PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Blood Cultures in the Evaluation of Uncomplicated Skin and Soft Tissue Infections

Jay R. Malone, Sarah R. Durica, David M. Thompson, Amanda Bogie and Monique Naifeh

Pediatrics; originally published online August 5, 2013;
DOI: 10.1542/peds.2013-1384

Blood Cultures in the Evaluation of Uncomplicated Skin and Soft Tissue Infections

AUTHORS: Jay R. Malone, MD, MS,[a] Sarah R. Durica, BA,[b] David M. Thompson, PhD,[a] Amanda Bogie, MD,[c] and Monique Naifeh, MD, MPH[a]

Sections of [a]General and Community Pediatrics and [c]Emergency Medicine, Department of Pediatrics, The University of Oklahoma, Oklahoma City, Oklahoma; and [b]The University of Oklahoma College of Medicine, Oklahoma City, Oklahoma

KEY WORDS

abscess, cellulitis, bacteremia, infant, child, adolescent, blood, culture, blood specimen collection

ABBREVIATIONS

CA-MRSA—community-acquired methicillin-resistant *Staphylococcus aureus*
CI—confidence interval
CRP—C-reactive protein
cSSTI—complicated skin and soft tissue infection
ED—emergency department
LOHS—length of hospital stay
MRSA—methicillin-resistant *Staphylococcus aureus*
SSTI—skin and soft tissue infection
WBC—white blood cell

Dr Malone conceptualized and designed the study, participated in data acquisition and initial data analysis, and drafted the initial manuscript; Ms Durica performed data acquisition; Dr Thompson performed data analysis and interpretation; Dr Bogie contributed to the conceptualization and design of the study; Dr Naifeh contributed to study design and participated in data interpretation; Ms Durica and Drs Thompson, Bogie, and Naifeh critically revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-1384

doi:10.1542/peds.2013-1384

Accepted for publication Jun 20, 2013

Address correspondence to Monique Naifeh, MD, MPH, Department of Pediatrics, The University of Oklahoma, 1200 Children's Ave, Suite 14000, Oklahoma City, OK 73104. E-mail: monique-naifeh@ouhsc.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Blood cultures are a common investigation in children admitted to the hospital with skin and soft tissue infections. The yield of blood cultures in this condition is unknown.

WHAT THIS STUDY ADDS: Blood cultures are not useful in children admitted to the hospital with uncomplicated skin and soft tissue infections, and they may be associated with increased length of hospital stay.

abstract

BACKGROUND: Blood cultures are often obtained in children hospitalized with skin and soft tissue infections (SSTIs). Because little evidence exists to validate this practice, we examined the yield of blood cultures in the evaluation of immunocompetent children with SSTIs.

METHODS: Medical records were reviewed for all children admitted between January 1, 2007 and December 31, 2009 after emergency department evaluation and diagnosis of cellulitis or abscess. We compared patients with SSTIs (n = 482) with those with complicated SSTIs (cSSTIs; n = 98). A cSSTI was defined as surgical or traumatic wound infection, need for surgical intervention, or infected ulcers or burns. The SSTI group included patients without complicating factors.

RESULTS: None of the patients in the SSTI group had a positive blood culture. In the cSSTI group, 12.5% of blood cultures were positive. The mean length of hospital stay (LOHS) of children with SSTIs was shorter than that of those with cSSTIs ($P < .001$). In the SSTI group, obtaining a blood culture was associated with a higher mean LOHS ($P = .044$).

CONCLUSIONS: Blood cultures are not useful in evaluating immunocompetent children who are admitted to the hospital with uncomplicated SSTIs, and they are associated with a nearly 1-day increase in mean LOHS. *Pediatrics* 2013;132:1–6

Skin and soft tissue infections (SSTIs) are a common pediatric problem, accounting for 1 in 500 to 1 in 150 pediatric emergency department (ED) visits.[1,2] Some management guidelines[1,3,4] suggest obtaining blood cultures to ensure early identification of bacteremia and prevention of subsequent sepsis. Obtaining a blood culture during an episode of SSTI is common practice, particularly in children who are admitted to the hospital for treatment with intravenous antibiotics.[2,5]

The rate of bacteremia in immunocompetent children with SSTIs is not known. In the pre–*Haemophilus influenzae* vaccine era, the rate of SSTI-associated bacteremia was ~20%,[6] but after introduction of the *H. influenzae* vaccine, the rate decreased to 2%.[7] In 1998, Sadow and Chamberlain reported that bacteremia during SSTI was largely associated with superinfected lesions originating from active varicella infection,[7] which is now much less common because of routine childhood vaccination.[8] However, since that study was published, the widespread emergence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has been implicated in invasive infections and now accounts for 45% to 75% of SSTIs.[9–13] The number of pediatric ED visits for SSTIs increased more than 170% between 1997 and 2005.[14] It remains unclear how the introduction of varicella and pneumococcal vaccines and the widespread emergence of CA-MRSA have affected rates of bacteremia in SSTIs.

