# Skin and Soft Tissue Infections in Young Infants

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## ABSTRACT

**Introduction:** The management of young infants with skin and soft tissue infection is not well-defined.

**Methods:** We performed a survey study of pediatric hospital medicine, emergency medicine, urgent care, and primary care physicians to assess the management of young infants with skin and soft tissue infection. The survey included 4 unique scenarios of a well-appearing infant with uncomplicated cellulitis of the calf with the combination of age ≤28 days vs 29–60 days and the presence vs absence of fever.

**Results:** Of 229 surveys distributed, 91 were completed (40%). Hospital admission was chosen more often for younger infants (≤28 days) versus older infants regardless of fever status (45% vs 10% afebrile, 97% vs 38% febrile, both $P<0.001$). Younger infants were more likely to get blood, urine, and cerebrospinal fluid studies ($P<0.01$). Clindamycin was chosen in 23% of admitted younger infants compared to 41% of older infants ($P<0.05$).

**Conclusions:** Frontline pediatricians appear relatively comfortable with outpatient management of cellulitis in young infants and rarely pursued meningitis evaluation in any afebrile infants or older febrile infants.


## INTRODUCTION

The management of young infants with skin and soft tissue infection (SSTI) has not been well-studied and, in the few available studies, appears to be highly variable in both diagnostic evaluation and therapy.[1-6] "Skin and soft tissue infection" can refer to a variety of clinical manifestations, including pustulosis, carbuncles, furuncles, cellulitis, and abscesses. In the literature addressing young infants with skin infections, the majority consider SSTI to include only pustulosis (pus-filled lesion <1cm), cellulitis, and abscess, while more severe associated processes (osteomyelitis, septic arthritis, bacteremia, meningitis) are considered "invasive bacterial infections" (IBI) and are studied separately.

In the literature reporting on young infants (≤90 days) with SSTI, fever is present in 3% to 20%, and IBI rate ranged from 0.6% to 11.9%, although if the study with the highest rate by Fortunov et al is removed, the resulting range in the remaining 5 studies is much smaller at 0.6% to 2.5%.[1-6] The study by Vidwan and Geis demonstrated a correlation of IBI with fever. The risk of IBI in afebrile infants was small at 0.6%; however, the risk in febrile infants was more meaningful at 7.7%.[1] While fever often dictates management in infants ≤60 days, this small base of literature demonstrates that fever is not present in the majority of reported cases. The evidence-based diagnostic evaluation for febrile infants ≤60 days is, therefore, not applicable in many cases. The threat of IBI is a driving force in the management of infants with possible infection, but rates of IBI are low in infants with SSTI, suggesting that invasive evaluation (eg, lumbar puncture) may not always be needed. The aim of this study was to describe the preferred diagnostic and management approach to a young infant with uncomplicated cellulitis.

## METHODS

This was a cross-sectional study using online surveys to assess respondent perspectives on the management of young infants

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**Table 1.** Description of Study Participants

| | Respondent N/Total Requested N (%) |
|---|---|
| Overall Survey Response Rate | 94/229 (41.0) |
| Overall Survey Completion Rate | 91/229 (39.7) |
| Service Division Response Rate[a] | |
| Urgent Care | 12/45 (26.7) |
| Primary Care | 34/116 (29.3) |
| Hospital Medicine | 26/30 (86.7) |
| Emergency Medicine | 19/35 (54.3) |
| | **Respondent N (% of Total)** |
| Years in Practice of Respondents (N = 87) | |
| 0-5 years | 36 (41.4) |
| 6-10 years | 21 (24.1) |
| 11-15 years | 12 (13.8) |
| ≥16 years | 18 (20.7) |

[a]As clinicians might work in multiple divisions, sum does not add to 100.

with SSTI. Surveys were distributed to physicians in the clinical areas of pediatric hospital medicine, pediatric primary care, pediatric emergency medicine, and pediatric urgent care within an urban Midwestern tertiary pediatric hospital system. The survey was available from June 2020 to September 2020. Participants were emailed an anonymous survey link with 3 reminders sent over the 12-week study period. The study was approved by the Institutional Review Board of the Medical College of Wisconsin, project #00037408.

