Fever

Paul L. McCarthy

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Paul L. McCarthy, MD*

IMPORTANT POINTS

1. **Etiologic, diagnostic, and management considerations vary for fever with no apparent source among infants younger than 3 months, children 3 to 36 months of age, and children who have fever lasting more than 7 to 10 days (so-called fever of unknown origin [FUO]).**
2. **Fever without apparent source is caused most often by bacterial or viral infections; in children who have FUO, collagen vascular disease, especially systemic juvenile rheumatoid arthritis, is also a common etiology.**
3. **The clinical evaluation, observation, history, and physical examination represent the most effective means of determining the cause of fever without apparent source.**
4. **For infants younger than 3 months of age, a full sepsis laboratory evaluation, including a complete blood count and white blood count differential, urinalysis, lumbar puncture, and cultures of cerebrospinal fluid, blood, and urine, is the most sensitive approach to detect bacterial infections.**
5. **Bacteremia or urinary tract infection should be considered in children 3 to 36 months of age in whom no cause for fever is apparent from the clinical evaluation. Urine culture is definitive for the latter. Increased risk for bacteremia is indicated by the child's appearance, height of fever, and degree of leukocytosis.**

Definition

The child who has fever with no apparent source is a common diagnostic and management challenge in pediatric practice. These children will be discussed in three domains, each of which has unique etiologic, diagnostic, and management considerations:

- The infant younger than 3 months of age with fever
- The child of 3 to 36 months of age with fever
- The child who has prolonged fever lasting more than 7 to 10 days (so-called fever of unknown origin [FUO]).

Recent work has noted that the upper limit of normal body temperature is 37.7˚C (99.9˚F) in adults and 37.9˚C (100.2˚F) in children. The lowest and highest (99th percentile) temperature varies with the time of the day, with the lowest occurring at 6 AM and the highest at 6 PM. Thus, the traditional teaching that normal body temperature is 37.0˚C (98.6˚F) is too restrictive. On the other hand, a temperature of 38.0˚C (100.4˚F) or greater in the infant or child represents abnormal temperature elevation or fever.

A variety of devices measure temperature from the skin, the tympanic membrane, or the urine. Although each offers ease of use, carefully performed studies have indicated that a rectal temperature, usually obtained with a glass mercury thermometer left in place for 3 minutes, is highly correlated with core body temperature. Devices that evaluate the temperature of the tympanic membrane, so-called ear thermometry, are not sufficiently accurate. This may be due to poor placement, which results in measuring the temperature of the ear canal wall, thus giving a falsely low reading. Axillary temperatures, although necessary in children who have anorectal malformations or who are immunocompromised, have a sensitivity of only 50% to 70%, depending on the method used, for detecting elevated temperature documented by rectal thermometry. For children older than 36 to 48 months of age who can hold the device beneath their tongues for 3 minutes, the mercury thermometer continues to be the best method for measuring temperature.

Epidemiology

Approximately 15% of visits to pediatricians are for acute episodes of fever. In the first 2 years of life, children average four to six such acute episodes. Episodes of fever in the first 3 months of life are less common than in the age range of 3 to 36 months.

At times, an infant may have an acute infection in the first 90 days of life but will not mount a fever response. For example, an infant may have septicemia and be afebrile or even hypothermic. Further, the occurrence of fever in the first 2 to 3 months of life is infrequent compared with the occurrence in older children. In one study of 575 patients in the first 2 months of life who were being followed for primary care, only six (1%) developed fever; in the same clinic, 55 of 390 children (14%) between 9 and 12 months of age developed a fever. In another report, only 2 of 149 (1.3%) consecutive febrile infants had fevers of 40˚C (104˚F) or more compared with 26 of 332 (8%) consecutively seen febrile children ages 3 to 36 months from the same institution. Finally, it appears that younger infants have fever less commonly than older infants. Several studies of consecutively evaluated febrile infants have noted that fever is twice as common in the second 30 days of life than in the first 30 days.

