum bicarbonate levels or marked left-shift polymorphonuclear neutrophils. [5]

Elevating limbs with cellulitis expedites resolution of the swelling. Cool sterile saline dressings may be used to remove purulent discharge from any open lesion.

Usually, cellulitis is presumed to be due to staphylococci or streptococci infection and is treated with beta-lactam antibiotics (eg, nafcillin, cefazolin). Other options in allergic patients include clindamycin or vancomycin. Ceftriaxone may be useful in the outpatient setting because it can be administered once daily. Agents with a broader spectrum of activity are recommended in selected patients, such as diabetic patients.

More specific antibiotic therapy may be indicated in patients who develop cellulitis in special settings (eg, after a human or animal bite, exposure to potentially contaminated fresh water or seawater). [57,82]

Treatment of cellulitis caused by uncommon organisms, such as *Vibrio* species or gram-negative bacteria, should be individualized to those recovered organisms. [83] In general, these organisms require treatment with drugs other than those discussed above. For instance, cellulitis due to *Vibrio* infection may be treated with tetracyclines, chloramphenicol, or aminoglycosides. [84]

Cutaneous cellulitis and soft tissue infections due to community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) represent an emerging problem also among patients who lack traditional risk factors.^[30]In such cases, management with standard gram-positive antibiotics may be ineffective, also because concomitant multiresistance to other antibiotics widely used in common empiric therapy, including erythromycin, may occur.^[82]

Bacterial strains are usually susceptible to gentamicin, tetracyclines, rifampin, trimethoprim/sulfamethoxazole, and vancomycin. [61,85] Clindamycin may be used in areas where inducible resistance is not prevalent. Daptomycin may also represent a cost-effective alternative for complicated skin infections. [86] Tigecycline may also offer a good MRSA coverage [78]. A randomized, open-label, comparator-controlled, multicenter, multinational study has demonstrated the efficacy of linezolid therapy and its superiority to vancomycin in the management of skin and soft tissue infections, including cellulitis, due to MRSA. [87] However, bacterial culture is still considered essential in order to determine the antibiotic susceptibility of the bacterial isolate and to adjust the systemic antimicrobial therapy according to sensitivity data.

If mycologic investigations performed to rule out tinea pedis as a possible cause of recurrent episodes of cellulitis detect the presence of fungal infection in toe webs or feet, treatment with topical antifungals is recommended. With severe chronic changes or if onychomycosis is providing a source for repeated infection, oral antifungals such as itraconazole or terbinafine may be considered.

Also see the clinical guideline summary from the Infectious Diseases Society of America, Practice guidelines for the diagnosis and management of skin and soft-tissue infections.

Surgical Care

Incision and drainage are indicated if suppuration has occurred.

Consultations

- Consult an infectious diseases specialist for recommendations on appropriate antibiotic therapy.
- Consult a surgeon for drainage of any abscess and debridement of any devitalized tissue,

especially if necrotizing fasciitis is suspected.

- Consult a dentist in case of facial cellulitis of odontogenic origin to plan tooth extraction or root canal treatment.
- Consult a critical care specialist in case of rapidly spreading infections with systemic symptoms.

Activity

Immobilization of the affected part may relieve pain.

Medication

The goals of pharmacotherapy are to eradicate the infection, to reduce morbidity, and to prevent complications.

Antibiotics

Systemic antimicrobials are the mainstay of therapy for cellulitis. Oral antibiotics may be used for mild or localized forms of cellulitis; intravenous antibiotics are indicated for more severe cases and for patients who are immunocompromised.

Dicloxacillin (Dycill, Dynapen)

Binds to one or more penicillin-binding proteins, which, in turn, inhibits synthesis of bacterial cell walls. For treatment of infections caused by penicillinase-producing staphylococci. May use to initiate therapy when staphylococcal infection is suspected.

