Goal. The goal of this lesson is to provide a review of and update for the treatment of select acute bacterial skin and skin structure infections that are commonly seen and treated in the community. This lesson reviews treatment recommendations published by the Infectious Disease Society of America (IDSA), and antimicrobials with methicillin-resistant Staphylococcus aureus (MRSA) activity.

Objectives. At the completion of this activity, the participant will be able to:

1. recognize the different types of skin and skin structure infections discussed in this lesson;
2. demonstrate an understanding of the emergence of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) in acute bacterial skin and skin structure infection;
3. identify empiric antimicrobial treatment options for impetigo, abscess, cellulitis, and other soft tissue infections; and
4. list fundamental prescribing and patient counseling points for the entities discussed.

Introduction
Acute bacterial skin and skin structure infections (ABSSSI), previously referred to as uncomplicated and complicated skin and skin structure infections (SSTI), present as a wide spectrum of disease. Disease may range from mild to severe, and includes impetigo, abscess, erysipelas, cellulitis, necrotizing fasciitis, and other soft tissue infections. Soft tissue refers to tissues that connect, support, or surround other structures and organs of the body that are not bone. Examples of soft tissue include muscle, tendons, fat, and blood vessels. The mechanism of such infections varies and may result secondary to minor or major abrasions, wounds, trauma, animal or human bites, or surgical site infections, among others.

ABSSSI are typically caused by gram-positive pathogens, including Staphylococcus aureus (S. aureus) and β-hemolytic streptococci. However certain gram-negative and anaerobic bacteria are also found in polymicrobial infections. Over the past decade, widespread emergence of community-associated [also referred to as acquired] methicillin-resistant S. aureus (CA-MRSA) has been reported. Previously, MRSA infections were limited to hospital-acquired infections or from other nosocomial sources.

While most uncomplicated SSTI can be successfully treated in the outpatient setting, complicated infections or those due to resistant organisms require intravenous treatment and/or hospitalization. Several newer intravenous antibiotics with MRSA coverage are available for the treatment of ABSSSI and include ceftaroline fosamil, daptomycin, linezolid, and telavancin. Outpatient parenteral antimicrobial therapy (OPAT) may be an option in select patients to prevent or shorten hospitalizations, decrease readmission rates, and reduce nosocomial infections and complications. Complicated skin and skin structure infections are one of the most common infections treated with parenteral antibiotics outside of the hospital.

The major types of skin and soft tissue infections that will be discussed in this lesson include impetigo, abscess, cellulitis, and erysipelas. With the exception of impetigo, treatment recommendations will be directed toward adults.

Impetigo
Impetigo is a contagious superficial bacterial skin infection commonly seen throughout the world. Its peak incidence is among children aged two to five years, but it can affect older children and adults. Impetigo occurs more frequently in tropical or subtropical climates, but is also prevalent in northern climates during the summer months.

Impetigo can occur as a result of either 1) bacterial invasion of previously normal skin, or 2) streptococcal colonization of intact skin followed by inoculation secondary to minor skin trauma, insect bites, etc. Risk factors include poverty, crowded living conditions, poor hygiene, and underlying scabies. Impetigo generally occurs on exposed parts of the body such as the face, especially around the nose and mouth, and on the arms.
or legs. Handwashing remains an important measure in reducing the spread among children.

The disease presents as multiple localized lesions that are either non-bullous or bullous, ranging from the size of a dime to a quarter. With both forms, the lesions enlarge and progress from papules to vesicles and pustules. Over about one week, the lesions break down leaving a brown crust and possibly depigmented areas. Systemic symptoms are usually absent, but regional lymphadenitis may occur in non-bullous impetigo. Ecthyma is a more extreme and less common form of impetigo where the infection invades a deeper layer of the skin.

Impetigo is almost exclusively caused by *Staphylococcus aureus* and/or β-hemolytic streptococci (primarily Group A). Since the 1990s, *S. aureus* has emerged as the most common pathogen involved in impetigo (70 percent of cases). A smaller number of cases are also due to CA-MRSA. Bullous impetigo is caused by strains of *S. aureus* that produce a toxin causing cleavage in the superficial skin layer.