We determined the prevalence of bacteremia, defined as a blood culture that yields a positive result, among immunocompetent children admitted to the hospital after ED evaluation and diagnosis of SSTI.

METHODS

Subjects

This retrospective case series included children aged 0 to 18 years who were admitted to The Children's Hospital of Oklahoma after diagnosis of SSTI during initial ED evaluation. The Children's Hospital of Oklahoma is an urban, university-affiliated pediatric hospital at a tertiary medical center. The ED treats ~40 000 children annually, and during the study period, patients were evaluated by residents in pediatrics, emergency medicine, and family medicine and attending physicians. This study was approved by the institutional review board of the University of Oklahoma Health Sciences Center.

A search of the hospital's electronic medical records listed all children who were seen in the ED between January 1, 2007 and December 31, 2009, diagnosed with SSTIs using ICD-9-CM codes for cellulitis and abscess (682.X), and admitted to the hospital. Children who were discharged from the hospital from the ED were excluded. Other exclusion criteria were immunocompromise, missing medical record, return ED visit for a single episode of cellulitis, diagnoses that the primary reviewer judged to be miscoded upon detailed chart review, incidental diagnosis of cellulitis at the time of admission for a reason other than SSTI, and development of cellulitis while admitted to the hospital for a reason other than SSTI.

Eligible patients were stratified into groups that distinguished those with complicated skin and soft tissue infection (cSSTI) from those with uncomplicated infections (SSTIs). The cSSTI group included patients with surgical or traumatic wound infection, need for surgical intervention, and infected ulcers or burns.[4] Routine incision and drainage was not considered surgical intervention. The SSTI group included all children without these complicating factors.

Measurements

The primary reviewer evaluated medical records from eligible patients using a standard form. Data extracted included demographics, length of hospital stay (LOHS), clinical presentation, past medical history, and laboratory results obtained in the ED including blood and wound cultures, complete blood count with differential, and C-reactive protein (CRP). A second reviewer independently checked 10% of the medical records to ensure accuracy of data collection.

Protocol

During the study period, blood cultures were collected in BACTEC Peds Plus/F culture vials (Becton, Dickinson and Company, Sparks, MD). One culture with a volume of 1 to 3 mL was drawn from each patient and incubated for 120 hours. Cultures were categorized as contaminated if they grew *Staphylococcus epidermidis*, viridans streptococci, diphtheroids, micrococcus, or propionibacterium species. Cultures containing any other organism were categorized as positive. Cultures were categorized as negative if no organism was found.

The primary reviewer judged medical records to be miscoded and excluded them from the study if the clinical history, physical examination, and physician assessment and plan made no mention of SSTI or symptoms of SSTI. All charts excluded for this reason were reviewed by a second reviewer. The primary reviewer also excluded medical records from patients who were immunocompromised, as evidenced by information that was available to the treating physician in the ED that indicated primary or secondary immunodeficiency.

Data Analysis

Categorical variables are reported as counts and percentages. Intergroup differences in percentages were tested by using Fisher's exact tests. Continuous variables, including age, are reported as means with SDs, and intergroup differences in means were

tested by using 2-sample *t* tests. Statistical significance was determined by using a critical α of .05.

A sample of 340 patients was needed to ensure, with 90% certainty, that the width of the confidence interval (CI) on the estimated rate of bacteremia in patients with SSTI would be no more than 2%. The sample size estimate assumes that 2% is the true prevalence of bacteremia in children with SSTIs.[7]

RESULTS

The initial database search identified 1812 children who were seen in the ED for SSTI during the 3-year study period (Fig 1). Of those, 657 were admitted to the hospital. Exclusion criteria were met by 77 patients. The primary investigator reviewed the remaining 580 charts and judged 482 patients to have uncomplicated SSTIs and 98 to meet criteria for cSSTIs.