Dosing

Adult

250-500 mg PO q6h, 1 h ac or 2 h pc

Pediatric

<40 kg: 25-50 mg/kg PO divided q6h >40 kg: Administer as in adults

Interactions

Decreases efficacy of oral contraceptives; increases effects of anticoagulants; probenecid and disulfiram may increase penicillin levels

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Monitor PT in patients taking anticoagulant medications; toxicity may increase in patients with renal impairment; epigastric pain, diarrhea, nausea, vomiting, dizziness, fatigue, abdominal pain, eosinophilia, fever, elevated liver transaminase levels, seizures, thrombocytopenia, agranulocytosis, leukopenia, pseudomembranous colitis, anaphylaxis, and anemia may occur

Cephalexin (Keflex, Biocef)

First-generation cephalosporin arrests bacterial growth by inhibiting bacterial cell wall synthesis. Bactericidal activity against rapidly growing organisms. Primary activity against skin florae; used for skin infections or prophylaxis in minor procedures.

Dosing

Adult

250-1000 mg PO q6h

Pediatric

25-100 mg/kg/d PO divided q6h

Interactions

Coadministration with aminoglycosides increases nephrotoxic potential

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Neutropenia, increased liver transaminase levels, thrombocytopenia, anaphylaxis, pseudomembranous colitis, diarrhea, nausea, vomiting, rash, headache, dizziness, and eosinophilia may occur; caution in patients hypersensitive to penicillin, with history of antibiotic-associated colitis, using nephrotoxic agents, with impaired renal function, or breastfeeding

Cefuroxime (Ceftin, Kefurox)

Second-generation oral cephalosporin antibiotic that inhibits cell wall synthesis and is bactericidal.

Dosing

Adult

250-500 mg PO bid for 10 d; absorption improved when taken pc

Pediatric

< 3 months: Not established

>3 months: 10-15 mg/kg PO bid for 10 d

Interactions

Disulfiramlike reactions may occur when alcohol is consumed within 72 h after administration; may increase hypoprothrombinemic effects of anticoagulants; may increase nephrotoxicity in patients receiving potent diuretics (eg, loop diuretics); coadministration with aminoglycosides increases nephrotoxic potential

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

May cause hemolytic anemia, thrombocytopenia, anaphylaxis, toxic epidermal necrolysis, Stevens-Johnson syndrome, seizures, agranulocytosis, interstitial nephritis, pseudomembranous colitis, neutropenia, diarrhea, nausea, thrombophlebitis, elevated liver enzymes, angioedema, rash, abdominal cramps, pruritus, eosinophilia, and elevated BUN/creatinine levels; caution in penicillin allergy, seizure disorder, when nephrotoxic agents are used, with history of antibiotic associated colitis, or with impaired renal function

Clindamycin (Cleocin)

Lincosamide for treatment of serious skin and soft tissue staphylococcal infections. Also effective against MRSA and aerobic and anaerobic streptococci (except enterococci). Inhibits bacterial growth, possibly by blocking dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest.

Dosing

Adult

150-450 mg PO g6h

Pediatric

25-40 mg/kg IV/IM divided q6-8h; not to exceed 4.8 g/d IV or 1.8 g/d PO

Interactions

Increases duration of neuromuscular blockade induced by tubocurarine and pancuronium; erythromycin may antagonize effects; antidiarrheals may delay absorption

Contraindications

Documented hypersensitivity; regional enteritis; ulcerative colitis; hepatic impairment; antibiotic-associated colitis

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe hepatic dysfunction; no adjustment necessary in renal insufficiency; associated with severe and possibly fatal colitis

Nafcillin (Nafcil, Unipen)

Penicillinase-resistant penicillin that inhibits cell wall synthesis and is bactericidal. Initial therapy for suspected penicillin G–resistant streptococcal or staphylococcal infections.

Use parenteral therapy initially in severe infections. Change to oral therapy as condition warrants. Because of thrombophlebitis, particularly in elderly patients, administer parenterally only for short term (1-2 d); change to oral route as clinically indicated.