Group A streptococci (GAS) that causes impetigo can also enter the respiratory tract resulting in strep throat. While impetigo and strep throat are mild illnesses due to GAS, “invasive GAS disease,” which is severe and life threatening, can also occur when it enters other parts of the body such as blood, lungs, and muscle. Post-streptococcal glomerulonephritis and rheumatic fever following impetigo have also been described.

The goal of treatment includes relieving discomfort, improving cosmetic appearance of the lesions, preventing further spread of the infection both in the patient and to others, and preventing recurrence. Topical therapy is recommended over systemic therapy in cases where only a small number of non-bullous lesions are present.

Mupirocin 2 percent ointment (Bactroban®) has a labeled indication for impetigo, with directions to apply to the affected area three times a day. According to the IDSA 2011 MRSA infection treatment recommendations, mupirocin 2 percent ointment can be used in children with minor skin infections such as impetigo.

Fusidic acid cream is also effective, however, it is not available in the U.S.

A third topical agent, retapamulin (Altabax®), also carries an FDA-approved indication for children (nine months of age and older) and adults. This agent is the first member in a new class of antibacterial agents called pleuromutilins. Retapamulin only needs to be applied twice daily, compared to three times a day with mupirocin. However, it is more expensive and is not FDA-approved for the treatment of MRSA due to mixed results in clinical trials.

Advantages of topical therapy include delivery of high concentrations of drug to only infected tissue, minimization of systemic absorption and toxicity, and avoidance of altering gastrointestinal flora. The use of topical agents in limited impetigo may also minimize bacterial resistance.

Oral antibiotics should be initiated in patients who do not tolerate a topical antibiotic, or in those with more extensive or systemic disease. The use of penicillin for primary treatment of GAS is no longer recommended. Since *S. aureus* now accounts for most cases, penicillinase-resistant penicillins or first-generation cephalosporins such as dicloxacillin, cephalaxin, and amoxicillin/clavulanate are preferred. Clindamycin, an option for penicillin-allergic patients, is also appropriate. Macrolides are no longer adequate therapy due to resistant strains of *S. aureus* or *S. pyogenes*. Fluoroquinolones should also be excluded since MRSA resistance to this class is extensive. In communities with a high prevalence of CA-MRSA, agents such as clindamycin, trimethoprim-sulfamethoxazole (TMP-SMX), and tetracyclines may be used. Note that tetracyclines should not be used in children less than eight years of age. Duration of treatment is based on clinical improvement, while seven days is considered sufficient in most cases.

**Abscess**

An abscess is a collection of pus within the dermis or subcutaneous tissues. Patients will present with nodules and surrounding erythema. The presence of an abscess is significant as it differs from cellulitis, and is more likely to be due to *S. aureus*.

Abscesses are treated primarily by incision and drainage. Therefore, it is important that they are distinguished from cellulitis. Antibiotic therapy is recommended for abscesses when associated with severe or extensive disease (involving multiple sites of infection), or rapid progression along with cellulitis; signs and symptoms of systemic illness; comorbidities or immunosuppression; extremes of age; abscess in an area difficult to drain (face, hand, and genitals); septic phlebitis; and lack of response to incision and drainage alone.

**Cellulitis and Erysipelas**

Cellulitis and erysipelas are diffuse, acute, spreading infections of the dermis. These infections present with edema and redness, are warm to touch, and sometimes cause inflammation of the regional lymph nodes. Systemic symptoms are usually mild, but can include fever, tachycardia, confusion, hypotension, and leukocytosis.

