

Pediatric Cellulitis: A Red Hot Concern

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Abstract (150 words):

Cellulitis and other skin and soft tissue infections (SSTIs) are a common reason for children to seek care, both in the primary care setting and the emergency department. Most children recover quickly from cellulitis, but a small subset will require hospitalization. Practitioners need to be skilled in the diagnosis and treatment of cellulitis, including recognition of the need for inpatient treatment. Cellulitis is a common skin and soft-tissue infection that is usually caused by streptococci bacteria or, less commonly, *Staphylococcus aureus*. Diagnosis of cellulitis, and exclusion of complicated or other more serious infections, can be challenging. Management of these infections has been highly variable, resulting in some difficulty identifying the ideal treatment regimen. The goal is to use the antibiotic with the narrowest spectrum for the shortest duration necessary to provide clinical improvement. Research to identify the best treatment for pediatric cellulitis will be important moving forward.

Pediatric Cellulitis: A Red Hot Concern

Is cellulitis really such a big problem?

Skin and soft-tissue infections (SSTIs) are a diverse group of infections, ranging from mild, superficial infections to severe, life-threatening infections. SSTIs, such as cellulitis and abscesses, are a common reason that patients seek medical care, with over 23 million emergency department (ED) visits and over 82 million primary care visits from 1993 to 2005.^{1,2} Over the past 20 years, mirroring the rising prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), medical providers have seen a dramatic increase in the number of patients seeking care for SSTIs, both in the ED and primary care settings.^{1,2} Hospitalizations are also increasing, with a 29% increase in admissions for SSTIs from 2000 to 2004.³

Unfortunately, children have not been immune to this phenomenon. Pediatric visits to emergency departments for SSTIs nearly tripled from 1997 to 2005. The number of pediatric hospitalizations for SSTIs has more than doubled from 1997 to 2009, rising to over 74,000 admissions per year.^{4,5} The cost associated with these admissions has also been increasing over time, indicating the growing economic burden these infections are placing on patients, families, and our healthcare system as a whole.^{5,6}

Appropriate diagnosis and treatment of SSTIs has always been important for the general pediatrician. The increasing number of children presenting with SSTIs and the greater proportion of those requiring hospitalization, however, has raised the stakes for this common pediatric problem. In 2014, the Infectious Diseases Society of America (IDSA) published evidence-based practice guidelines for the diagnosis and treatment of SSTIs in both adult and pediatric patients.⁷ These recommendations can be a welcome guide for the practitioner who is faced with the dramatic increase in the frequency and severity of infections, as well as the emergence of resistance to many of the antibiotics which have been used to treat SSTIs in the past. In this article, we will review the diagnosis and management of cellulitis in children, including severe infections requiring hospitalization.

How can I accurately diagnose cellulitis?

Cellulitis is a bacterial infection of the skin and subcutaneous fat that is typically acute in onset, with diffuse erythema that spreads over the course of hours to days. The term erysipelas is sometimes used synonymously with cellulitis, though this can also refer to a more superficial infection of the upper dermis with more well defined margins of erythema. More simply, erysipelas can also refer to a cellulitis involving only the face.⁷

Cellulitis often begins after bacteria penetrate the skin to create an infection within the underlying skin and soft tissues. Bacteria usually gain access via areas of minor local trauma such as an abrasion or an insect bite that have disrupted the skin barrier. Often, these breaks in the skin are small and unapparent.⁷ The most common locations for pediatric SSTIs tend to be on the lower extremities or buttocks, though infections over the trunk and arms can also occur with some frequency.⁶

Information gained from the history combined with findings from the physical exam is usually sufficient to make a diagnosis of cellulitis. Typical exam findings include erythema, swelling, warmth and tenderness to the affected area. Occasionally, there can be inflamed regional lymph nodes or associated lymphangitis, recognized by the presence of red, linear streaks spreading proximally from the

area of cellulitis.⁷ If swelling is significant, the skin surface may develop a *peau d'orange* appearance. Systemic symptoms are usually mild and can include fever, tachycardia and leukocytosis, though symptoms can progress to include hypotension and altered mental status with more severe infections.

What tests should I order when I suspect cellulitis?

Routine lab testing is usually not necessary in uncomplicated SSTIs. In one recent study by Malone et al, over 90% of children admitted to the hospital for SSTIs had laboratory investigation, including blood cultures, but <1% of patients had a positive culture.⁸ In fact, in their study, there were no true positive blood cultures and length of stay was nearly 1 day longer if a culture had been ordered for a patient with an uncomplicated SSTI. This highlights not only the lack of utility, but also the potential harm to patients that could result from obtaining blood cultures in uncomplicated SSTIs, since a false positive blood culture often results in hospitalization or prolonged hospitalization, further laboratory testing and an extended antibiotic course. Likewise, other labs such as complete blood count, C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), offer non-specific findings and usually do not impact the overall clinical course.

Laboratory testing may be warranted for children in whom the rate of bacteremia is likely to be higher. These include immunocompromised patients, patients with severe systemic symptoms, and those with complicated infections. In the Malone study cited above, the rate of positive blood cultures in patients with complicated infections was 12.5%. Complicated SSTIs are usually considered to be infections associated with surgical or traumatic wound infections, infected burns or ulcers, or infections requiring surgical intervention beyond routine incision and drainage.