Dosing

Adult

500 mg to 2 g IV/IM q4-6h; not to exceed 12 g/d IM or 20 g/d IV

Pediatric

50-100 mg/kg/d IV/IM divided q6-12h; not to exceed 12 g/d

Interactions

Associated with warfarin resistance when administered concurrently; effects may decrease with bacteriostatic action of tetracycline derivatives

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

To optimize therapy, determine causative organisms and susceptibility; >10 d of treatment required to eliminate infection and prevent sequelae (eg, endocarditis, rheumatic fever); perform culture after treatment to confirm infection is eradicated

Vancomycin (Lyphocin, Vancocin)

Intravenous antibiotic used to treat serious infections, especially for MRSA. Bactericidal and inhibits cell wall synthesis.

To avoid toxicity, current recommendation is to assay trough levels after third dose drawn 0.5 h prior to next dosing. Use CrCl to adjust dose in patients diagnosed with renal impairment.

Dosing

Adult

500 mg IV q6h or 1 g q12h; adjust dose for renal insufficiency

Pediatric

<7 days, <1200 g: 15 mg/kg IV q24h <7 days: 10-15 mg/kg IV q8-18h >7 days: 10-15 mg/kg IV q8-24h >7 days, >2000 g: 15-20 mg/kg IV q8h

Infants/children: 10 mg/kg IV q6h; not to exceed 1 g/dose, peak 25-40 mcg/mL, trough 5-10 mcg/mL

Interactions

Erythema, histaminelike flushing, and anaphylactic reactions may occur when administered with anesthetic agents; when taken concurrently with aminoglycosides, risk of nephrotoxicity may increase above that with aminoglycoside monotherapy; effects in neuromuscular blockade may be enhanced when coadministered with nondepolarizing muscle relaxants

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in renal failure and neutropenia; red man syndrome is caused by intravenous infusion that is too rapid (dose administered over a few min) but rarely occurs when dose is administered as 2-h administration or PO or IP administration; red man syndrome is not an allergic reaction; emergence of antimicrobial resistance among *S aureus* may occur

Linezolid (Zyvox)

Prevents formation of functional 70S initiation complex, which is essential for bacterial translation process. Bacteriostatic against enterococci and staphylococci and bactericidal against most strains of streptococci.

Dosing

Adult

400-600 mg PO/IV q12h for 10-14 d

Pediatric

Not established

Interactions

May cause hypertension when used concomitantly with adrenergic agents, including pseudoepinephrine, sympathomimetic agents, vasopressors, or dopaminergic agents (reduce dose of dopamine or epinephrine if concurrent use required); serotonin syndrome may occur if used concomitantly with serotonergic agents,

including TCAs, meperidine, dextromethorphan, trazodone, venlafaxine, and selective serotonin reuptake inhibitors

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Has mild MAOI properties and potential for same interactions as other MAOIs; caution in uncontrolled hypertension, pheochromocytoma, carcinoid syndrome, or untreated hyperthyroidism; caution in patients who are at increased risk for bleeding, have preexisting thrombocytopenia, receive concomitant medications that may decrease platelet count or function, or may require >2 wk of therapy (monitor platelet counts); unnecessary use may lead to development of resistance

Ceftriaxone (Rocephin)

Third-generation cephalosporin with broad-spectrum, gram-negative activity; lower efficacy against gram-positive organisms; higher efficacy against resistant organisms. Arrests bacterial growth by binding to one or more penicillin-binding proteins.

Dosing

Adult

1-2 g IV/IM qd or divided bid depending on severity of infection; not to exceed 4 g/d

Pediatric

Neonates >7 days: 25-50 mg/kg/d IV/IM; not to exceed 125 mg/d

Infants and children: 50-75 mg/kg/d IV/IM divided q12h; not to exceed 2 g/d

Interactions

Probenecid may increase levels; coadministration with ethacrynic acid, furosemide, and aminoglycosides may increase nephrotoxicity

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); superinfections and

promotion of nonsusceptible organisms may occur with prolonged use or repeated therapy; caution in breastfeeding

Cephazolin (Ancef, Kefzol, Zolicef)

First-generation semisynthetic cephalosporin that arrests bacterial cell wall synthesis, inhibiting bacterial growth. Resistance occurs by alterations in penicillin-binding proteins. Primarily active against skin florae, including *S aureus*. Typically used alone for skin and skin-structure coverage.