While the terms cellulitis and erysipelas may be used interchangeably by physicians, there are distinguishing features. Erysipelas is a non-complicated form of cellulitis and is almost always a streptococcal infection (and occasionally *S. aureus*) that involves the superficial layers of the dermis. It is characterized by well-demarcated, raised areas of vivid erythema. Erysipelas is more common in infants, young children, and older adults, and more frequently affects the lower extremities. Prompt diagnosis and treatment corresponds...
with a very good prognosis. The infection rarely extends into the deeper layers of the skin and soft tissues.

Alternately, cellulitis extends further into the deeper dermis and subcutaneous tissue and has less defined margins. Cellulitis is either purulent or nonpurulent. Purulent cellulitis is defined as cellulitis with associated purulent drainage or exudate in the absence of a drainable abscess.

Cellulitis and erysipelas result when organisms enter through breaches in the skin, most often on the lower legs. Other common sites include the upper extremities, trunk, perineum, or head and neck. Predisposing factors for these infections include conditions that make the skin more fragile or make local host defenses weaker. Examples include obesity, previous cutaneous damage, edema from venous insufficiency or lymphatic obstruction, and prior radiation therapy. The break in skin may be due to trauma, pre-existing skin infections such as impetigo, ulceration, or eczema among others. The breaks can be so small that they are not clinically apparent. Surgical procedures that disrupt lymphatic drainage (e.g., axillary node dissection for breast cancer) increase the risk of cellulitis.

Blood culture results are positive in fewer than 5 percent of cases. Other potential sources for culture include peripheral blood, needle aspirates, and skin biopsies. Surgical specimens in cases with purulence, abscess, or necrosis may be cultured, but many cases are nonpurulent.

Traditionally, cellulitis and erysipelas were managed empirically with agents that covered β-hemolytic streptococci and methicillin-sensitive S. aureus (MSSA). For classic erysipelas, penicillin has remained first-line therapy. However, because these two infections can be difficult to distinguish, they are often treated the same.

In 2005, IDSA released guidelines for SSTI, listing the following antibacterials as suitable agents for empiric outpatient treatment: dicloxacillin, cephalaxin, or clindamycin. Treatment may also need to be directed to other organisms including gram-negative organisms which can produce cellulitis in certain circumstances. Table 1 lists risk factors for other pathogens that may be involved in cellulitis. At the time of preparing the 2005 guidelines, IDSA did not recognize the role of CA-MRSA in cellulitis and, therefore, did not recommend empiric coverage. However, in 2011, IDSA published their first guideline specifically for the treatment of MRSA with recommendations on the management of some of the most common clinical syndromes encountered including skin and skin structure infections. These two guideline documents are the basis of the recommendations in this lesson.

### Increasing Prevalence of CA-MRSA

The prevalence of CA-MRSA has increased in the last decade and is currently a prominent cause of purulent ABSSSI in the United States. Data from a Los Angeles emergency department (ED) indicated that infections from CA-MRSA more than doubled within a five-year period in patients presenting with purulent ABSSSI, from 29 percent in 2001 to 64 percent in 2005.

CA-MRSA strains are more virulent than health care-associated (HA-MRSA) strains and may carry genes that involve toxins associated with tissue necrosis and more serious disease. CA-MRSA skin infections range from cutaneous abscesses to necrotizing fasciitis. CA-MRSA can also cause severe systemic infections including pneumonia and bloodstream infections. Unlike HA-MRSA, many CA-MRSA strains are susceptible to gentamicin, tetracyclines, lincosamides, and TMP-SMX. CA-MRSA refers to MRSA infections that occur in outpatients or within 48 hours of hospitalization, and lack nosocomial exposures such as indwelling device, recent hospitalization, surgery, dialysis, or residence

