FEVER IN CHILDREN LESS THAN 36 MONTHS OF AGE—QUESTIONS AND STRATEGIES FOR MANAGEMENT IN THE EMERGENCY DEPARTMENT

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Abstract—Fever is a common pediatric complaint in the Emergency Department. Emergency Physicians often must be conservative in their management of febrile children, as patient follow-up is not always available. A unified approach for the management of febrile infants will be discussed in this article. © 2003 Elsevier Inc.

Keywords—fever; infant; child; bacteremia

INTRODUCTION

Febrile illnesses in infants and children account for 10–20% of pediatric visits to Emergency Departments (EDs) (1,2). Fever is defined as a core temperature greater than 38°C (100.4°F) (3). It is the role of the Emergency Physician to determine which of these cases may represent serious illnesses that require further evaluation and treatment.

There are several tools that may be useful in evaluating the febrile infant. The Rochester Criteria were developed by Dagan et al. in 1985 to determine a subset of infants under the age of 3 months who are less at risk of occult bacterial infection and can be managed on an outpatient basis (4). These criteria include no evidence of focal infection, a peripheral white blood cell count between 5000 and 15,000 white blood cells/mm³ with less than 1500 bands/mm³, and urinalysis yielding normal findings. Baker et al. subsequently developed alternative criteria, the Philadelphia Criteria, to determine which infants are at high risk of bacterial infection (5). These criteria include a peripheral white blood cell count of at least 15,000/mm³, a spun urine specimen that has 10 or more white cells per high-power field or that is positive on bright-field microscopy, cerebrospinal fluid (CSF) with a white-cell count of 8 or more per cubic millimeter or a positive Gram’s stain, or a chest radiograph showing an infiltrate. Both sets of criteria have been widely used in the evaluation of the young febrile infant.

With the advent of the Hemophilus influenzae vaccine came the recognition that the incidence of occult bacteremia would be affected, and Baraff’s extensive literature review in 2000 resulted in the publication of new guidelines for management of fever in the ED (8). Now that use of the pneumococcal vaccine is becoming more widespread, the incidence of bacteremia and subsequent focal infections are changing. Management of febrile young children in the ED differs markedly from management in a primary care setting. This article reviews the current, conservative ED management strategies and guidelines for fever without a source (Figures 1 and 2) and discusses some of the common questions regarding fever in infants and children evaluated in the ED. Although Baraff’s recommendation is to use 39.5°C as a definition for fever in children over 3 months of age, our
The institution uses a temperature of 39°C (102.2°F) as not all children have yet been fully vaccinated against *S. pneumoniae* (whether due to inadequate primary care or national shortages of the vaccine) and studies on this unimmunized population to date have used the cutoff of 39°C. In both patient populations, however, following a protocol as detailed in the flow diagrams maintains uniformity of approach for all febrile infants.

**STRATEGIES FOR MANAGEMENT**

In febrile infants less than 2 months of age, antibiotic administration as early as possible is optimal and a “Febrile Infant Protocol” has been proposed (9). This includes identification of febrile infants in triage, provision of acetaminophen by the triage nurse, and provision of a parent information sheet about fever and the need for evaluation (see Figure 3). If the parents consent to pro-
ceed with treatment, there is immediate transfer of the patient to a patient care room with nursing initiation of bladder catheterization, intravenous line placement (if the patient is 28 days old or less) and blood sampling for a CBC and blood culture prior to evaluation by a doctor. The doctor then evaluates the infant, performs a lumbar puncture, and antibiotics are administered, with the goal of antibiotic administration within 2 h of arrival in the ED. If intravenous access is unsuccessful within 2 h, antibiotics are administered intramuscularly. This approach significantly reduces overall time to antibiotic administration in this age group. For management summary in this age group, see Figure 1 and Table 1.

In the 2–36 month age group, management depends upon laboratory test results and care is more patient-specific with regards to the need for chest X-ray, CSF studies, and antibiotic administration (see Figure 2 and Table 2).
QUESTIONS

Q: How prevalent is occult bacteremia now in the post-H. influenzae era and the age of the pneumococcal vaccine?