An increase in the occurrence of fever is seen between November and March in children 3 to 36 months of age, coinciding with the circulation within the community of acute infections caused by respiratory and gastrointestinal viral pathogens such as respiratory syncytial virus and rotavirus, respectively. Interestingly, there is also an accentuation in the occurrence of fever in infants younger than 90 days of age between November and March, but approximately 40% of febrile

*Professor of Pediatrics and Chief of General Pediatrics, Yale University School of Medicine, New Haven, CT.

episodes are seen in July through September. This latter phenomenon is due to the circulation of enteroviruses at that time of the year. There is also speculation and some documentation in the literature that immature thermoregulation may predispose infants to elevated body temperatures when the environmental or ambient temperature is very high, as in summer months.

It is difficult to obtain a precise estimate of the occurrence of FUO in children. Most reports concern hospitalized patients. One author reporting on FUO at a large children's hospital documented only 100 children with this admitting diagnosis over a 6-year period. Hence, this entity appears to be less common than acute episodes of fever, but it presents a significant diagnostic challenge.

Pathogenesis

Fever in children is due to a resetting of the thermoregulatory center in the hypothalamus by the action of cytokines released in response to various inciting agents. In children who have both acute and prolonged fevers, these agents most often are viral or bacterial pathogens. Less commonly, especially in prolonged fever, the agent may be circulating immune complexes, as seen in autoimmune disease. In malignant disease, pyrogens that cause fever may be released by tumor cells.

Once reset, the thermoregulatory center maintains a higher body temperature through such mechanisms as cutaneous vasoconstriction (heat conservation) or shivering (thermogenesis). Because the febrile response is less mature in young infants, no fever or hypothermia may occur in the presence of infection. The orchestrated fever response to an inciting agent (usually infectious) differs from elevated body temperature in which there is no resetting of the thermoregulatory center. One may see this phenomenon in the child who is left in an automobile when the temperature of the environment (ambient temperature) is high; homeostatic responses, such as sweating, are not adequate to compensate for the high ambient temperature. Children have a greater surface area per kilogram of body weight, thus making them more prone to heat injury from high environmental temperatures. The youngest infants, in whom surface area per kilogram of body weight is the greatest, are most susceptible to this type of heat injury.

In children who have FUO, fever is due most often to infectious agents, either viruses or bacteria, but autoimmune disease and tumors also are common etiologies. The pathophysiology of fever appears similar in this group to that seen in children who have acute fever.

Clinicians must be vigilant about the possibility of a focal lesion affecting the function of the thermoregulatory center and leading to elevated body temperature. Central nervous system (CNS) tumors may result in abnormal thermoregulation, and children who have acute subdural hematomas also may manifest elevated body temperature.

The limit of physiologic thermoregulation appears to be about 41.1˚C (106˚F). This degree of fever was present in only 100 children of 210,000 seen in our emergency department over a 10-year period, and these children had a high occurrence of CNS insults, such as meningitis, or other bacterial infections.

Clinical Aspects

The most challenging aspect of evaluating febrile children who have no apparent source of fever is to differentiate those who have a serious illness from those who do not.

In infants younger than 3 months of age and children 3 to 36 months old who have fever, most serious illnesses are caused by infectious agents. Table 1 indicates the diagnoses in 305 infants younger than 3 months of age who were seen at one medical center. Approximately 1 in 10 children had either meningitis/bacteremia, urinary tract infection (UTI), soft-tissue infection, or pneumonia. These illnesses often are caused by Gram-negative organisms or group B *Streptococcus* (GBS) and less commonly by *Listeria monocytogenes* and enterococci. Organisms seen commonly in older febrile children, including *S pneumoniae*, *Haemophilus influenzae* type b, and group A *Streptococcus*, also may be causative. Infection by Gram-negative organisms or GBS is an indicator that the immune system is relatively less competent in this age group. Gradually, during the first 90 days of life, infection caused by Gram-negative organisms or GBS becomes less frequent as the immune system matures. Another phenomenon associated with immaturity of the immune system in the febrile infant is the occurrence of bacteremia presenting as sepsis, which is due to the overwhelming nature of the infection.