### Table 1

#### Risk factors for associated pathogens in cellulitis*

<table>
<thead>
<tr>
<th>Reported risk factors for MRSA</th>
<th>Risk factors associated with other pathogens</th>
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<tbody>
<tr>
<td>• Previous history of hospitalization or surgery within the past year</td>
<td>Diabetic foot infections</td>
</tr>
<tr>
<td>• Residence in a long term care facility within the past year</td>
<td>Often polymicrobial, including gram-positive and gram-negative aerobes and anaerobes</td>
</tr>
<tr>
<td>• Hemodialysis</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>• Previous MRSA infection or colonization</td>
<td>Gram-positive, gram-negative including <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>• Recent antibiotic use</td>
<td>Intravenous drug use</td>
</tr>
<tr>
<td>• Contact sports</td>
<td><em>Staphylococcus aureus, Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>• Patient report of “spider bite”</td>
<td>Human bites</td>
</tr>
<tr>
<td>• Purulent soft tissue infections</td>
<td>Polymicrobial mixture of oral anaerobes and aerobes</td>
</tr>
<tr>
<td>• Crowded living environments, such as homeless shelters, prisons, etc.</td>
<td>Dog and cat bites</td>
</tr>
<tr>
<td>• Intravenous drug use</td>
<td>Polymicrobial mixture of pathogens derived from the animal and host skin flora</td>
</tr>
<tr>
<td>• Men who have sex with men</td>
<td></td>
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<tr>
<td>• Household contacts with MRSA infection</td>
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</tbody>
</table>

* Derived from retrospective studies; may not discriminate between MRSA and non-MRSA infections. Adapted from Am J Med. 2011;124(12).p1116.
in a long-term care facility.

The IDSA document cites a study in which 73 percent of cases of nonpurulent cellulitis tested positive for serology to detect streptococci, indicating that it is still the predominant bacteria for nonpurulent cellulitis. On the other hand, a large study of purulent soft tissue infections in EDs across the U.S. found that 76 percent of cases were due to *S. aureus*, including 59 percent by CA-MRSA.

Hence, 2011 IDSA guidelines provide the following recommendations. 1) For outpatients with purulent cellulitis (e.g., cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess), empiric therapy for CA-MRSA is recommended pending culture results. Listed options include clindamycin, TMP-SMX, a tetracycline (doxycycline or minocycline), and linezolid. Empiric therapy for infection due to β-hemolytic streptococci is likely to be unnecessary. 2) For outpatients with nonpurulent cellulitis (e.g., cellulitis with no purulent drainage or exudate and no associated abscess), empiric therapy for infection due to β-hemolytic streptococci is recommended. Listed options include cephalaxin, dicloxacillin, and clindamycin. The role of CA-MRSA is unknown in nonpurulent cases, and empiric coverage for CA-MRSA if no response or systemic toxicity is known.

Cultures are recommended in patients who have not responded adequately to initial treatment or if there is a concern for a cluster or an outbreak. Five to 10 days of therapy is recommended, but should be individualized based on the patient’s clinical response for both types of cellulitis.

Patients with systemic toxicity and/or rapidly progressing or worsening infection despite receiving appropriate oral antibiotics may require inpatient management (i.e., intravenous antimicrobials) and surgical intervention. Hospitalized patients with complicated SSTI, defined as deeper soft tissue infections, surgical/traumatic wound infections, major abscesses, cellulitis, and infected ulcers and burns, should be treated with surgical debridement, broad spectrum antibiotics, and empiric therapy for MRSA pending culture results. Listed options include IV vancomycin, PO or IV linezolid, IV daptomycin, IV telavancin, and IV or PO clindamycin. A beta-lactam antibiotic, such as cefazolin or nafcillin, may be initiated in hospitalized patients with nonpurulent cellulitis and modified to MRSA therapy if there is no clinical response. Table 2 summarizes the recommended antimicrobial therapy for patients with cellulitis.

### Recurrent MRSA SSTIs
Health care providers may instruct patients on measures to prevent recurrent MRSA infection such as keeping draining wounds covered with clean, dry bandages; maintaining good personal hygiene with regular bathing and handwashing with soap and water or alcohol-based hand gel; and avoiding the re-use or sharing of personal items that have contacted infected skin.