Table 1 lists patient demographics and clinical features. In the SSTI group (n = 482), the mean age was 3.4 years (SD: 3.8) with a range of 4 days to 16 years. Of these, 50% were male, and 56.2% had received at least 1 dose of antibiotics before ED presentation. The mean temperature was 37.5°C (SD: 1.2), and 26.6% had temperatures >37.9°C.

In the cSSTI group (n = 98), the mean age of 5.8 years (SD: 4.7), with a range of 6 days to 16 years, was significantly older than the uncomplicated group ($P < .001$). The cSSTI group also had more males (64.2%; $P = .011$). Forty-nine percent received at least 1 dose of antibiotics before ED presentation, and mean temperature was 37.5°C (SD: 1.0) with 24.5% of temperatures >37.9°C.

In the uncomplicated SSTI group, patients with and without a blood culture had similar presenting temperature (37.5°C vs 37.1°C, $P = .095$), CRP (60 mg/L vs 47 mg/L, $P = .39$), and white blood cell (WBC) count (17.7 vs 15.5, $P = .15$). Patients with a blood culture were more likely to have a CRP drawn (97.8% vs 74.1%, $P < .001$).

Patients with uncomplicated SSTIs most often presented with infections located on the extremities (32.3%) or the buttocks or perineum (26.8%) (Table 2). The most common site of infection in the cSSTI group was the face or neck (39%), and no children in the cSSTI group had infections of the buttocks or perineum ($P < .001$). The cSSTI group also had a higher number of periorbital infections than the SSTI group (11 vs 0, $P < .001$).

Laboratory investigations were performed in the majority of cases (Table 3). Blood cultures were performed in 94.4% of uncomplicated and 81.6% of complicated cases. No positive blood cultures were detected in the SSTI group, which suggests that the chance of obtaining a positive blood culture during an episode of uncomplicated SSTI is <1%

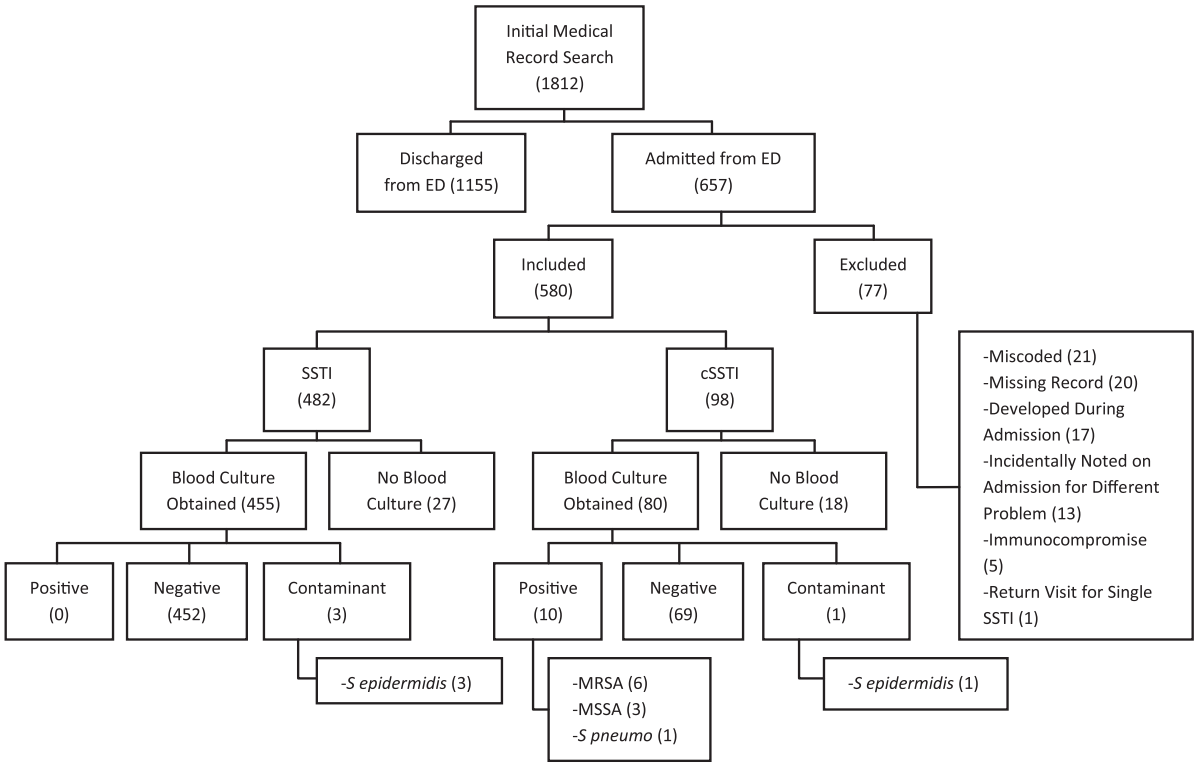

FIGURE 1
Study design diagram.