Dosing

Adult

1 g IV q8h

Severe infection: 2 g IV q6h

Pediatric

50-100 mg/kg/d IV divided q6-8h; not to exceed 6 g/d

Interactions

Probenecid prolongs effect; coadministration with aminoglycosides may increase renal toxicity; may yield false-positive urine-dip test results for glucose

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); superinfections and promotion of nonsusceptible organisms may occur with prolonged use or repeated therapy

Cephradine (Velosef)

First-generation semisynthetic cephalosporin that arrests bacterial cell wall synthesis, inhibiting bacterial growth. Broad-spectrum bacterial antibiotic active against gram-positive and gram-negative bacteria. Also highly active against most strains of penicillinase-producing staphylococci.

Dosing

Adult

250-500 mg PO q6h; alternatively, 500-1000 PO mg q12h

Pediatric

6.25-25 mg PO q6h

Interactions

Loop diuretics may increase nephrotoxicity of cephalosporins; probenecid may increase plasma concentrations of cephalosporins; iron supplements may reduce efficacy (take iron supplements ≥ 2 h before or after administration)

Contraindications

Documented hypersensitivity to the cephalosporin; porphyria

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Evidence indicates partial cross-allergenicity between penicillins and cephalosporins; therefore, use with caution in patients with known hypersensitivity to penicillins

Cefadroxil (Duricef)

First-generation semisynthetic cephalosporin that arrests bacterial growth by inhibiting bacterial cell wall synthesis. Bactericidal activity against rapidly growing organisms, including *S aureus*, *S pneumoniae*, *S pyogenes*, *Moraxella catarrhalis*, *E coli*, *Klebsiella* species, and *Proteus mirabilis*.

Dosing

Adult

1-2 g/d PO divided bid

Pediatric

30 mg/kg/d PO divided bid; not to exceed 2 g/d

Interactions

Probenecid may decrease clearance of cephalosporins; aminoglycosides and furosemide may increase nephrotoxicity; iron supplements may decrease efficacy

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); prolonged use may result in superinfection

Imipenem and cilastatin (Primaxin)

Used for severe disease. Used to treat multiple-organism infections in which other agents do not have broad-spectrum coverage or are contraindicated because of their potential for toxicity.

Dosing

Adult

500 mg IV q6h

Pediatric

<12 years: Not established; 15-25 mg/kg/dose IV q6h, not to exceed 4 g/d, suggested for >3 mo

>12 years: 50 mg/kg/d IV divided q6h; not to exceed 4 g/d

Interactions

Coadministration with cyclosporine may increase adverse CNS effects of both agents; coadministration with ganciclovir may result in generalized seizures

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Adjust dose in renal insufficiency (adult adjustments)

CrCl (mL/min) 80-50: 0.5 g q6-8h

CrCl 50-10: 0.5 g q8-12h

Hemodialysis: 0.25-0.5 g after hemodialysis, then q12h

Avoid use in children <12 y with CNS infections

Ertapenem (Invanz)

Bactericidal activity results from inhibition of cell wall synthesis and is mediated through ertapenem binding to penicillin-binding proteins. Stable against hydrolysis by a variety of beta-lactamases, including penicillinases, cephalosporinases, and extended-spectrum beta-lactamases. Hydrolyzed by metallobeta-lactamases.

Dosing

Adult

IV: 1 g qd for 14 d infused over 30 min

IM: 1 g qd for 7 d

Pediatric

Not established

Interactions

Probenecid may reduce renal clearance and increase half-life, but benefit is minimal and does not justify coadministration

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Pseudomembranous colitis may occur; seizures and adverse CNS reactions may occur; when using with lidocaine to administer IM, avoid inadvertent injection into blood vessel

Cotrimoxazole (Bactrim, Septra)

Inhibits bacterial growth by inhibiting synthesis of dihydrofolic acid. May be considered alternative to vancomycin in selected cases of MRSA infection.

