Treatment of Skin and Soft Tissue Infections

Loren G. Yamamoto, MD, MPH, MBA

Abstract: Group A streptococcus and Staphylococcus aureus are the most common bacterial etiologies of skin and soft tissue infections that range in virulence from very mild to limb/life threatening. Antibiotic coverage recommendations are varying and subject to controversy. Antibiotic resistance patterns are evolving with many different biochemical mechanisms. Rapid bacterial identification using mass spectrometry is on the horizon. Therapeutic considerations should include cost and adherence issues.

Key Words: skin infections, soft tissue infection, group A streptococcus, Staphylococcus aureus, staph aureus, impetigo, toxic shock, necrotizing fasciitis, intertrigo, bacterial virulence, bacterial resistance, antibiotics, antibiotic resistance

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TARGET AUDIENCE

This CME article is intended for pediatric emergency medicine physicians, emergency medicine physicians, pediatricians, nurse practitioners, nurses, physician assistants, and any other medical personnel involved in the care of children presenting with acute care conditions that could present with skin and soft tissue infections.

LEARNING OBJECTIVES

After completion of this CME article, readers should have improved their knowledge of and enhanced their competence to:

1. Clinically distinguish the various types of skin and soft tissue infections.
2. Identify the bacterial etiologies of skin and soft tissue infections.
3. Initiate effective antibiotic strategies to treat skin and soft tissue infections.

Skin and soft tissue infections commonly present to the emergency department (ED), urgent care, acute care, and primary care settings. Although most of these are not serious, treatment failure can result in the need for hospitalization. In addition, some patients can harbor uncommon and occult yet life-threatening conditions that are essential for the clinician to diagnose and treat immediately. The skin is a barrier to infection, but this can be breached via glands, follicles, wounds, bug bites, and common skin conditions such as eczema.

Impetigo and Its Relatives

Impetigo is a common infection. Culturing impetigo lesions classically yields both Staphylococcus aureus and Streptococcus pyogenes (also known as a group A beta-hemolytic streptococcus, group A streptococcus, GAS). This seemingly simple and common infection has great controversy in many aspects. Its history is informative of these controversies. In the early 1980s, a treatment strategy that was used taught that although both organisms were present, treating the GAS alone would be sufficient for clinical resolution. Even at that time, S aureus was largely penicillin resistant; thus, treating many patients with penicillin during this period did in fact result in clinical cures despite S aureus’ penicillin resistance.

Impetigo was also successfully treated with amoxicillin, erythromycin, and the emerging new cephalosporin class at that time. Clindamycin was not used during this period because it had developed a notorious reputation of pseudomembranous colitis. Even chloramphenicol was used more commonly than clindamycin in the early 1980s. Methicillin (intravenous [IV]), nafcillin (IV) oxacillin (IV or orally [PO]), cloxacillin (PO), and dicloxacillin (PO) were subsequently used as the desire to treat the S aureus component increased, although the data supporting this change in practice are difficult to substantiate. These drugs were known as penicillinase-resistant penicillins (a misnomer because their use was largely limited to S aureus, not other penicillinase-producing organisms). The suspension forms of these drugs had a bitter metallic taste, which prompted most pediatricians to treat patients with cephalosporins instead. Methicillin-resistant S aureus (MRSA) gradually became more common. Methicillin resistance corresponded with cephalosporin resistance as well, rendering both drug classes ineffective in treating MRSA. As the MRSA frequency increased, practitioners changed their treatment to clindamycin and trimethoprim-sulfamethoxasole (TMP-SMX), which had better coverage of S aureus. Unfortunately, whereas GAS was 100% sensitive to penicillins and cephalosporins, there was some modest resistance to clindamycin and what was thought to be frequent resistance to TMP-SMX. The history is interesting here because the strategy in the 1980s was to primarily treat the GAS component, but this gradually evolved to primarily treat the S aureus component. The data supporting this change are lacking, yet the current practice is so pervasive that no clinician would currently ignore the S aureus component.