A: Probably less than 2%.

Baraff’s extensive literature review in 2000 concludes that for children less than 3 months of age, in low-risk infants the prevalence of occult bacteremia is 0.2–1%, occult urinary tract infection (UTI) is 0.2–1%, bacterial enteritis is 0.2–1%, and bacterial meningitis is 0% (dependent on study methodology) (8). In the same study, the 3–36-month age group is also analyzed. Three large, prospective, randomized, controlled trials from 1987 to 1994 are compared, revealing an overall prevalence of 2.6–6.1% of occult bacteremia in children with a temperature over 39°C. There is a substantially higher risk for those with either temperature over 40°C or with temperature over 39.5°C and peripheral white blood cell count (WBC) > 15,000/mm³. The major pathogen in these studies was S. pneumoniae, with occasional cases caused by Salmonella and N. meningitides (after H. influenzae is excluded—some studies predate widespread H. influenzae vaccination). Alpern et al. published a study subsequent to this analysis, evaluating bacteremia in children aged 2–24 months who presented to the pediatric ED in whom they found a prevalence of bacteremia of 1.9%. Of these pathogens, S. pneumoniae accounted for 83% and no H. influenzae was identified (10).

Before the H. influenzae Type b vaccine, the prevalence of occult bacteremia ranged from 2.3–11.6%, which has been reduced by over 90% (11). The pneumococcal vaccine is expected to reduce the incidence of pneumococcal illness by at least 89% according to phase III trials (12). Thus, further studies regarding the prevalence of bacteremia after widespread immunity has developed are likely to drastically change the approach to the febrile infant and child.

Q: Does bacteremia always have to be treated with parenteral antibiotics?

A: Not always.

In one study of children with proven pneumococcal bacteremia, those who received parenteral antibiotics on the initial ED visit had no positive blood or cerebrospinal fluid (CSF) cultures on a follow-up visit (13). Initial treatment with either oral or parenteral antibiotics resulted in no difference in subsequent focal infections, although those treated with only oral antibiotics were less likely to be improved and had a higher rate of persistent bacteremia. A meta-analysis in 1998 showed the same rate of subsequent serious bacterial infection in patients with S. pneumoniae bacteremia regardless of whether treatment was oral or parenteral (14). Another later study found that an oral course of antibiotics of 7–10 days resulted in adequate resolution of pneumococ-
cal bacteremia in all cases (15). It seems reasonable, therefore, to treat all patients who are in the high risk category with an initial dose of parenteral antibiotics, and if *S. pneumoniae* is found on blood culture, to consider outpatient treatment with appropriate oral antibiotics for 7–10 days in children over 2–3 months of age. Other pathogens grown on blood culture also merit consideration—there has been shown to be a rate of false-positive blood cultures (i.e., non-pathogenic) of around 0.9% (16). For any patient aged 3–36 months whose blood culture reveals a pathogen, prompt re-evaluation is necessary. At least one study has shown that a single dose of parenteral antibiotics at the initial visit can eradicate bacteremia in patients with bacteremia caused by *S. pneumoniae*, *H influenzae* type b, *Salmonella* and *N. meningitides* (17). If the patient is non-toxic, has no focal bacterial infection, and is well-appearing at a 24-h follow-up visit and received parenteral antibiotics at the first visit, a reasonable course of action would be to commence oral antibiotics, selected on the basis of what pathogen is grown and sensitivities (although duration of therapy is not well established). However, if patients with a positive blood culture have a persistent fever, are ill-appearing, have developed a bacterial focus of infection, or are less than 3 months of age, inpatient parenteral antibiotic therapy should be instituted (8).

Q: What does “without a source” mean? Are viral infections such as Respiratory Syncytial Virus (RSV) bronchiolitis considered sources?

A: While the rate of bacteremia has been reported to be lower in patients with bronchiolitis, bacteremia cannot be absolutely ruled out.