Experts define recurrent disease as two or more separate SSTI episodes at different sites over a six-month period. Environmental hygiene measures, with appropriate detergents or commercially available cleaners, may be used in patients with recurrent infections within a household or commu-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Recommended antimicrobial therapy for patients with cellulitis</th>
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<tbody>
<tr>
<td><strong>Antimicrobial</strong></td>
<td><strong>Dose</strong></td>
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<tr>
<td><strong>Outpatient purulent cellulitis</strong></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 mg PO TID</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>1-2 DS tab PO BID</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg PO BID</td>
</tr>
<tr>
<td>Minocycline</td>
<td>200 mg x 1, then 100 mg PO BID</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg PO BID</td>
</tr>
</tbody>
</table>

| **Outpatient nonpurulent cellulitis** |  |
| Treatment for streptococci and MSSA |  |
| Cephalaxin | 500 mg PO QID |
| Dicloxacillin | 500 mg PO QID |
| Empiric coverage for CA-MRSA if no response or systemic toxicity |  |
| Clindamycin | 300-450 mg PO TID |

| **Hospitalized patients with cellulitis** |  |
| Treatment for MRSA |  |
| Vancomycin | 15-20 mg/kg/dose IV every 8-12 hour |
| Linezolid | 600 mg PO/IV BID |
| Daptomycin | 4 mg/kg/dose IV QD |
| Telavancin | 10 mg/kg/dose IV QD |
| Clindamycin | 600 mg PO/IV TID |

| If nonpurulent cellulitis, may consider treatment for streptococci and MSSA with modification to MRSA-active therapy if no response |  |
| Nafcillin or Oxacillin | 1-2 g IV every 4 hours |
| Cefazolin | 1 g IV every 8 hours |
nity, and should be geared toward cleaning high-touch surfaces (i.e., surfaces that come into frequent contact with bare skin such as counters, doorknobs, bath tubs, and toilet seats).

Decolonization with mupirocin nasal and/or chlorhexidine topical antiseptic solution may be an option in patients who develop recurrent SSTI despite optimizing wound care and hygienic measures. While oral antimicrobial therapy for decolonization is not routinely recommended, it may be considered if infections recur regardless of measures. However, there are no published data to support the efficacy of decolonization in patients with recurrent MRSA SSTI. The optimal regimen, frequency of application, and duration of therapy are unclear.

Antimicrobials for the Treatment of CA-MRSA in SSTI

Trimethoprim-sulfamethoxazole (TMP-SMX), widely known by the trade names Bactrim™ or Septra®, is prescribed as one to two double-strength tablets orally twice daily for the treatment of MRSA in adults. This agent is not FDA-approved for the treatment of any staphylococcal infection; however, 95 to 100 percent of CA-MRSA strains are susceptible to it in vitro and it is an important option for outpatient management of SSTI. TMP-SMX is classified as pregnancy Category C/D, and is not recommended for women in the third trimester of pregnancy (or for children <2 months of age). Caution should be exercised when using this agent in the elderly, especially in those receiving concurrent inhibitors of the renin-angiotensin system and in those with chronic renal insufficiency because of an increased risk of hyperkalemia.

Oral tetracycline antibiotics that may be used for MRSA include doxycycline and minocycline. The adult dose for doxycycline is 100 mg orally twice daily. It is FDA-approved for the treatment of SSTI due to S. aureus, but not specifically for those caused by MRSA. For minocycline, a 200 mg oral loading dose is recommended, followed by 100 mg twice daily. These agents have in vitro activity and appear to be effective for this indication, but data are limited and lacking to support use in more invasive infections. Tigecycline (Tygaci®), a derivative of tetracycline, is an FDA-approved intravenous agent for the treatment of complicated SSTIs in adults. However, FDA recently issued a warning to consider alternative agents in patients with serious infections because of an increase in all-cause mortality. Tetracyclines are classified as pregnancy Category D, and are not recommended for children less than eight years of age because of the potential for tooth enamel discoloration and decreased bone growth.