The survey included 4 hypothetical scenarios of a well-appearing infant with uncomplicated cellulitis of the calf. The patient's skin exam was described as "mildly indurated area on the calf without fluctuance," and it was clearly stated in the scenario to be "consistent with a diagnosis of uncomplicated cellulitis." The combination of the infant's age (≤ 28 days vs 29–60 days) and the presence or absence of fever made each of the 4 scenarios unique (Appendix A). Participants were asked to select diagnostic tests, disposition, and antibiotics for each clinical scenario. Possible diagnostic evaluation included (multiple tests could be chosen) blood culture, urine studies, cerebrospinal fluid (CSF) studies, chest radiograph, complete blood cell count (CBC), herpes simplex virus (HSV) studies, skin swab, needle aspirate, skin ultrasound, or no further evaluation.

For disposition, participants could choose either inpatient or outpatient care. Antibiotic choice utilized skip logic based on the disposition response. If inpatient was chosen, intravenous antibiotic choices included clindamycin, nafcillin or oxacillin, ceftriaxone or cefotaxime, vancomycin, cefazolin, ampicillin, piperacillin-tazobactam, cefepime, acyclovir, and gentamicin. If outpatient was chosen, oral antibiotics options included clindamycin, cephalexin, amoxicillin, amoxicillin-clavulanate, cefdinir, cefuroxime, and cefixime. There was no limit to the number of antibiotics a participant could select. Participant demographics collected included the participants' specialty and number of years in practice. Participants were required to answer each question before responding to the next and were able to change their previous responses. The data were summarized using descriptive statistics. For management decisions, the McNemar's test was used to compare scenarios by age (17 days vs 52 days) and fever status (febrile vs afebrile). For antibiotic usage, since it was based on the disposition response, analyses were done separately for inpatient and outpatient antibiotics, and the generalized linear mixed models with binary distribution and logit link function were used. Statistical software SAS 9.4 was used for all the analyses. A $P$ value of <0.05 was considered statistically significant.

## RESULTS

A total of 229 surveys were administered and 91 were completed (40%). Most (37%) survey respondents practiced in primary care, and most (41%) were in practice less than 5 years (Table 1).

Participants were significantly more likely to choose inpatient admission for younger infants versus older infants regardless of fever status (45% vs 10% when afebrile, 97% vs 38% when febrile, both $P < 0.001$). The patient's age was a significant factor in diagnostic evaluation. In the afebrile scenarios, respondents were more likely to choose blood cultures (76% vs 52%, $P < 0.001$), CBC (76% vs 52%, $P < 0.001$), urine studies (39% vs 17%, $P < 0.001$), CSF studies (38% vs 6%, $P < 0.001$), and HSV studies (6% vs 1%, $P = 0.046$) for the 17-day-old infant vs the 52-day-old infant. Respondents were significantly less likely to choose "no further evaluation" for younger infants compared to older infants in the absence of a fever (22% vs 39%, $P < 0.001$) (Table 2).

Respondents were significantly more likely to choose inpatient admission for febrile infants of both ages compared to afebrile infants (97% vs 45% for 17 days, 38% vs 10% for 52 days, both $P < 0.001$). They were significantly more likely to choose no further evaluation for afebrile infants of both ages ($P < 0.001$). Conversely, respondents were more likely to select blood cultures, CBC, urine studies, CSF studies, and ultrasound for infants with fever compared to infants the same age without a fever (Table 2). Management decisions by age and fever status are summarized in the Figure. The relationships between years of practice and management choices were not statistically significant, with the exception that physicians with less than 10 years of practice were more likely to order urine studies on the 17-day-old infant with fever, and physicians with more than 16 years of practice were more likely to order a chest x-ray on the 17-day-old infant with fever ($P = 0.011$ and $P = 0.0098$, respectively).

Antibiotic selection varied. Ampicillin and cephalosporins were the most commonly selected inpatient intravenous (IV) antibiotic in 17-day-old infants (64% and 67%, respectively), whereas clindamycin was chosen in only 23% of admitted 17-day-old infants. In 52-day-old infants, cephalosporins and clindamycin were the most commonly selected antibiotics (45% and 41%, respectively). Sixteen respondents (10%) selected IV vancomy-

cin. Clindamycin was the most commonly selected outpatient antibiotic in 17-day-old infants (31%) compared to a 1st generation cephalosporin in 52-day-old infants (49%) (Table 3).