Fever without a source is any fever without an identifiable focus of serious infection. Thus, a febrile child should have no signs such as meningismus, altered mental status, respiratory distress, circulatory failure, or hemorrhagic rash. Most clinicians would agree that such infants and children merit investigation as to the source of their symptoms. Less certainty exists about recognized illnesses that may be perceived as causing some degree of fever—are children with viral syndromes also at risk for occult bacteremia?

It has been found that febrile children aged 2–24 months with symptoms of bronchiolitis such as wheeze and retractions may have a lower than baseline incidence of bacteremia and urinary tract infection (UTI) (18,19). In a 1997 study of 156 patients identified with bronchiolitis, there was none with bacteremia and 1.9% with UTI, compared with controls who had a 2.7% prevalence of bacteremia and a 13.6% prevalence of UTI. Greenes and Harper also analyzed children presenting with fever over 39°C and recognizable viral syndromes such as croup, varicella, bronchiolitis and stomatitis (20). Of this subgroup of patients, 65% had blood cultures drawn, and of these only 0.2% (2 patients) revealed a pathogen (*S. pneumoniae* and Group A Streptococcus). Similarly, a study by Alpern et al. showed a rate of bacteremia of 0.7% in children with bronchiolitis (although this is not a statistically significant difference from the baseline prevalence of bacteremia of 1.9%) (10). Thus, although the rate of bacteremia may be lower in this subgroup, a recognizable syndrome such as RSV bronchiolitis does not absolutely exclude bacteremia.

Q: If a source such as otitis media or pneumonia is found, is a blood culture necessary?

A: Yes, in a select subset of children.

The prevalence of bacteremia in children aged 3–36 months with clinical otitis media and fever was as high as 5% in 1991, with a statistically significant rise in bacteremia for those with temperatures over 40°C (21). Since the advent of the *H. influenzae* vaccine, one study found that of patients aged 2–24 months who were evaluated for occult bacteremia, those with otitis media were 2.2 times more likely to have bacteremia compared with those without a focus of infection (12). Similarly, lobar pneumonia has been found to have a comparable prevalence of bacteremia, with one study finding a prevalence of bacteremia of 1.2% (although the pathogen was *Haemophilus influenzae*, type b) and another finding a prevalence of 2.7% (predominantly *S. pneumoniae*), although this was likely an overestimate, as not all patients with pneumonia had blood cultures (22,23). It would seem, then, that in children with a fever over 39°C who have an otitis media or pneumonia and are younger than 24 months, a blood culture still should be utilized. However, if a course of oral antibiotics is instituted to treat otitis or pneumonia, they usually provide adequate coverage against bacteremia. Clinicians should take both the age of the infant and the degree of fever into account when deciding whether a CBC and blood culture should be obtained before treating an otitis or pneumonia, as an initial dose of parenteral antibiotics and close follow-up may be preferable in younger infants, especially those under 6 months of age, ill-appearing children, or patients who have not been fully immunized.

Q: What kind of urine sample is adequate for analysis?

A: If they’re not potty trained, they need to be catheterized.

In a large study by Al-Orifi et al., 7584 urine specimens were collected from children under the age of 2 years, either by bag collection or catheterization (24). Of these, 62.8% of the bag specimens (compared with 9.1% of the catheterized specimens) grew a contaminant—a total of 3440 contaminated urine specimens, resulting in significant subsequent costs of unnecessary treatment, repeat cultures and follow up. Although suprapubic aspirate is the gold standard for urine culture, most Emer-
emergency Physicians do not routinely perform such an invasive procedure and a catheterized sample is now acceptable.

Q: If there are no respiratory symptoms, is a chest X-ray necessary for a fever work-up?

A: If there is significant leukocytosis and a high fever (> 39–39.5°C), a chest X-ray may be helpful.

Occult pneumonia has been shown to have an incidence of at least 19% in children under 5 years of age with no respiratory symptoms, fever over 39°C, and a white blood cell count of greater than 20,000 (25). However, it is entirely possible that the infiltrates seen on the initial radiograph are of viral origin and may spontaneously clear. The current guidelines for evaluation of a febrile child with a white blood count greater than 15,000 cells/mm³ recommend parenteral ceftriaxone be given empirically with follow-up in 24 h. Because the patient will receive a dose of antibiotics regardless of the presence or absence of respiratory symptoms, an alternate reasonable approach is to obtain an X-ray study during the follow-up visit, if appropriate. The child can then be re-examined for respiratory symptoms, fever resolution, and a longer course of antibiotics instituted if necessary.