Clindamycin, also an acceptable empiric treatment of purulent cellulitis, should be prescribed as 300 to 450 mg orally three times a day. Although not specifically FDA-approved for the treatment of MRSA infection, it has become widely used for the treatment of SSTI. The D zone test is recommended for detection of inducible clindamycin resistance in erythromycin-resistant, clindamycin-susceptible isolates, and is readily available. While Clostridium difficile-associated disease may occur with virtually any antibiotic, it may occur more frequently following clindamycin treatment when compared with other oral agents.

Linezolid (Zyvox®) is a gram-positive agent that is bacteriostatic against enterococci and staphylococci, and bactericidal against most strains of streptococci. It is of the oxazolidinone class, and exhibits its antimicrobial effect via inhibition of bacterial protein synthesis. Linezolid is active against problematic organisms such as MRSA, penicillin-resistant Streptococcus pneumoniae, and vancomycin-resistant enterococci (VRE). Resistance surveillance data indicates that more than 99 percent of S. aureus strains are susceptible to linezolid. It is FDA-approved for the treatment of complicated SSTIs and nosocomial pneumonia. The dosage is 600 mg orally or IV every 12 hours in children ≥12 years and adults. Linezolid does not require dosage adjustments in patients with either renal or hepatic impairment. It is rather expensive compared to other oral agents available for CA-MRSA.

Adverse effects were observed in some animal studies and there are no adequate, well-controlled studies in pregnant women. Therefore, this agent is classified as pregnancy Category C. Excretion in breastmilk is unknown, thus caution is advised.

Linezolid is contraindicated with concurrent use or within two weeks of MAO inhibitors; and in patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis, and/or those taking sympathomimetics, vasopressive agents, and dopaminergic agents unless closely monitored for increased blood pressure. Additionally, linezolid should not be administered to patients taking SSRIs, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), meperidine or buspirone, unless closely monitored for signs or symptoms of serotonin syndrome.

Tyramine, an amino acid that helps regulate blood pressure, is naturally occurring in the body and is found in certain foods. Ingestion of foods rich in tyramine such as aged cheeses, cured meats, fermented cabbage, soy sauce, or broad bean pods, such as fava beans, should be avoided as this can cause sudden and severe high blood pressure. Food that has been improperly stored or spoiled can create an environment where tyramine concentrations may increase.

Thrombocytopenia has been reported with linezolid use and may limit its use in patients with pre-existing myelosuppression. Weekly CBC (complete blood count) monitoring is recommended, and the agent should be discontinued in circumstances where myelosuppression occurs or worsens. It has
also been associated with neuropathy and lactic acidosis. Other common adverse events include headache, diarrhea, insomnia, dizziness, rash, nausea, and vomiting.

**Vancomycin** is a glycopeptide that inhibits bacterial cell wall synthesis by blocking glycopeptide polymerization. While its use in ABSSSI does have some limitations, it is the most common choice for parenteral treatment of CA-MRSA with nearly 50 years of clinical use. Vancomycin is available in multiple generic formulations, reasonably well tolerated, associated with a low incidence of adverse effects, and is relatively inexpensive. Unfortunately, the susceptibility of MRSA to this antibiotic may be decreasing with increasing reports of clinical failure. The vancomycin breakpoints for susceptible, intermediate, and resistant minimum inhibitory concentrations (MIC) have been reduced in laboratory standards to reflect the changes that have been seen in MRSA vancomycin susceptibility. Studies have indicated that vancomycin tissue penetration is variable.