(95% CI: 0%–0.81%). In the cSSTI group, 10 positive cultures were observed (12.5%; 95% CI: 6.2%–22.0%; $P < .001$).

In the SSTI group, 75.7% of patients (365/482) had a wound culture, of which 68.4% (250/365) grew MRSA. In the cSSTI group, 67.3% of patients (66/98) had a wound culture, and 37.9% (25/66) of those grew MRSA.

Mean LOHS differed significantly between the 2 groups ($P < .001$, Table 4). Children admitted with SSTIs had a mean LOHS of 3.2 days (SD: 2.3, range 1–21 days), whereas children with cSSTIs had a mean LOHS of 6.6 days (SD: 10.9, range 1–72 days). In the SSTI group (Table 4), patients in whom a blood culture was obtained had a mean LOHS that was 0.91 days longer than patients without a blood culture (95% CI: 0.026–1.8 days; $P = .044$).

DISCUSSION

SSTIs are an increasingly common cause of outpatient visits and pediatric ED visits. This is the first study in the CA-MRSA era to specifically examine the prevalence of bacteremia in children with SSTIs. More than 90% of children admitted to the hospital for SSTIs undergo laboratory investigations, including blood cultures. However, our study found that blood cultures are positive in <1% of patients with uncomplicated SSTIs and so do not improve patient management.

In our cohort, 83% of patients were judged to have uncomplicated SSTIs, and 94% of those had blood cultures obtained. Among those with uncomplicated SSTIs, there were no positive but 3 contaminated blood cultures. This preponderance of contaminated cultures parallels the findings of 2 recent studies of antibiotic choice in SSTIs, both of which noted false-positive to true-positive cultures in a ratio of 3:1.[2,15] Similar false-positive blood culture rates were also noted in the 1998 study by Sadow and Chamberlain, who examined the utility of blood cultures in the post–*Haemophilus influenzae* vaccination era.[7] They collected data in 1994–1995, before the introduction of the varicella vaccine in 1995 and the pneumococcal conjugate vaccine in 2000. They detected 5 cases of bacteremia, of which 3 were associated with varicella and one was *Streptococcus pneumoniae*. Routine vaccination against both of these pathogens is now common practice.

Additionally, Sadow and Chamberlain's study was performed just as CA-MRSA infections were beginning to increase in incidence. Although CA-MRSA has been implicated in a wide range of severe infections, including bacteremia and sepsis, it remains unclear whether CA-MRSA causes bacteremia in a higher percentage of cases than methicillin-sensitive *Staphylococcus aureus*. Despite a high prevalence of MRSA (68.4%) detected in wound cultures in children with uncomplicated SSTI, no cases of bacteremia were detected. In the cSSTI group, 60% of the detected cases of bacteremia were MRSA, although this figure should be viewed cautiously because there were only 10 isolates.

Children with uncomplicated versus complicated SSTI differed with regard to several demographic and laboratory measures. Mean age was higher in children with cSSTIs (5.8 vs 3.4 years; $P < .001$), possibly because of the inclusion of infection secondary to traumatic injury in the definition of complicated infection. Blood cultures were performed more frequently in children with uncomplicated infection (94.4% vs 81.6%; $P < .001$). This could be a result of

TABLE 1 Patient Demographics and Clinical Features ($N = 580$)

	SSTI ($n = 482$)	cSSTI ($n = 98$)	P
Age, mean (SD)	3.4 (3.8)	5.8 (4.7)	<.001
Male gender, *n* (%)	241 (50)	63 (64.2)	.011
Temperature (°C), mean (SD)	37.5 (1.2)	37.5 (1.0)	.99
Fever (>37.9°C), *n* (%)	128 (26.6)	24 (24.5)	.9
Heart rate, mean (SD)	138 (30)	133 (31)	.1353
Prior antibiotics (yes), *n* (%)	271 (56.2)	48 (49.0)	.22

TABLE 2 Location of Cellulitis ($N = 580$)

	SSTI ($n = 482$), *n* (%)	cSSTI ($n = 98$), *n* (%)	P
Extremity	155 (32.3)	23 (23.5)	.09
Buttock or perineum	129 (26.8)	0 (0)	<.001
Face or neck[a]	93 (19.3)	38 (38.8)	<.001
Hand or foot	36 (7.5)	9 (9.2)	.41
Trunk	35 (7.3)	13 (13.3)	.07
Genitals	25 (5.2)	2 (2.0)	.29
Scalp	9 (1.9)	2 (2.0)	.99
Periorbital	0 (0)	11 (11.2)	<.001

[a] Excluding periorbital.