## DISCUSSION

There have been several small, retrospective studies on the topic of young infants with SSTI that demonstrate variability in diagnostic evaluation and therapy choices.[1-6] By using a survey method, we tried to ascertain physician management decisions in the idealized circumstance of a well-appearing infant with no concern for a complication. There is an abundance of guidelines and evidence supporting admission and thorough diagnostic evaluation, including CSF sampling, in young infants with a fever.[7-10] The difficulty comes when clinicians encounter an infant with a clear source of infection, such as an SSTI. Rates of CSF sampling in studies looking at young infants with SSTI ranged from 25% to 67%.[1-6] Rates of blood cultures in the same population ranged from 13% to 96%.[1-4] In 37% to 47% of cases, no further diagnostic evaluation (either blood or CSF) was done.[1,2,6] Admission was longest and 10 times more expensive for those infants who had CSF studies done.[2] For the sake of comparison, 26% to 58% of infants 29-60 days old with a febrile urinary tract infection had CSF sampling.[11-13] Young afebrile infants ≤ 28 days with acute otitis media had CSF studies in 34% of cases and blood cultures in 53% of cases compared to 33% and 13%, respectively, in infants 29-56 days old.[14]

In our study, 92% of respondents recommended CSF studies be obtained on the 17-day-old febrile infant, in keeping with the standard of care for a febrile infant ≤28 days.[8-10] For the 17-day-old infant without fever, however, only 38% recommended CSF evaluation, which was lower than expected given the high-risk age of the infant. Less than one-quarter of respondents recommended CSF evaluation in the 52-day-old infants both with and without fever, reflecting the overall more liberal practices in this age group. As expected, the younger infant and the febrile infant had a more thorough evaluation and were significantly more likely to have a blood culture, CSF evaluation, and urine studies compared to the older and afebrile infant, respectively ($P < 0.01$ for all).

The decision to admit an infant with SSTI has been shown to vary. Even in studies with the youngest cohorts of infants ≤ 30

**Table 2.** Management Differences (Total N = 87, Abbreviated)[a]

**Management by Age (Fever Controlled)**

| | Afebrile | | | Febrile | | |
|---|---|---|---|---|---|---|
| | **17 days** | **52 days** | ***P* value** | **17 days** | **52 days** | ***P* value** |
| Recommended Evaluation (N, %) | | | | | | |
| Blood culture | 66 (75.9) | 45 (51.7) | < 0.001 | 87 (100) | 80 (92.0) | 0.008 |
| Urine studies | 34 (39.1) | 15 (17.2) | < 0.001 | 75 (86.2) | 50 (57.5) | < 0.001 |
| Cerebrospinal fluid studies | 33 (37.9) | 5 (5.8) | < 0.001 | 80 (92.0) | 12 (13.8) | < 0.001 |
| Complete blood cell count | 66 (75.9) | 45 (51.7) | < 0.001 | 85 (97.7) | 80 (92.0) | 0.025 |
| Herpes simplex virus studies | 5 (5.8) | 1 (1.2) | 0.046 | 15 (17.2) | 1 (1.2) | <0 .001 |
| No further evaluation | 19 (21.8) | 34 (39.1) | < 0.001 | 1 (1.2) | 5 (5.8) | 0.10 |
| Disposition (N, %) | | | | | | |
| Admission | 39 (44.8) | 9 (10.3) | < 0.001 | 84 (96.6) | 33 (37.9) | < 0.001 |