Dosing

Adult

160/800 mg PO q12h for 10-14 d

Pediatric

<2 years: Do not administer

>2 years: 6-12 mg of trimethoprim/kg/d in 2 doses

Interactions

May increase PT when used with warfarin (perform coagulation tests and adjust dose accordingly); coadministration with dapsone may increase blood levels of both drugs; coadministration of diuretics increases incidence of thrombocytopenia purpura in elderly persons; phenytoin levels may increase with coadministration; may potentiate effects of methotrexate in bone marrow depression; hypoglycemic response to sulfonylureas may increase with coadministration; may increase levels of zidovudine

Contraindications

Documented hypersensitivity; megaloblastic anemia due to folate deficiency; age <2 mo

Precautions

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Do not use during last trimester of pregnancy, owing to potential toxicity to newborn (eg, jaundice,

hemolytic anemia, kernicterus)

Dosage adjustments (adult adjustments)

CrCl (mL/min) 80-50: Recommended IV dose q18h

CrCl 50-10: Recommended IV dose q24h

CrCl <10: Not recommended HD: 4-5 mg/kg after HD

During peritoneal dialysis: 0.16-0.8 g q48h

Discontinue at first appearance of rash or sign of adverse reaction; obtain CBC counts frequently; discontinue therapy if significant hematologic changes occur; goiter, diuresis, and hypoglycemia may occur with sulfonamides; prolonged IV infusions or high doses may cause bone marrow depression (if signs occur, give 5-15 mg/d leucovorin); caution in folate deficiency (eg, chronic alcoholism, elderly persons, those receiving anticonvulsant therapy, or those with malabsorption syndrome); hemolysis may occur in G-6-PD-deficient individuals; AIDS patients may not tolerate or respond to TMP-SMZ; caution in renal or hepatic impairment (perform urinalyses and renal function tests during therapy); give fluids to prevent crystalluria and stone formation

Amoxicillin/clavulanate (Augmentin)

Amoxicillin inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins. Addition of clavulanate inhibits beta-lactamase – producing bacteria. Good alternative antibiotic for patients allergic to or intolerant of macrolide class. Usually well tolerated and provides good coverage of most infectious agents. Good alternative when *S pyogenes* or anaerobes are considered likely.

Dosing

Adult

500 mg/125 mg q8h PO or IV for 10-14 d

Pediatric

<3 months: 125 mg/5 mL PO susp; 30 mg/kg/d (based on amoxicillin component) divided bid for 7-10 d >3 months: If using 200 mg/5 mL or 400 mg/5 mL susp, 45 mg/kg/d PO divided q12h; if using 125 mg/5 mL or 250 mg/5 mL susp, 40 mg/kg/d PO divided bid for 7-10 d

>40 kg: Administer as in adults

Interactions

Coadministration with warfarin or heparin increases risk of bleeding; may act synergistically against selected microorganisms when coadministered with aminoglycosides; coadministration with allopurinol may increase incidence of amoxicillin rash; may decrease efficacy of oral contraceptives when administered concomitantly

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Hepatic impairment may occur with prolonged treatment in elderly persons; diarrhea may occur; adjust dose in renal impairment; cross-allergy may occur with other beta-lactams and cephalosporins

Antibiotic, Tetracycline Derivative

Doxycycline

Broad-spectrum, synthetically derived bacteriostatic antibiotic in the tetracycline class. Almost completely absorbed, concentrates in bile, and is excreted in urine and feces as a biologically active metabolite in high concentrations.

Inhibits protein synthesis and, thus, bacterial growth by binding to 30S and possibly 50S ribosomal subunits of susceptible bacteria. May block dissociation of peptidyl t-RNA from ribosomes, causing RNA-dependent protein synthesis to arrest.