TABLE 3 Laboratory Investigations ($N = 580$)

	SSTI ($n = 482$)	cSSTI ($n = 98$)	P
Blood culture performed, *n* (%)	455 (94.4)	80 (81.6)	<.001
Blood culture positive, *n* (%)	0 (0)	10 (12.5)	<.001
Blood culture contaminant, *n* (%)	3 (0.7)	1 (1.3)	.11
Complete blood count performed, *n* (%)	477 (99.0)	96 (98.0)	.1
WBC count $\times 10^9$/L, mean (SD)	17.6 (6.9)	15.2 (7.6)	.0024
Neutrophils, mean (SD)	10.6 (5.3)	9.9 (6.5)	.26
Bands, mean (SD)	0.2 (0.7)	0.37 (1.1)	.052
Band/neutrophil ratio, mean (SD)	0.02 (0.08)	0.05 (0.2)	.015
CRP performed, *n* (%)	465 (96.5)	83 (84.7)	<.001
CRP, mean (SD)	59.4 (64.2)	87.1 (101.1)	.0011

TABLE 4 LOHS (N = 580)

	SSTI (n = 482)			cSSTI (n = 98)		P
LOHS (days), mean (SD)	3.18 (2.3)			6.62 (10.9)		<.001
	Blood Culture Drawn (n = 455)	No Blood Culture Drawn (n = 27)	P	Blood Culture Drawn (n = 80)	No Blood Culture Drawn (n = 18)	P
LOHS (days), mean (SD)	3.24 (2.31)	2.33 (1.47)	.044	7.30 (11.89)	3.61 (2.17)	.194

a greater percentage of children with cSSTI being admitted to surgical services that may perform laboratory investigations less often than medical services. Differences between the 2 groups in WBC, band/neutrophil ratio, and CRP, though statistically significant, were not large enough to be clinically meaningful.

Mean LOHS differed significantly between the SSTI and cSSTI groups and also differed within the SSTI group. Among patients with SSTI, those who underwent blood cultures stayed in the hospital nearly 1 day longer (3.2 days) than those who did not (2.3 days; $P <$ .044). It is possible that patients without a blood culture were initially less ill appearing than those who did receive a blood culture. However, no differences were detected in presenting temperature, CRP, or WBC. Blood cultures were obtained in a large proportion of patients whose initial clinical appearance seems unlikely to have affected the decision to obtain a culture and therefore the LOHS. Rather, it is more likely that the longer mean LOHS was a result of blood culture monitoring. Although a case series design cannot prove causality, this conclusion is clinically logical, because care providers are most comfortable declaring a culture negative after 48 hours.

Our study had several limitations. First, its retrospective study design limited our interpretation of history and clinical appearance to clinician reports in the medical record. Therefore, we may have incorrectly assigned some patients to the SSTI or cSSTI groups. Second, 56.2% of patients in the SSTI group had received at least 1 dose of antibiotics before their blood culture. This may have caused some blood cultures to be negative in children who were bacteremic before receiving antibiotics. Third, blood cultures were not obtained in 5.6% of the SSTI group or 18.4% of the cSSTI group, which limits our ability to determine the precise incidence of bacteremia during SSTIs. Fourth, although our cohort included infants <60 days old, we did not study enough patients in this age range to extend our conclusions to this high-risk group. Dedicated research is needed to determine the bacteremia risk in young infants with SSTIs. Finally, our study examined only the 36.3% of children presenting to the ED with SSTIs who were admitted to the hospital. Although this allowed us to select for children who were presumably more ill appearing and had a greater number of laboratory examinations performed, some of the children who were discharged from the hospital from the ED may have been initially bacteremic. Though unlikely, this possibility limits our ability to determine with certainty the true incidence of bacteremia during SSTI. Therefore, the applicability of our study is limited to hospitalized patients.