In 2009, the American Society of Health-System Pharmacists (ASHP), IDSA, and the Society of Infectious Diseases Pharmacists jointly issued a consensus statement on the therapeutic monitoring of vancomycin in adults. The panel agreed that antibiotics other than vancomycin should be considered when vancomycin MIC values are $\geq 2 \text{ mg/L}$ because it is unlikely that effective serum concentrations will be achieved when keeping within therapeutic trough levels. The IDSA MRSA treatment guidelines note that, for most patients with SSTI who have normal renal function and are not obese, 1 gm IV every 12 hours is sufficient. It is recommended that trough serum vancomycin levels always be maintained above $10 \text{ mg/L}$ to avoid development of resistance. Additionally, the panel recommends dosing vancomycin at 15 to 20 mg/kg/dose (based on actual body weight and not to exceed 2 gm/dose) every eight to 12 hours for seriously ill patients with MRSA infections and normal renal function. A loading dose of 25 to 30 mg/kg should also be considered in such instances. For these large doses, prolonging the infusion time to two hours, and using an antihistamine may reduce the risk of red man syndrome and possible anaphylaxis. For severe infections, higher trough concentrations of 15 to 20 mg/L are recommended to optimize pharmacodynamics, improve tissue penetration, and prevent resistance development. Serum trough concentrations should be obtained just prior to the fourth dose; monitoring of peak concentrations is not recommended.

Vancomycin has long been considered a nephrotoxic and ototoxic agent. Yet, according to the consensus statement, there are limited data suggesting a direct causal relationship between toxicity and specific serum vancomycin concentrations. In summary, trough monitoring is best suited for patients receiving aggressive dosing, those receiving concurrent nephrotoxins, patients with unstable renal function, or those receiving prolonged courses of therapy. There are limited data to support the safety of sustained trough serum vancomycin concentrations of 15 to 20 mg/L.

**Daptomycin** (Cubicin®) is a lipopeptide class antibiotic that disrupts cell membrane function via calcium-dependent binding, resulting in bactericidal activity in a concentration dependent manner. It is FDA-approved for adults with SSTI due to *S. aureus* among other indications. The dose is 4 mg/kg of total body weight once daily IV for seven to 14 days. The frequency of administration should be reduced to every 48 hours in patients with CrCl <30mL/min. Elevations in creatine phosphokinase (CPK), which are rarely treatment-limiting, have occurred in patients receiving higher doses such as 6 mg/kg for other indications. Patients should be monitored, however, for signs and symptoms of infection with suggested CPK weekly monitoring during therapy. The label recommends more frequent monitoring with current or previous statin therapy, unexplained CPK increases, or renal impairment. Daptomycin may also cause false prolongation of the PT and increase of INR with certain reagents. This agent is classified as pregnancy Category B.

**Telavancin** (Vibativ®), the active form of ceftaroline fosamil, is a broad spectrum cephalosporin with potent activity against MRSA. It exerts bactericidal activity by binding to key penicillin binding proteins, with enhanced affinity to several resistant pathogens including MRSA and strains that vancomycin and daptomycin are ineffective against. However, unlike many other new agents discussed in this lesson, ceftaroline is active against common gram-negative and some anaerobic bacteria. For complicated SSTI, the dose is 600 mg IV every 12 hours. Renal dosage adjustments are required for CrCl <50 mL/min. It is the only $\beta$-lactam with activity against MRSA.

**Ceftaroline** (Teflaro®), an intravenous lipoglycopeptide that inhibits cell wall synthesis leading to cell membrane depolarization. This powerful agent is bactericidal against gram-positive pathogens including MRSA, as well as vancomycin-intermediate and vancomycin-resistant *S. aureus* (VISA, VRSA). It is FDA-approved for complicated SSTI in adults dosed at 10 mg/kg IV every 24 hours. It is classified as pregnancy Category C, as adverse developmental outcomes were observed in animal data. Telavancin may prolong the QT interval and should be avoided in patients with a history of QT prolongation or certain cardiac conditions. Caution should also be exercised in patients with renal impairment or in those receiving other nephrotoxic medications. In two clinical trials, nephrotoxicity was more commonly seen in patients treated with telavancin than among those treated with vancomycin. Although renal dysfunction seems reversible upon cessation of therapy, the manufacturer’s label recommends monitoring renal
function during therapy and after discontinuation. The label also provides recommendations for dosage adjustments in patients with CrCl <50mL/min. Monitoring of serum levels is not available.