Currently, GAS is still universally sensitive to penicillin and beta-lactams. The sensitivity of GAS to antibiotics other than beta-lactams is more difficult to determine. Most laboratories do not run sensitivity tests for GAS because it is 100% penicillin sensitive. In searching for antibiotic sensitivity in the literature, sensitivity to clindamycin seems to be fairly consistent at approximately 98%, but sensitivity to erythromycin ranges widely from 52% to 95%. In addition, many reports indicate that erythromycin sensitivity within a region can vary greatly during periods of high or low macrolide use. Thus, one should assume that GAS sensitivity to erythromycin is unpredictable. Staphylococcus aureus has clearly evolved to a different organism, but it is unclear if the early recommendation of ignoring the S aureus in the treatment of impetigo is still correct. Organisms can vary in 2 basic ways that are often considered the same, but they are clearly different: resistance and virulence.

Resistance refers to difficulties encountered in the treatment of the organism, of which antibiotic resistance dominates. Methicillin-resistant S aureus refer to S aureus that are resistant to methicillin (also resistant to cephalosporins and all the antistaph penicillins). Staphylococcus aureus is a penicillinase producer but

Professor of Pediatrics, University of Hawai’i John A. Burns School of Medicine and Kapi’olani Medical Center for Women & Children, Honolulu, HI. The author and staff in a position to control the content of this CME activity and their spouses/life partners (if any) have disclosed that they have no financial relationships with, or financial interest in, any commercial organizations pertaining to this educational activity.

Reprints: Loren Yamamoto, MD, MPH, MBA, Department of Pediatrics, 1319 Punahou St, 7th Floor, Honolulu, HI 96826 (e-mail: Loren@hawaii.edu).

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it possesses additional resistance factors rendering beta-lactamase inhibitor additives, such as clavulanic acid, tazobactam, and sulbactam, useless most of the time. The MRSAs are not homogeneous. There are multiple known subtypes. Community-acquired MRSAs tend to be sensitive to clindamycin, whereas hospital-acquired MRSAs are almost always clindamycin resistant. As clindamycin use increases, it is likely that clindamycin resistance will increase.

Virulence refers to the organism’s ability to inflict substantial harm on the body. The best example of this is the classic observation by microbiologists in the early 1900s in which it was noted that mice died when injected with colonies of smooth pneumococci (possessing a polysaccharide capsule), but the mice survived when injected with colonies of rough pneumococci (nonencapsulated). Encapsulated pneumococci are more virulent than nonencapsulated pneumococci. The polysaccharide capsule is a virulence factor that shields the organism from opsonization and other attempts by the immune system to neutralize the organism. We now know that pneumococcal vaccines target the polysaccharide capsules of the most virulent strains. Nonencapsulated pneumococci often result in simple nasopharyngeal colonization, sinusitis, and otitis media. Encapsulated pneumococci are the strains most often associated with invasive pneumococcal disease such as pneumococcal meningitis. Similarly, Haemophilus influenzae type B has a polysaccharide capsule virulence factor, whereas nontypable H influenzae is less virulent.

Staphylococcus aureus strains that produce toxic shock toxin can kill a patient (ie, it is highly virulent), whereas an ordinary S aureus without this toxin might cause impetigo (ie, its virulence is low). Both virulent and nonvirulent S aureus can be MRSA or methicillin-sensitive S aureus; thus, resistance does not necessarily correlate with virulence. Other virulence factors of S aureus are staphylococcal scaled skin syndrome (SSSS) epidermylocytolytic toxin, exotoxins associated with septic shock, and other factors that increase the invasiveness of the organism. For example, consider these 2 cases: a patient with a simple bee sting developed a modest cellulitis of the elbow. He shortly thereafter developed staphylococcal pneumonia, empyema, pneumothorax, and septic shock. Another patient presented with extensive impetigo and developed staphylococcal pneumonia, empyema, and septic shock. In considering these patients developed invasive disease whereas most patients have infections limited to cellulitis and impetigo, this could be due to host immunity factors, the quantitative load of organisms, and/or the virulence of the organism. Other S aureus virulence factors include membrane-damaging toxins, cell wall–anchored proteins, clumping factors A and B, fibronectin-binding proteins, Panton-Valentine leucocidin, alpha-hemolysin, phenol-soluble modulins, arginine catabolic mobile element, etc. Another type of resistance occurs when GAS is in close proximity to another penicillinase-producing organism such as S aureus. The penicillinase creates tiny microenvironments that are free of any penicillins, permitting GAS to survive. Although there are published treatment guidelines for impetigo, controversy remains. The GAS remains penicillin sensitive, yet S aureus is almost always resistant. It is currently