**Management by Fever Status (Age Controlled)**

| | 17 days | | | 52 days | | |
|---|---|---|---|---|---|---|
| | **Febrile** | **Afebrile** | ***P* value** | **Febrile** | **Afebrile** | ***P* value** |
| Recommended Evaluation (N, %) | | | | | | |
| Blood culture | 87 (100) | 66 (75.9) | < 0.001 | 80 (92.0) | 45 (51.7) | < 0.001 |
| Urine studies | 75 (86.2) | 34 (39.1) | < 0.001 | 50 (57.5) | 15 (17.2) | < 0.001 |
| Cerebrospinal fluid studies | 80 (92.0) | 33 (37.9) | < 0.001 | 12 (13.8) | 5 (5.8) | 0.008 |
| Complete blood cell count | 85 (97.7) | 66 (75.9) | < 0.001 | 80 (92.0) | 45 (51.7) | < 0.001 |
| Herpes simplex virus studies | 15 (17.2) | 5 (5.8) | 0.002 | 1 (1.2) | 1 (1.2) | > 0.99 |
| Ultrasound | 26 (29.9) | 16 (18.4) | 0.002 | 21 (24.1) | 13 (14.9) | 0.011 |
| No further evaluation | 1 (1.2) | 19 (21.8) | < 0.001 | 5 (5.8) | 34 (39.1) | < 0.001 |
| Disposition (N, %) | | | | | | |
| Admission | 84 (96.6) | 39 (44.8) | < 0.001 | 33 (37.9) | 9 (10.3) | < 0.001 |

[a]Associations with chest x-ray, skin swab, and needle aspirate were not statistically significant. Complete data are available in Appendix B.

**Figure.** Management by Age and Fever Status

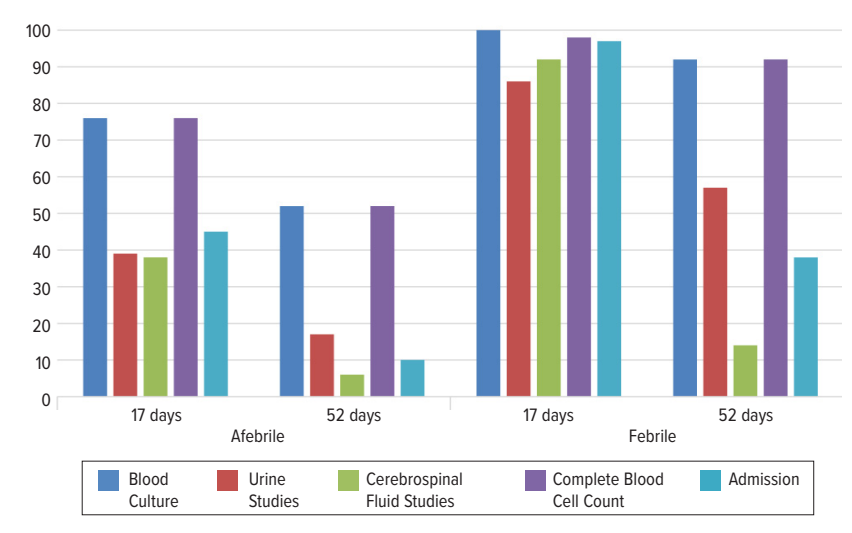

**Table 3.** Antibiotics by Age (Abbreviated)[a]

| Inpatient Antibiotic Choice by Age | | | |
|---|---|---|---|
| | **17 days (N=123, %)** | **52 days (N=42, %)** | ***P* value** |
| Nafcillin/oxacillin | 5 (4.1) | 1 (2.4) | 0.41 |
| Ampicillin | 79 (64.2) | 8 (19. 0) | <0.001 |
| 1st gen cephalosporin | 7 (5.7) | 2 (4.8) | 0.96 |
| 3rd gen cephalosporin | 40 (32.5) | 12 (28.6) | 0.64 |
| 4th gen cephalosporin | 36 (29.3) | 5 (11.9) | 0.027 |
| Clindamycin | 28 (22.8) | 17 (40.5) | 0.048 |
| Vancomycin | 12 (9.8) | 4 (9.5) | 0.74 |
| **Outpatient Antibiotic Choice by Age** | | | |
| | **17 days (N=51, %)** | **52 days (N=132, %)** | ***P* value** |
| Amoxicillin | 4 (7.8) | 5 (3.8) | 0.50 |
| Amoxicillin-clavulanate | 4 (7.8) | 7 (5.3) | 0.71 |
| 1st gen cephalosporin | 22 (43.1) | 65 (49.2) | 0.40 |
| Clindamycin | 16 (31.4) | 39 (29.6) | 0.81 |

[a]Infrequently chosen antibiotics without significant associations were excluded from the Table. Complete data are available in Appendix C.