Dosing

Adult

100 mg twice daily

Pediatric

<8 years: Not recommended

Interactions

Bioavailability decreases with antacids containing aluminum, calcium, magnesium, iron, or bismuth subsalicylate; tetracyclines can increase hypoprothrombinemic effects of anticoagulants; tetracyclines can decrease effects of oral contraceptives, causing breakthrough bleeding and increased risk of pregnancy

Contraindications

Documented hypersensitivity; severe hepatic dysfunction

Precautions

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Photosensitivity may occur with prolonged exposure to sunlight or tanning equipment; reduce dose in renal impairment; consider drug serum level determinations in prolonged therapy; tetracycline use during tooth development (last half of pregnancy through age 8 y) can cause permanent discoloration of teeth; Fanconilike syndrome may occur with outdated tetracyclines

Follow-up

Further Inpatient Care

• If necrosis ensues, promptly remove diseased tissues by surgical debridement. [88] Plastic reconstruction with skin grafting or cutaneous flap resurfacing may be required to achieve final

wound closure.

 In case of partial inefficacy of parenteral antibiotics in patients showing hemorrhage and/or bullous cellulitis, administration of adjuvant systemic corticosteroids (prednisone 0.5 mg/kg/d for 5-8 d) may improve the response to treatment.^[89]

Transfer

 Transfer severely ill patients with cellulitis to an intensive care unit for closer observation and aggressive management.

Deterrence/Prevention

- Support stockings may help in cellulitis of the lower extremities.
- Cuts and fissures should be washed and kept clean while healing.
- Patients with recurrent streptococcal cellulitis may be helped with penicillin G (250 mg bid) or erythromycin (250 mg qd or bid).^[90]
- If recurrent episodes of cellulitis are suspected to be secondary to tinea pedis, treat with topical or systemic antifungals.
- Pneumococcal vaccine should prevent cellulitis due to such organisms in children. A study noted
 that 96% of the serotypes that cause facial cellulitis are included in the heptavalent-conjugated
 pneumococcal vaccine recently licensed in the United States.

Complications

- Local suppuration with abscess formation and skin necrosis (gangrenous cellulitis) may occasionally be observed.
- Myonecrosis, fasciitis, acute carpal tunnel syndrome (in upper limb cellulitis), and osteomyelitis may occur. [23]
- Thrombophlebitis may develop, particularly in the lower extremities.
- Bacteremia with seeding of distant sites may complicate cellulitis.
- · Meningitis may complicate facial cellulitis.
- Scarlet fever complicating streptococcal cellulitis has been observed but is rare. [91]
- Bacterial- and toxin-related effects may result in shock and multisystem organ failure. [10,88]
- Glomerulonephritis and bacterial endocarditis are possible complications.
- Recurrence of cellulitis may cause local persistent lymphedema. The final result is a permanent hypertrophic fibrosis to which the term elephantiasis nostras has been given.

Prognosis

• The prognosis of patients with uncomplicated cellulitis generally is excellent. Appropriate antibiotic

therapy generally results in complete resolution of the illness.

Patient Education

- Educate patients regarding proper skin hygiene to prevent cellulitis.
- For excellent patient education resources, visit eMedicine's Diabetes Center. Additionally, see eMedicine's patient education article Cellulitis.

Miscellaneous

Medicolegal Pitfalls

- Failure to diagnose other severe soft tissue infections or deep involvement (eg, gas gangrene, necrotizing fasciitis, septic arthritis) is a potential pitfall.
- Failure to hospitalize patients with severe cellulitis or signs of systemic sepsis or toxin-mediated disease for intravenous antibiotic therapy and closer observation may result in disease progression.
- Failure to assess preexisting allergy to antibiotics before starting treatment may represent a pitfall.

Special Concerns

- Cellulitis of the lower extremities is more likely to be complicated by thrombophlebitis in geriatric patients.
- Scar cellulitis is common in areas of previous burns, particularly areas that required treatment with grafts.

Multimedia



Media file 1: Cellulitis involving the hand.







Media file 3: Cellulitis involving the abdominal wall.

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Keywords

cellulitis, infection of the skin, skin infection, soft tissue infection, infection of the soft tissue, *Streptococcus* pyogenes, *Staphylococcus* aureus, *S* aureus

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Disclosure: Nothing to disclose.

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Acknowledgments

The authors and editors of eMedicine gratefully acknowledge the contributions of previous Chief Editor, William D. James, MD, to the development and writing of this article.

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