![FIGURE 1. MLS resistance. This is an agar plate of S aureus. There is no zone of inhibition around the E (erythromycin) disk on the left. There is a large zone of inhibition around the C (clindamycin) disk on the right, but in the area between the 2 disks, the clindamycin zone of inhibition is smaller with visible colonies growing adjacent to the clindamycin disk. The presence of erythromycin has induced resistance to clindamycin in this area. This picture is known as the D-test because it results in a D-shaped zone of inhibition around the clindamycin disk.](image)
unthinkable to treat impetigo with penicillin, although this had been done 30 years ago. Clindamycin is commonly used, yet there is increasing resistance by both GAS and *S aureus*. The GAS is cephalosporin sensitive; however, it will not cover MRSA. The TMP-SMX is more reliable in covering *S aureus*, but its coverage of GAS is thought to be poor based on older susceptibility studies. In vitro GAS susceptibility to TMP-SMX is dependent on thymidine present in the growth media because its presence bypasses the folate inhibition mechanism of action. When tested in non-thymidine-containing media, GAS was found to be sensitive to TMP-SMX. However, this in vitro testing needs to be confirmed to be valid in vivo because thymidine and other substrates are present in variable concentrations in the host as well. Table 1 shows some theoretical coverage rates depending on resistance rates in your community. Other than using linezolid, the highest theoretical success rate is achieved with TMP-SMX (assuming that this covers GAS), and cephalexin + clindamycin (which some might feel is too much antibiotic treatment for a relatively minor problem). Although most practitioners use clindamycin to treat impetigo, as clindamycin resistance increases, this treatment strategy will become less effective.

Whereas oral antibiotic strategies have some controversy, topical treatment with mupirocin is highly effective for superficial infections such as impetigo. If the number of lesions is limited, topical mupirocin is reasonably easy for a patient/parent to apply and there are minimal systemic adverse effects. If the number of lesions is high, then topical treatment becomes extensive that might prove to be difficult to apply or the patient/parent might not be willing to do this. Multiple tubes will be necessary increasing the cost of treatment, but many oral antibiotic strategies are similarly expensive. Oral antibiotic dosing might be easier, but it has systemic absorption and adverse effects that could be avoided with topical therapy.

**Impetigo With Febrile Erythroderma**

Some patients with impetigo will simultaneously present with a febrile erythroderma. Fever alone can increase the perfusion of the skin giving the patient the appearance of a slight erythroderma. A true erythroderma in conjunction with any GAS-associated condition such as impetigo, is most likely to be due to uncomplicated scarlet fever; however, some patients will have early streptococcal or staphylococcal toxic shock syndrome (TSS). It is critically important to distinguish the two because scarlet fever can usually be managed with oral antibiotics as an outpatient, whereas TSS requires intensive care unit management with fluid resuscitation and, in some cases, with vasoactive inotrope infusions. If the patient is obviously exhibiting signs and symptoms of shock, then the patient clearly needs to be admitted to the intensive care unit. However, most cases are not this obvious and, in fact, most cases are scarlet fever and not TSS. Because there is no readily available diagnostic test to distinguish the two, it probably is best to begin anti-GAS and anti-*S aureus* antibiotic treatment in the ED and monitor the patient for several hours. Laboratory testing can help to provide reassuring or nonreassuring information, yet these are not diagnostic. If the patient continues to improve during a prolonged ED observation, it is more likely that the patient’s erythroderma is due to scarlet fever, and the patient can be discharged from the ED after confirming the presence of reliable home observers and follow-up can be assured. If the patient has TSS, it is more likely that signs and symptoms of shock will develop. These can be variable, but even though tachycardia is nonspecific, its persistence should raise concern. Other concerning symptoms include lightheadedness, irritability, lethargy, combativeness, behavior changes, muscle pain, vomiting, and/or lower-than-expected urine output. If in doubt, extend the ED observation period or admit the patient to the hospital.