Q: If the white blood count is normal, is a lumbar puncture really necessary?

A: Yes, if the infant is younger than 60 days, or 60–90 days and you intend to give antibiotics.

A recent prospective study analyzed the peripheral blood WBC count in infants aged 3–89 days presenting with fever over (38°C) (100.4°F) (26). Of 5353 evaluated infants, 22 were found to have meningitis caused by organisms including E. coli (n = 11), group B streptococcus (n = 9), and S. pneumoniae (n = 1). Of these infants, 16 had a peripheral WBC of less than 15,000 cells/mm³—in fact, 9 of the 22 had a white blood count of between 5,000 and 15,000 cells/mm³. If WBC alone were used as the deciding factor for performance of lumbar puncture, more than half of infants with meningitis would have been missed. Thus, in this age group, a lumbar puncture should be performed if the patient is inconsolable, lethargic, has a change in behavior, or if there is clinical suggestion of meningitis. If a lumbar puncture is not performed in the 60–90-day age group (see management strategy, Table 1), antibiotics should not be given and follow-up within 24 h is imperative.

Q: Should antibiotics be given before a lumbar puncture is performed?

A: If possible, a lumbar puncture should be performed prior to initiating antibiotics as CSF can become sterile within an hour of antibiotic administration. However, antibiotics should be given immediately in the unstable patient.

A retrospective study by Kanegaye et al. reviewed patients aged 1–16 years with meningitis between 1992 and 1996 (27). This was defined as those who had a CSF culture positive for a known bacterial pathogen, a positive CSF antigen study or Gram’s stain in conjunction with a CSF WBC of > 10/mm³, blood culture positive with CSF WBC of > 100/mm³ or, in the absence of bacterial isolate, CSF WBC of > 4000/mm³. Isolated pathogens included S. pneumoniae, N. meningitides and group B streptococcus. After treatment with a third generation cephalosporin, it was found that time to CSF sterility for those with N. meningitides was less than 1 hour for 3 of 9 patients, and all CSF samples were sterile within 2 h. For S. pneumoniae, time to sterility was 4–10 h for 5 of 7 patients, and for group B streptococcus there was an 8-hour window. Thus, in patients in whom meningitis is a possibility, CSF optimally should be obtained before antibiotics are given in order for an accurate diagnosis to be made. However, if the patient is unstable or the lumbar puncture is technically difficult to perform, then antibiotics should be administered prior to obtaining specimens of CSF for evaluation. Ideally, a blood culture will have been performed.

Q: What about the “bundled baby”—can this raise the temperature?

A: No, not the core temperature.

A case-controlled study in 1994 compared infants who were clothed in diaper and coveralls only with those bundled in coveralls, cap, receiving blanket and thermal blanket (28). After 65 min it was found that although mean skin temperature was significantly increased in bundled babies, there was no significant difference in the

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<td>0–1 month</td>
<td>≥ 38°C (≥ 100.4°F)</td>
<td>CBC/blood culture, UA/urine culture, CSF studies +/– CXR</td>
<td>Admit</td>
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</tr>
<tr>
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<td>CBC/blood culture, UA/urine culture, CSF studies +/– CXR</td>
<td>Admit high risk</td>
<td>Discharge low risk with 24 hour follow up</td>
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<td>Ceftriaxone</td>
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CBC = Complete blood count; UA; = urinalysis; CSF = cerebrospinal fluid; CXR = chest X-ray.

Table 1. Evaluation of Fever in Children Aged 0–2 Months—Summary

A: If there is significant leukocytosis and a high fever (> 39–39.5°C), a chest X-ray may be helpful.