days, 12% to 36% were discharged home to complete outpatient antibiotic treatment.[3,5] In an older cohort of infants ≤90 days examined by Vidwan and Geis, 58% of afebrile infants and 59% of febrile infants were discharged home from the emergency department.[1] The large majority of respondents (97%) recommended admission of the febrile 17-day-old infants in our study, which is consistent with standard of care for a febrile infant in this age group. We were surprised to find that less than half (45%) of respondents recommended admission for the afebrile 17-day-old infant. Likewise, only 38% recommended admission for the febrile 52-day-old infant. Although this infant would not qualify as "low risk" in the febrile neonate algorithm for our institution due to the presence of a visible infection, our expectation was that more clinicians would consider the infant "high risk" and admit.

Choice of antibiotic for SSTI in young infants is not well agreed upon in the literature. Streptococci species and methicillin-sensitive *Staphylococcus aureus* (MSSA) are the most commonly implicated pathogens in nonpurulent cellulitis, and empiric therapy should be targeted toward these organisms.[15] There is good evidence that infants ≤60 days should be treated with a third-generation cephalosporin alone or in combination with ampicillin (if ≤28 days) as empiric therapy for possible sepsis.[9,16,17] Soft tissue infections are often treated with drugs targeting methicillin-resistant *Staphylococcus aureus* (MRSA), such as clindamycin or vancomycin.[18-20] Markham et al found that clindamycin was the most common (80%) antibiotic used in young infants with SSTI, and only 21% of infants received vancomycin. Combination therapy (ie, anti-staphylococcal drug with neonatal sepsis drugs) was used in 45% and was associated with a 30% longer length of stay and 40% higher costs.[4] We found a shift in the use of IV clindamycin in infants who were admitted: 52-day-old infants were significantly more likely to receive clindamycin (41% vs 23%, $P=0.048$) in addition to a 3rd or 4th generation cephalosporin. However, at our institution, 20% of all Staphylococcus aureus isolates are resistant to clindamycin, and there is evidence of rising clindamycin resistance among MSSA isolates over the last decade.[21] As empiric bacterial coverage for common SSTI organisms, clindamycin is not an ideal regimen, and these findings represent an opportunity for improved antibiotic stewardship.

Of note, at the time of our survey, we did not have any guideline for pediatric SSTI at our institution. Subsequently, a clinical practice guideline for the hospital medicine group was published in 2020 but excluded young infants. Therefore, clinical decisions were made at the discretion of the managing physician. Additionally, there is no national guideline published by the American Academy of Pediatrics or other group, to our knowledge, to drive management of SSTI in infants this age.

There were several limitations to this study. This was a survey study limited to respondents within a single tertiary care pediatrics system. We attempted to capture the physicians most likely to manage young infants by including primary care, hospital medicine, urgent care, and emergency medicine physicians; however, there are other pediatric and family practice physicians outside of our system who are also managing infants within our community. The response rate to our survey was only about 40%, and it is possible that there was bias related to the degree of comfort in managing infants with cellulitis and those physicians who chose to take the survey. The survey was administered during the pandemic, which may have affected response rates due to burnout from the large volume of emails related to pandemic concerns and other competing clinical obligations. The survey was developed by the authors of the study who practice pediatric hospital and emergency medicine, and response options were chosen based on prior literature and resources available within our health system. However, no previously validated survey on this topic exists. Inherent to all survey studies, participant answers may not reflect actual clinical practice.

## CONCLUSIONS

Our findings suggest that physicians at our institution are quite comfortable with outpatient management of infants ≤28 days when afebrile and infants 29–60 days regardless of fever status. Likewise, diagnostic evaluation for meningitis with CSF studies was rarely recommended in afebrile infants regardless of age or febrile infants over 29 days. As expected, in accordance with febrile neonate guidelines, infants ≤28 days with fever were managed more aggressively, with the large majority being recommended for admission and CSF studies. With regard to antibiotic usage, we found a significant shift towards the use of clindamycin in older infants, which is not likely to be explained by any inherently higher risk of resistant bacteria and would potentially be a good target for future antimicrobial stewardship efforts.

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**Appendices:** Available at www.wmjonline.org

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