**Cellulitis**

Cellulitis can be caused by both GAS and *S aureus*. It is difficult to confirm the causative organism with certainty. Surface cultures can be misleading, blood cultures are most often negative, and leading edge or other soft tissue cultures have not proven to be useful. Cellulitis due to *S aureus* is usually localized under a cutaneous lesion, often with a small abscess or draining purulence. Cellulitis due to GAS is usually extensive with a central open lesion, most commonly on the lower extremities, but sometimes on the face. Its color is magenta, and the history is often that the large area of redness appeared in a relatively short period, which

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**TABLE 1. Antibiotic Sensitivity of GAS and *S aureus*. Theoretical Therapeutic Success Rate (Both Organisms Sensitive to the Antibiotic)**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>GAS Sensitivity</th>
<th><em>S aureus</em> Sensitivity</th>
<th>Theoretical Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Amoxicillin/clavulinate</td>
<td>100%</td>
<td>70%</td>
<td>70%</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>100%</td>
<td>69%</td>
<td>69%</td>
</tr>
<tr>
<td>Erythromycin&lt;sup&gt;3,5,7&lt;/sup&gt;</td>
<td>70%</td>
<td>55%</td>
<td>39%</td>
</tr>
<tr>
<td>Clindamycin&lt;sup&gt;3,5,7&lt;/sup&gt;</td>
<td>98%</td>
<td>76%</td>
<td>74%</td>
</tr>
<tr>
<td>Cephalexin + Clindamycin</td>
<td>100%</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>Penicillin + Clindamycin</td>
<td>100%</td>
<td>76%</td>
<td>76%</td>
</tr>
<tr>
<td>TMP-SMX (assumes GAS mod resistant)</td>
<td>50%</td>
<td>95%</td>
<td>48%</td>
</tr>
<tr>
<td>TMP-SMX (assumes GAS sensitive)</td>
<td>100%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Rifampicin&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>100%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Tetracycline&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>70%</td>
<td>99%</td>
<td>70%</td>
</tr>
<tr>
<td>Ciprofloxacin&lt;sup&gt;3,6&lt;/sup&gt;</td>
<td>99%</td>
<td>82%</td>
<td>81%</td>
</tr>
<tr>
<td>Linezolid&lt;sup&gt;3&lt;/sup&gt;</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Vancomycin&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Staphylococcus aureus* sensitivity numbers are from the 2015 emergency department nonurine isolates from Kapi‘olani Medical Center for Women & Children. Presumably, these are mostly community acquired because they are ED patients (no inpatients in this group). Sensitivities vary between communities. The GAS sensitivities are 100% for all beta-lactams and otherwise based on values from the literature (see citation numbers).
raises concern that this could be an overwhelming infection. The term *erysipelas* can be used together (near synonyms) with GAS cellulitis, or when it is limited to the superficial epidermis (as opposed to true cellulitis, which is a deeper infection), or when associated with lymphangitis or lymphadenitis. Because GAS is always sensitive to penicillin, one could treat this with penicillin, but it takes great fortitude and confidence to treat such a large cellulitis with such a narrow-spectrum drug. It is useful to advise patients that after effective treatment has commenced, they should anticipate a darkening of the erythromeda and, often, the formation of tiny blisters with eventual superficial desquamation on the surface of the cellulitis. This can be alarming if the patient is not expecting it. The major reason for treatment failure is the presence of an abscess that requires drainage. The GAS cellulitis is diffuse and it forms more rapidly making the presence of an abscess less likely. Atypical factors such as more extensive swelling or pain might be suggestive of an abscess, but there are no good studies to confirm the reliability of these signs. In the emerging age of bedside ultrasound, it makes sense that clinicians should scan the cellulitis region with the high-resolution, high-frequency linear probe because it is likely that the depth of an abscess would be less than 4 to 5 cm. Although tiny abscesses might be difficult to confirm, these might not require drainage. Ultrasonographic cobblestoning has been described with cellulitis, but this likely does not add to the diagnostic certainty of cellulitis because this can be readily visualized without ultrasound. The main role of ultrasound is to identify an abscess.

Cellulitis due to *S aureus* is more likely to have an associated abscess. Because its size is smaller and localized, abscess identification can usually be done clinically in most instances. However, applying a bedside ultrasound probe to the area will be more reassuring. A questionable abscess finding can be followed by applying a bedside ultrasound probe to the area will be more reassuring. This practice avoids incising unnecessarily or incising in the wrong location.