Occult pneumonia has been shown to have an incidence of at least 19% in children under 5 years of age with no respiratory symptoms, fever over 39°C, and a white blood cell count of greater than 20,000 (25). However, it is entirely possible that the infiltrates seen on the initial radiograph are of viral origin and may spontaneously clear. The current guidelines for evaluation of a febrile child with a white blood count greater than 15,000 cells/mm³ recommend parenteral ceftriaxone be given empirically with follow-up in 24 h. Because the patient will receive a dose of antibiotics regardless of the presence or absence of respiratory symptoms, an alternate reasonable approach is to obtain an X-ray study during the follow-up visit, if appropriate. The child can then be re-examined for respiratory symptoms, fever resolution, and a longer course of antibiotics instituted if necessary.

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A case-controlled study in 1994 compared infants who were clothed in diaper and coveralls only with those bundled in coveralls, cap, receiving blanket and thermal blanket (28). After 65 min it was found that although mean skin temperature was significantly increased in bundled babies, there was no significant difference in the
core temperature of the infants. If rectal temperatures are used to measure temperature in the ED, as recommended, a temperature over 38°C for infants 0–90 days and over 39°C for infants older than 90 days should be considered a fever, regardless of their clothing.

Q: Should high-dose acetaminophen (oral or rectal) be used for high fever?
A: No, but opinions vary.

Regarding oral high-dose acetaminophen (APAP), Tréluwer et al. conducted a double blind study in 121 infants aged 4 months to 9 years who had an initial temperature of 39–40.5°C and had taken no antipyretics in the prior 24 h (29). An oral dose of either 15 or 30 mg/kg of APAP was given, and for the higher dose there was found to be a decrease in the time to bring the temperature down to 38.5°C, a longer period of time spent at or below that temperature, and a lower overall temperature by 0.5°C. The clinical significance of such a small difference in temperature between the two groups is minimal, and further studies regarding safety of additional 15-mg/kg doses subsequent to the 30-mg/kg dose are yet to be undertaken. Another study looked at 70 febrile patients aged 6 months to 6 years who were randomized to receive 15 mg/kg oral APAP, 15 mg/g rectal APAP, or 30 mg/kg rectal APAP (30). There was no significant difference in temperature decrement between the groups.

It should be noted that many (if not most) of the pediatric population with fever have already received acetaminophen prior to presentation in the ED, so the utility of high-dose acetaminophen as a loading dose in the ED is uncertain. The very real possibility of adverse effects also bears consideration as cases of liver failure associated with excessive acetaminophen administration are well documented (31). Chronic acetaminophen overdose in infants and children also has been well documented and cannot be overemphasized (32). Studies showing a small benefit of high-dose antipyretics must be balanced with the very real risks, especially if parents perceive increased doses as being necessary without adequate knowledge of the dangers to their children.

Q: Should acetaminophen be alternated with ibuprofen for persistent fever?
A: There is no good evidence to support this theory, although it is often a recommended treatment approach.

In 1972, Steele et al. studied the alternating use of acetaminophen with aspirin, finding a decrease in neither the rate nor the degree of temperature, although the effect was more sustained (33). No controlled studies have been done to determine either optimal methods or safety of alternating acetaminophen and ibuprofen to date, and yet this practice remains widespread (34). Disagreement also exists over the optimal alternating regime—should APAP be given every 4 h and ibuprofen every 6, resulting in a synchronous 12-h dose, or should APAP be given every 6 h so that there is a medication given every 3 h? Even if the correct milligram dosage is recommended by pediatricians, many do not ask parents which formulation they possess, which can lead to vastly inaccurate calculations. For example, a parent may give a child a teaspoon of Infant Tylenol (80 mg/0.8 mL) rather than Children’s Tylenol (160 mg/5 mL), a dose of 500 mg—clearly excessive for a 12-kilogram child.