In December 2013, Cubist Pharmaceuticals announced that FDA had accepted the company’s New Drug Application for its investigational antibiotic, tedizolid phosphate (PO and IV) with priority review. Cubist is seeking FDA approval of tedizolid for the treatment of ABSSSI. If approved, tedizolid will be the second oral FDA-approved antibiotic for the treatment of complicated SSTI caused by MRSA and an alternative to linezolid.

Conclusion
Skin and soft tissue infections are common across all ages. While generally caused by *S. aureus* and β-hemolytic streptococci, it is important to note the increasing prevalence of MRSA. Treatment options are expanding. For the most up to date information, refer to the IDSA guidelines.

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The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CE activity and is targeted to pharmacists in all practice settings.

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Acute Bacterial Skin and Skin Structure Infections: Review and Update

1. Acute bacterial skin and skin structure infections are typically caused by:
   a. gram-positive pathogens.  c. anaerobes.
   b. gram-negative pathogens.

2. Which of the following diseases presents as multiple localized non-bullous or bullous lesions?
   a. Abscess  c. Erysipelas
   b. Cellulitis  d. Impetigo

3. Since the 1990s, which pathogen has emerged as most commonly involved in impetigo?
   a. S. pyogenes  c. CA-MRSA
   b. S. aureus  d. Group A Streptococcus

4. An impetigo treatment option for penicillin-allergic patients is:
   a. cephalexin.  c. dicloxacillin.
   b. clindamycin.  d. fluoroquinolones.

5. Which of the following skin and skin structure infections (SSTIs) is described as a collection of pus within the dermis or subcutaneous tissue?
   a. Abscess  c. Erysipelas
   b. Cellulitis  d. Impetigo

6. Abscesses are primarily treated with antibiotics.
   a. True  b. False

7. Cellulitis differs from erysipelas in that cellulitis:
   a. is almost always due to streptococci.
   b. involves the superficial layers of the dermis.
   c. is more common in infants and young children.
   d. extends into the deeper dermis and subcutaneous tissue.

8. According to the 2011 IDSA guidelines, which of the following antimicrobials is considered a suitable agent for empiric outpatient treatment of purulent cellulitis?
   a. Dicloxacillin  c. TMP/SMX
   b. Cephalexin  d. Ciprofloxacin

9. Which MRSA strain is more virulent and may carry genes that involve toxins associated with tissue necrosis?
   a. CA-MRSA  b. HA-MRSA

10. Published data support the efficacy of decolonization in patients with recurrent MRSA SSTI.
    a. True  b. False

11. Trimethoprim-sulfamethoxazole should be used with caution in the elderly because of an increased risk of:
    a. hypertension.  c. hypokalemia.
    b. hypotension.  d. hyperkalemia.

12. Compared to other agents used to treat CA-MRSA, Clostridium difficile-associated disease may occur more frequently following treatment with:
    a. daptomycin.  c. clindamycin.
    b. linezolid.  d. doxycycline.

13. Which of the following agents is FDA-approved for treatment of complicated SSTIs and nosocomial pneumonia?
    a. TMP-SMX  c. Linezolid
    b. Clindamycin

14. The susceptibility of MRSA to which of the following antibiotics may be decreasing with increasing reports of clinical failure?
    a. Vancomycin  c. Daptomycin
    b. Linezolid  d. Ceftaroline

15. Which of the following agents is active against common gram-negative and some anaerobic bacteria?
    a. Telavancin  c. Daptomycin
    b. Vancomycin  d. Ceftaroline

Complete the lettered box corresponding to your answer.

1. [a] [b] [c]  6. [a] [b]  11. [a] [b] [c] [d]
2. [a] [b] [c] [d]  7. [a] [b] [c] [d]  12. [a] [b] [c] [d]
3. [a] [b] [c] [d]  8. [a] [b] [c] [d]  13. [a] [b] [c] [d]
4. [a] [b] [c] [d]  9. [a] [b]  14. [a] [b] [c] [d]
5. [a] [b] [c] [d]  10. [a] [b]  15. [a] [b] [c] [d]

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