In abscesses alone, in which there is no cellulitis, the American College of Emergency Physicians recommends against the practice of culturing the abscess fluid and initiating antibiotics, citing evidence that these are not necessary, as part of their “Choosing Wisely” campaign. However, a treatment guideline document agrees with this approach only for mild abscesses. This likely explains why nearly all drained abscesses get better despite moderate antibiotic resistance rates. Because most abscesses have some degree of cellulitis, antibiotic treatment might still be necessary for moderate cellulitis, but the criteria defining when to withhold and when to use antibiotics requires guidelines with greater clarity. One study of outpatient abscesses drained in the ED comparing treatment with TMP-SMX versus no antibiotics after drainage found better clinical cures in the TMP-SMX group (80.5% vs. 73.6%).

**Necrotizing Fasciitis**

Associated with GAS in its most virulent form, this is perhaps the most dangerous condition discussed in this report. It results in a severe threat to life and limb. The actual infection is most often polymicrobial, yet GAS is frequently a dominant pathogen. An early diagnosis is often missed because its external appearance is often unimpressive. The classic triad includes localized pain, swelling, and erythema, which are not specific enough for an obvious early diagnosis. Severe pain, bullae, skin necrosis (purple color), and crepitus are more specific signs when present. Roughly 70% of cases are initially misdiagnosed, most commonly as cellulitis or an abscess. Plain x-ray findings are usually nondiagnostic. A computed tomography scan or magnetic resonance imaging scan may help to confirm the diagnosis once the clinical suspicion is high enough, but neither modality is highly sensitive or specific without clinical correlation. This results in a delay in treatment often resulting in the necessity for more extensive soft tissue or muscle debridement or limb amputation. Common locations tend to be the scrotum, perineum, abdominal wall, and the extremities. Immunocompromised patients, diabetics, and IV drug abusers are at higher risk, but this still occurs in healthy patients with small initial wounds or lesions that are often characterized as trivial. Some early publications suggested that tissue necrosis indicative of NF could be confirmed with the finger test in which a gloved finger, inserted through a 2-cm incision overlying the site of infection, dissects into the tissues with minimal resistance. In current practice, this test is not used because it has been supplanting by imaging or, in cases with a strong-enough clinical suspicion, immediate treatment with surgical debridement and antibiotic therapy.

In addition to GAS and *S aureus*, other organisms include *Clostridium perfringens* (gas gangrene), *Vibrio vulnificus* (marine organism, injury by fish fins), *Aeromonas hydrophila* (water and soil organism) polymicrobial anaerobes, and Gram-negative organisms. These unusual organisms (eg, *marine vibrio*) require additional antibiotic coverage (eg, doxycycline, quinolones), thus the history of the wound can be important in antibiotic selection. Candida and fungal infections typically occur in immunocompromised hosts.

Bedside ultrasound has been described as a tool to facilitate the diagnosis, but these cases are few and far between, thus no clinician is likely to have sufficient experience with these to develop the pattern recognition for this. Clinicians will have to learn and remember the ultrasound appearance from previously published images so that it can be recognized when encountered. One report describes the “STAFF” sign, which is a series of ultrasound findings that include positive subcutaneous thickening, air, and fascial fluid, spelling out STAFF.
Necrotizing fasciitis requires immediate surgical debridement and broad-spectrum antibiotics that should include clindamycin and penicillin. Because this is a polymicrobial disease condition, broad-spectrum antibiotics, beta-lactamase inhibitors, and metronidazole can be used to more effectively cover these organisms. IV immune globulin and hyperbaric oxygen therapy might have benefits as well, however, a Cochrane systematic review on hyperbaric oxygen concluded that no trials sufficiently met their criteria for review.