The recommendation of aggressive treatment of fever also reinforces the “danger” of fever itself—Crocetti et al. in 2001 reinforced that fever phobia in parents still exists, with 56% of their respondents worried about the potential harmful effects of fever in their children (35). A survey of Pediatric ED nurses in 2000 revealed that 29% thought that permanent brain damage can result from high fever, 38% believed another antipyretic should be added an hour after a first dose if the child is still febrile, and 11% were not sure what temperature constitutes a fever (36). Even 65% of pediatricians who responded to a questionnaire in one study believed that an elevated body temperature in and of itself could become dangerous to a child, with 60% citing a temperature of 40°C (104°F) or above as significant and stating that the most serious complications of fever were brain damage (21%) and death (26%) (37). Another often cited reason for fever control is to “prevent febrile seizures,” a strategy that in controlled studies has proven ineffective with both APAP and ibuprofen (38,39).

However, fever control is useful in infants (beyond the automatic lumbar puncture age of 2 months) who are febrile and fussy on initial ED presentation. If, after fever reduction, the child is happy and playful, then a lumbar puncture may be avoidable.

Q: Do parents always understand the importance of immunizations?
A: No!

With the advent of the Internet, parents think that they are now more information savvy than ever before. Unfortunately, web sites now proclaim any opinion as information and many myths about the evils of immunization are easily found. Commonly touted myths are that the MMR vaccine and mercury-containing preservative (thimerosal) in vaccines cause autism, DTaP causes sudden infant death syndrome, Hepatitis B vaccine causes multiple sclerosis, and vaccine-related deaths are common. Other reasons cited for avoiding vaccination include the conclusion that chickenpox is a harmless disease, and there is no risk of children contracting vaccinable illness because the diseases have been eliminated from the United States. All of these myths have
been debunked in the literature, and all vaccines are now available in thimerosal-free formulations (40–43).

CONCLUSION

Occult bacteremia and other significant bacterial illnesses continue to be a valid concern in the febrile child younger than 36 months of age. However, despite the risk of serious bacterial infection, some physicians still fail to adequately diagnose and treat neonates with fever, with one study reporting 15% of physicians discharging febrile neonates under the age of 2 weeks and nearly 8% treating the same age group with oral antibiotics (44). Fortunately, with the increasing rate of pneumococcal vaccination, the rate of bacteremia will, in all likelihood, diminish, and the current guidelines will need to be revised. Lee et al. published a cost-effective analysis of a hypothetical cohort of children, assuming a current rate of occult bacteremia of 1.5% (45). According to their model, if the rate of bacteremia falls to less than 0.5% after widespread pneumococcal vaccination, empiric testing and treatment for occult bacteremia may be able to be eliminated. Until such time as the rate of bacteremia is shown to be this low, the Emergency Physician should continue to follow established guidelines in order to find and treat those with possible bacterial disease without over-treating those less at risk. Tables 1 and 2 outline our recommendations for evaluation of fever in children aged 0–36 months. These guidelines are intended to supplement clinical judgment and may be tailored to meet the needs of each specific institution. It is anticipated that the American College of Emergency Physicians and the American Academy of Pediatrics will publish clinical fever guidelines as newer data on bacteremia become available.

Acknowledgments—We thank Taylor Fletcher, MD (Palomar-Pomerado Hospitals) for the format of Tables 1 and 2.

Table 2. Evaluation of Fever in Children Aged 2–36 Months—Summary

<table>
<thead>
<tr>
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<tr>
<td>2–3 months</td>
<td>≥ 38°C (≥ 100.4°F)</td>
<td>CBC/blood culture/UA or CSF studies</td>
<td>Admit high risk</td>
<td>Ceftriaxone/Ceftriaxone if LP performed</td>
</tr>
<tr>
<td>3–36 months</td>
<td>≥ 39°C (≥ 102.2°F)</td>
<td>CBC (see Figure 2) +/− Blood culture if: WBC &lt; 5K or &gt; 15K ANC &gt; 10K + UA or urine culture (see Figure 2) +/− CXR</td>
<td>Discharge with 24-h follow up</td>
<td>Ceftriaxone if CXR/urine indicate high risk</td>
</tr>
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CBC = complete blood count; UA = urinalysis; CSF = cerebrospinal fluid; CXR = chest X-ray; LP = lumbar puncture; ANC = absolute neutrophil count.

REFERENCES