Similar to laboratory testing, imaging is usually unnecessary in uncomplicated SSTIs. However, there is evidence that ultrasound can be a useful adjunct to the physical exam when there is uncertainty about the presence of an abscess.⁹

How should I treat cellulitis?

Ideally, treatment would be directed at the specific organism causing cellulitis in your particular patient. However, the underlying cause for individual cases of cellulitis can be difficult to confirm, since cultures from the blood or affected tissues of patients with cellulitis often fail to yield an organism. It is widely accepted that the vast majority of uncomplicated cellulitis is due to infection with streptococci bacteria, usually group A. *Staphylococcus aureus* is another notable, though less frequent, cause of cellulitis. *S. aureus* should be suspected when there is a history of penetrating trauma or if there is purulence associated with the cellulitis.⁷ A family history or personal history of prior infections with *S. aureus* may increase the level of concern for this organism as well.

As with most infections in the era of antimicrobial stewardship, the goal for treatment of cellulitis is to use the antibiotic with the narrowest spectrum of activity necessary to adequately treat the infection. Unfortunately, there is no consensus as to the best treatment course for patients with cellulitis, in part because of the diverse regimens used in the literature that is available.¹⁰ With the most likely causes of cellulitis in mind, recommendations for the treatment of mild cases of cellulitis are to start with an oral

antibiotic effective against streptococci, such as penicillin, amoxicillin, dicloxacillin, cephalexin, or clindamycin (See TABLE 1).

If there is suspicion for *S. aureus*, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), oral medications such as doxycycline, clindamycin or trimethoprim-sulfamethoxazole (TMP/SMX) can be considered as well. Due to their lack of efficacy against streptococci, TMP/SMX and doxycycline should be paired with a β -lactam antibiotic such as cephalexin or amoxicillin if coverage for both bacteria is felt to be warranted.⁷ In this instance, clindamycin can offer a good single agent option to avoid multiple prescriptions since it generally offers good coverage against both streptococci and MRSA.

Use of an antibiogram with local resistance patterns should always be considered when making the choice of the best antibiotic to treat cellulitis, as there can be significant regional variations in antibiotic resistance. The ideal duration of treatment for children is not clearly defined, but a duration between 5-10 days is likely adequate for most uncomplicated cellulitis. In a trial of adults with uncomplicated cellulitis, a 5-day course of antibiotics was as effective as a 10-day course.¹¹ The clinician can also follow the clinical response to antibiotic therapy as a means of assessing adequacy of the duration of antibiotic course.

Which patients with cellulitis require hospitalization?

Though most cellulitis improves with appropriate outpatient management, a subset of patients may require hospitalization for a variety of reasons (see TABLE 2). Poor adherence or failure to respond to outpatient treatment are two common reasons for admission to the hospital. Immunocompromised children also deserve a high level of caution due to their reduced capability to ward off infections; they may benefit from admission for close monitoring and/or intravenous (IV) antibiotics.

Concern for a more severe infection should also prompt evaluation in the emergency department or even direct admission to the hospital. A number of signs or symptoms may indicate the presence of a more serious infection. On general assessment, children may be ill-appearing or there may be findings of systemic inflammatory response syndrome (SIRS). For children, SIRS is typically defined as having at least two of the following: Temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$, tachycardia or tachypnea (relative to what is normal for age), or white blood cell count $> 12,000 \text{ cells/mm}^3$ (or $> 10\%$ bands on the differential).¹² Other findings such as hypotension, altered mental status or lethargy should also raise concern for a more severe or systemic infection.

Focal exam findings at the site of infection can also raise concern for an infection that requires urgent hospital evaluation. Fluctuance on physical exam is suggestive of a fluid collection that may require incision and drainage, particularly if there is worsening or lack of improvement after a trial of antibiotics. Severe pain that seems out of proportion to the clinical findings, skin necrosis, crepitus, swelling or tenderness beyond the involved skin, or a hard, wooden induration to the subcutaneous tissue are all concerning findings that may suggest an infection involving deeper tissues such as necrotizing fasciitis. Necrotizing fasciitis is a rare but serious skin and soft-tissue infection of subcutaneous tissue and fascia that is rapidly progressive and destructive and has a high mortality rate. Consideration of necrotizing fasciitis warrants urgent evaluation in an emergency department. Frighteningly, these infections, especially early in their course, can be difficult to distinguish from a simple cellulitis that should respond to antibiotics.⁷ A careful history and physical exam along with

appropriate anticipatory guidance for families about what to expect are essential to help differentiate the two and provide the most appropriate and timely care.

What will happen to my patient in the hospital?