**Rapid Organism Identification**

The age of organism identification via mass spectrometry (MS) has arrived. In the past, organisms were identified by growing them on petri plates and identifying morphologic features by Gram stain light microscopy and metabolic features of the organism (eg, coagulase, disaccharide metabolism enzymes). Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF) MS analyzes a laser protein, lipid, and nucleic acid fingerprint of the organism, which can be compared to a catalog of organisms to identify the organism rapidly. Organism subtypes can be determined in this fashion. These subtypes can have known virulence factors and antibiotic sensitivity patterns giving clinicians this useful information at an earlier point in the patient’s clinical course. Proteins produced by organisms can be identified by MS, which can also enable antibiotic sensitivity (eg, beta-lactamase or penicillin-binding proteins) and virulence (eg, SS toxin, Gram-negative endotoxin) determination. Because this methodology does not require repeated incubation cycles, identification and sensitivity times can be reduced by eliminating the second incubation commonly used for final identification and antibiotic sensitivity. This time savings can be even more pronounced for fastidious or slow-growing organisms such as acid-fast bacilli. Most of the progress in MS has been with Gram-negative organisms, but very soon, all organisms will be identified and characterized in this fashion. Many clinical laboratories are already using these methods; however, these methods are evolving rapidly, and it will take time before MS methods for organism identification and sensitivity will become routine.

Nucleic acid–based methods such as rapid polymerase chain reaction amplification of bacterial genomes, fluorescence in situ hybridization, and microarrays can provide similar information of bacterial identification, resistance, and virulence factors. These methods currently compete with MS methods as they develop to improve sampling, turnaround times, and accuracy.

**Other Skin Soft Tissue Infections**

This topic is broad, and the focus of this report has largely been on GAS and *S. aureus*. These are, by far, the most common bacterial etiologies. These 2 organisms collectively result in a wide range of virulence, disease processes, antibiotic resistance patterns, and clinical treatment strategies.

Lemierre disease can present with tonsillitis and neck swelling appearing to be a soft tissue infection of the neck. However, it is a septic thrombophlebitis of the internal jugular vein most often due to *Fusobacterium necrophorum* requiring hospitalization. Although Lemierre disease is uncommon, in a cohort of college students presenting with an acute sore throat versus asymptomatic controls, *F. necrophorum* was found in 20.5% of sore throats and 9.4% of controls, whereas GAS was found in 10.3% of sore throats and 1.1% of controls. Other publications suggest that *F. necrophorum* is prevalent, which suggests that it only rarely progresses to cause Lemierre disease.

Ludwig angina is an uncommon infection originating from the mouth that can present with swelling and redness of the neck and submandibular region. Both Lemierre disease and Ludwig angina are generally discussed within the scope of head and neck infections, rather than skin and soft tissue infections.

Skin and soft tissue infections by parasites and viruses are not covered in this report. Animal bites by domestic dogs and cats have other controversies related to coverage of their unique organisms. Amoxicillin-clavulinate is commonly recommended, yet this might not cover *S. aureus* well. In addition, animal exposures and bites have other concerns such as rabies, cat-scratch disease, toxoplasmosis, tularemia, Lyme disease, Rocky Mountain spotted fever, and other unusual animal organisms that are beyond the scope of this article.

### Therapeutic Considerations

Clindamycin can be a very expensive pediatric drug. If one uses a dose of 30 mg/kg per day (10 mg/kg per dose, 3 times a day for 10 days), Table 2 shows the dosing and the retail cost of the clindamycin. Because most children can swallow pills by 6 years, training them to do so can result in a substantial cost savings. In practice, many 6- to 12-year-old children are unwilling to swallow pills. Encouraging children to learn to swallow pills in the 6- to 8-year age range is reasonable, which can result in tremendous cost savings for the system. Emergency department nurses can frequently train children to do this by administering the first dose in the ED. This has the advantage of starting the treatment immediately without resorting to the parenteral route, and it confirms that the child can swallow pills/capsules, permitting the ED physician to prescribe it as such. If the trial fails, then a prescription for the suspension/liquid form is provided instead. Similarly, the cost for the suspension/liquid forms of cephalaxin and amoxicillin are higher than the pill/capsule forms.

### TABLE 2. Retail Cost of Oral Clindamycin at 30 mg/kg per Day Divided in 3 Doses (TID) for 10 Days. The Cost of the Liquid Forms Is Much Higher Than the Equivalent Dose of Capsules. Non-Generic Suspension Costs Are In Parentheses