Despite these limitations, several findings of this large case series are important. First, blood cultures performed in patients admitted to the hospital with uncomplicated SSTIs yield an extremely low number of positive results. Second, although some laboratory findings differ between patients with uncomplicated and complicated SSTIs, these differences do not provide useful clinical predictive value. Given the limited value of these tests, physicians might reasonably limit their use to children with complicated infections. Third, patients with cSSTIs have a high rate of bacteremia, and blood cultures are important in treating those patients. However, obtaining blood cultures in children with uncomplicated SSTI is seldom useful and may be harmful, as we found that obtaining a blood culture is associated with a longer mean LOHS.

This is the first study to examine the yield of blood cultures in patients with SSTIs since the introduction of the varicella and pneumococcal vaccines, and it is the first to do so in the CA-MRSA era. We agree with recent research on pediatric SSTIs that has called for additional prospective research to define criteria for hospitalization. We conclude that blood cultures are not useful in the management of uncomplicated SSTI in hospitalized children, and clinicians should discontinue their use in this setting.

REFERENCES

1. Fleisher GR. Infectious disease emergencies. In: Fleisher GR, Ludwig S, Henretig FM, eds. *Textbook of Pediatric Emergency Medicine*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:783–851
2. Kam AJ, Leal J, Freedman SB. Pediatric cellulitis: success of emergency department short-course intravenous antibiotics. *Pediatr Emerg Care*. 2010;26(3):171–176
3. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious

Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. 2011;52(3):e18–55

4. Stevens DL, Bisno AL, Chambers HF, et al; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft-tissue infections [published correction appears in *Clin Infect Dis*. 2006;42(8):1219]. *Clin Infect Dis*. 2005;41(10):1373–1406
5. Gouin S, Chevalier I, Gauthier M, Lamarre V. Prospective evaluation of the management of moderate to severe cellulitis with parenteral antibiotics at a paediatric day treatment centre. *J Paediatr Child Health*. 2008;44(4):214–218
6. Fleisher G, Ludwig S, Henretig F, Ruddy R, Henry W. Cellulitis: initial management. *Ann Emerg Med*. 1981;10(7):356–359
7. Sadow KB, Chamberlain JM. Blood cultures in the evaluation of children with cellulitis. *Pediatrics*. 1998;101(3). Available at: www.pediatrics.org/cgi/content/full/101/3/e4
8. Marin M, Zhang JX, Seward JF. Near elimination of varicella deaths in the US after implementation of the vaccination program. *Pediatrics*. 2011;128(2):214–220
9. Moran GJ, Krishnadasan A, Gorwitz RJ, et al; EMERGEncy ID Net Study Group. Methicillin-resistant S. aureus infections among patients in the emergency department. *N Engl J Med*. 2006;355(7):666–674
10. Chen AE, Goldstein M, Carroll K, Song X, Perl TM, Siberry GK. Evolving epidemiology of pediatric *Staphylococcus aureus* cutaneous infections in a Baltimore hospital. *Pediatr Emerg Care*. 2006;22(10):717–723
11. Kaplan SL, Hulten KG, Gonzalez BE, et al. Three-year surveillance of community-acquired *Staphylococcus aureus* infections in children. *Clin Infect Dis*. 2005;40(12):1785–1791
12. King MD, Humphrey BJ, Wang YF, Kourbatova EV, Ray SM, Blumberg HM. Emergence of community-acquired methicillin-resistant *Staphylococcus aureus* USA 300 clone as the predominant cause of skin and soft-tissue infections. *Ann Intern Med*. 2006;144(5):309–317
13. Purcell K, Fergie J. Epidemic of community-acquired methicillin-resistant *Staphylococcus aureus* infections: a 14-year study at Driscoll Children's Hospital. *Arch Pediatr Adolesc Med*. 2005;159(10):980–985
14. Hersh AL, Chambers HF, Maselli JH, Gonzales R. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. *Arch Intern Med*. 2008;168(14):1585–1591
15. Khangura S, Wallace J, Kissoon N, Kodeeswaran T. Management of cellulitis in a pediatric emergency department. *Pediatr Emerg Care*. 2007;23(11):805–811

Blood Cultures in the Evaluation of Uncomplicated Skin and Soft Tissue Infections

Jay R. Malone, Sarah R. Durica, David M. Thompson, Amanda Bogie and Monique Naifeh

Pediatrics; originally published online August 5, 2013;
DOI: 10.1542/peds.2013-1384