While some primary care physicians continue to admit and care for their own patients who require hospitalization, it is becoming increasingly common that pediatric hospitalists are taking care of these children when they are admitted to the hospital. There will often be many things that are happening simultaneously when a child with cellulitis is admitted to the hospital. First and foremost is to determine whether the child is clinically stable, and whether there are concerning signs or symptoms that indicate a more serious infection that requires prompt evaluation and treatment. It is often helpful to outline the area of erythema or induration at the beginning of a hospitalization, as this can help in determining whether these signs are improving or worsening over time. If there are concerns for a deeper or progressive infection, imaging such as ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) may be used to help clarify the extent of the infection. Consultation with surgical or infectious disease specialists is also considered in cases that may require surgical debridement or may not be responding to treatment as expected.

Ensuring appropriate treatment with antibiotics is also a high priority early in the hospital course for any child admitted with cellulitis. As with outpatient treatment, the most appropriate antibiotic regimen chosen is likely to vary somewhat based on local resistance patterns and patient allergies. However, the microbiology involved in these infections is still essentially the same. Most therapeutic regimens should therefore be directed towards the most likely infectious agents: *streptococci* and *S. aureus*. Intravenous (IV) antibiotics are likely to be used initially in hospitalized patients. This is particularly the case if the patient is ill appearing, is rapidly worsening or worsening despite appropriate oral antibiotics, or is unable to take medications by mouth.

To cover streptococcal organisms and/or methicillin-sensitive *S. aureus* (MSSA), initial IV antibiotic considerations should include cefazolin, clindamycin, nafcillin, or oxacillin. MRSA is a less frequent cause of uncomplicated cellulitis, but may be more likely if there is abscess formation, if there is a history of penetrating trauma or if the patient has a prior history of MRSA infections. Trimethoprim-sulfamethoxazole, clindamycin or vancomycin can be considered if treatment for MRSA is felt to be necessary. Linezolid is also an effective option for treatment of MRSA infections, though it is typically only used as a last resort when there is felt to be no better alternative.

Further studies are needed to clarify the best treatment regimen for these patients. In the meantime, discussion of and adherence to published clinical practice guidelines may help to reduce use of inappropriate antibiotics. In their study of children treated for SSTIs at 7 academic and community hospitals, Moore et al found that over two-thirds of the patients received either overly broad-spectrum antibiotics and/or were treated for >10 days.¹³ Based on these results, there is clearly room for more education and quality improvement around treatment of pediatric SSTIs. Until such efforts are successful, trying to find the narrowest spectrum antibiotic and the shortest duration required to obtain clinical improvement should be the goal in order to reduce medication side-effects and future emergence of antibiotic resistant bacteria.

Aside from the management of the child's acute infection, the inpatient team will try to meet any other needs that may be present as well. For example, pain medications may be used to improve a

patient's level of comfort as the infection improves, and IV fluids may be administered to patients who are unable (or unwilling) to drink appropriately to maintain hydration. Many pediatric facilities are also equipped with Child Life specialists who can help reduce anxiety around any procedures that might be needed during their stay or simply help them adjust and feel more at ease with being in the hospital, which can be a traumatic transition for some children.

When will my hospitalized patient be ready to go home, and how can I best care for the patient after discharge?

The majority of children admitted for cellulitis improve quickly, resulting in fairly short hospitalizations. The average length of stay in the United States (US) for otherwise healthy children admitted for SSTIs has been decreasing over recent years and is now < 3 days.⁵ Criteria for discharge are usually considered to be resolution of any systemic symptoms that were present on admission as well as improvement at the site of infection. Improvement is typically indicated by pain, swelling and erythema that are decreased from what was present at the time of admission. If the affected area was outlined on admission, it should be well within the original outline at the time of discharge. Once improvement is noted, patients are transitioned to an appropriate oral antibiotic regimen to complete their treatment course.

Follow-up with a primary care provider within 2-5 days after discharge is usually beneficial to ensure the infection is continuing to improve as expected, and to help the patient and family with any new or ongoing concerns that they might have following their hospitalization.

Summary and Future Direction

Cellulitis and other SSTIs represent a growing burden to the pediatric population and require continued attention from the pediatric community. Familiarity with the microbiology of these infections, as well as the signs of a severe infection are needed in order to provide the most appropriate care for these children. Additional studies are needed to help clarify the best antibiotic regimens that should be used. Until that time, clinical practice guidelines and antimicrobial stewardship efforts should be used to guide our treatment and we should refrain from ordering unnecessary laboratory and imaging tests in uncomplicated cases.

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Table 1

Cellulitis Treatment Options		
<u>Bacteria to Treat</u>	<u>Oral Antibiotics</u>	<u>Parenteral Antibiotics</u>
Streptococci	penicillin amoxicillin dicloxacillin cephalexin clindamycin	cefazolin naftillin oxacillin clindamycin
MRSA	clindamycin TMP/SMX doxycycline* linezolid	clindamycin vancomycin linezolid

*For children over 8 years of age

TMP/SMX = trimethoprim-sulfamethoxazole

MRSA = methicillin-resistant *staphylococcus aureus*

Table 2

Cellulitis: Reasons for Hospitalization
Failure of Outpatient Management
Poor Adherence to Medication
Immunocompromised Patient
Toxic or Ill Appearance
Presence of SIRS Criteria
Hemodynamic Instability
Altered Mental Status/Lethargy
Concern for Severe Infection