<table>
<thead>
<tr>
<th>Dose</th>
<th>150-mg Capsules</th>
<th>300-mg Capsules</th>
<th>75 mg/5 mL, Suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-kg infant</td>
<td>100 mg TID</td>
<td>$10</td>
<td>$160 ($338)</td>
</tr>
<tr>
<td>20-kg 4 year old</td>
<td>200 mg TID</td>
<td>$15</td>
<td>$320 ($676)</td>
</tr>
<tr>
<td>30-kg 7 year old</td>
<td>300 mg TID</td>
<td>$20</td>
<td>$480 ($1014)</td>
</tr>
<tr>
<td>40-kg 12 year old</td>
<td>400 mg TID</td>
<td>$31</td>
<td>$640 ($1352)</td>
</tr>
<tr>
<td>75-kg teen/adult</td>
<td>600 mg TID</td>
<td>$960 ($2028)</td>
<td></td>
</tr>
</tbody>
</table>

Capsules: 150-mg capsules at $0.17 per capsule, 300-mg capsules at $0.51 per capsule. Suspension: generic 75 mg/5 mL, 100-mL bottle at $80 (nongeneric retail price, $169). TID indicates 3 times a day.
The taste of clindamycin can be poor. Earlier forms of clindamycin liquid are no longer on the market. In a more recent study comparing 3 forms of clindamycin suspension, 1 form was better than the other 2 forms. The better tasting form was rated to taste just slightly poorer (but within overlapping 95% confidence intervals) than amoxicillin. A practitioner cannot determine which form of clindamycin will be dispensed to the patient. A pharmacist will not taste the drug for the patient as a condition of purchase. The patient will get what the pharmacy dispenses, and the patient will find out how it tastes after he or she has obtained it. Advising patients that it likely will have a bad taste will prepare parents for this therapeutic challenge.

The taste of TMP-SMX suspension is not favorable either. If it is confirmed that TMP-SMX covers GAS well in vivo, its coverage for both GAS and S. aureus is excellent; however, this increasing use of TMP-SMX will likely increase the number of cases of Stevens-Johnson syndrome and toxic epidermal necrolysis. It should be documented in the medical record that patients/parents have been advised of this risk and that they accept this risk. Dosing TMP-SMX for a 60-kg patient for 10 days would cost (retail) $75 (20 mL twice daily) for the suspension and $5 for the tablets.

Quinolones and tetracyclines are other considerations, yet both of these have unattractive issues with children. New antibiotic classes bring new options that are almost always too expensive for routine use. Insurance companies will often not include these in their coverage lists, which means that patients must pay out of pocket for the most expensive drug options, rendering these options essentially useless for all but wealthy patients. Linezolid is an example of this. It has several advantages rendering these options essentially useless for all but patient treatment of skin and soft tissue infections. At an adult dose of 600 mg twice daily for 10 days, the retail price for the generic IV preparation is $7518, whereas the same adult dose given orally (twenty 600-mg tablets) has a generic retail price of $125.55 Linezolid use is often restricted by antibiotic stewardship programs. The most intriguing new group of antibiotics are dalvabanic and oritavancin. These are parenteral broad-spectrum drugs that cover S. aureus including MRSA and GAS. A single dose will last for a long period in the range of 2 weeks. One dose will treat most clinical infections, which eliminates therapeutic adherence concerns. These drugs are new, very expensive (in the range of $3000), and novel so that therapeutic usage is far from mainstream, yet they can be advantageous in select circumstances. Physician judgment should prevail.

Poor drug adherence is always a concern. Because medications are almost never dispensed at the site of service, the patient must travel to a pharmacy. This can take time, and there are always uncertainties about insurance coverage and the ability of the patient to obtain the medications. Administering the initial dose in the ED or clinic has the advantage of initiating therapy sooner while giving the patient more time to obtain the remainder of the therapeutic course. A single dose of oral clindamycin or SMX-TMP will give the patient roughly 8 to 12 hours to obtain the next dose. A single dose of intramuscular ceftriaxone will give the patient roughly 24 hours to obtain the next dose; however, this will not cover MRSA. Benzathine penicillin injections have a duration of 3 weeks; however, drug levels are low and insufficient to prevent MRSA infection. Progressing to a system in which the medications are dispensed from the ED or other site of service will confirm that the patient received the antibiotics, which likely improves therapeutic adherence.

In conclusion, GAS and S. aureus are the most frequent organisms involved in skin and soft tissue infections ranging from mild to limb/threatening infections. Other organisms play significant roles in uncommon and more serious infections. Anti-biotic strategies are controversial and evolving. Bacterial identification methods are evolving and advancing rapidly.

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