The occurrence of serious illnesses in older children who have acute episodes of fever is shown in Table 2. The most common serious illnesses are meningitis, bacteremia, UTI, pneumonia, soft-tissue infections, and bacterial enteric infections. In children 3 to 36 months

TABLE 1. Diagnoses in 305 Febrile Infants <60 Days of Age*

	NUMBER	% OF TOTAL
Viral illness	256	83.8
Bacterial illness		
Meningitis/Bacteremia†	11	3.6
Urinary tract infection	7	2.3
Enteric pathogen	8	2.6
Soft-tissue infection	6	2.0
Total bacterial	32	10.5
Other	17§	5.5

Adapted from Caspe W, Chamudes O, Louie B. The evaluation and treatment of the febrile infant.* Pediatric Infect Dis. *1983;2:131–135.
†***Of these 11 patients, two had meningitis and bacteremia and nine had bacteremia only.***
§***Four (1.3%) had pneumonia.***

of age, bacterial meningitis, bacteremia, and focal soft-tissue infections (such as periorbital cellulitis) are caused most commonly by *H influenzae* type b and *S pneumoniae*. It is not uncommon in this age group, especially among children 3 to 24 months of age, for bacteria to circulate in the blood without the patient appearing to have sepsis or initial serious focal soft-tissue infection. These children, who initially appear to have minor viral infections or otitis media, are referred to as having occult bacteremia.

In one study of 482 febrile children who had positive blood cultures, approximately two in three were hospitalized immediately, presumably due to focal soft-tissue infection or the appearance of sepsis; one in three had occult bacteremia.

Table 3 indicates the etiologic organisms in children who have occult bacteremia. The first column represents data collected, for the most part, prior to the uniform use of vaccine against *H influenzae* type b; this organism is currently a less frequent cause of bacteremia and bacterial focal soft-tissue infection such as meningitis and periorbital cellulitis. *S pneumoniae* is causing an increasing proportion of cases of bacteremia.

Bacterial and viral infections continue to be the most common etiology among children who have prolonged fevers (lasting more than 7 to 10 days). Table 4 outlines the diagnoses in 100 children who had FUO and is representative of the diagnoses reported by other investigators. In the children younger than 6 years of age in this series, infectious illnesses caused most often by either bacteria or viruses predominated (34/52); in the children 6 years of age or older, infectious illnesses still predominated (18/48), but a substantial portion had collagen vascular diseases (most often systemic juvenile rheumatoid arthritis). Six children had malignancies, primarily leukemia and lymphoma. A diagnosis not reported in this series but always a significant consideration in a child who has persistent fever is Kawasaki disease, especially in those who have an incomplete clinical picture with only three or four of six of the major diagnostic criteria. It is also important to consider uncommon diagnoses, such as inflammatory bowel disease, vasculitis (eg, Behçet disease), or CNS abnormalities, such as a tumor.

The most common specific etiology of FUO in this series was bacterial infections (34 of 100 patients), especially among the younger children (20 of 52). Approximately two thirds of these bacterial infections were not highly unusual, such as with brain abscess, but rather such relatively common entities as UTI, pneumonia, meningitis, septicemia, tonsillitis, sinusitis, and focal soft-tissue infections (eg, osteomyelitis).

Symptoms and Signs

Careful history taking, observation of the child's state of well-being, and the physical examination are fundamental to diagnosing the etiology of a fever. Table 5 indicates the sensitivity of this clinical evaluation

TABLE 2. Serious Illnesses During 996 Episodes of Acute Infectious Illness in Febrile Children <36 Months of Age*

DIAGNOSIS	NUMBER	%
Bacterial meningitis	9	0.9
Aseptic meningitis	12	1.2
Pneumonia	30	3.0
Bacteremia	10	1.0†
Focal soft-tissue infection	10	1.0
Urinary tract infection	8	0.8§
Bacterial diarrhea	1	0.1
Abnormal electrolytes, abnormal blood gas	9	0.9
Total	89	8.9

From McCarthy PL. Acute infectious illnesses in children.* **Compr Ther. *1988;14(3):52–57.*
†Some studies have noted a mean occurrence of bacteremia of approximately 4% if the fever is ≥39˚C (102.2˚F).
§In some studies, the occurrence of urinary tract infection has been as high as 5% in febrile children.

TABLE 3. Organisms Isolated From Blood in Outpatients Who Have Occult Bacteremia*

ORGANISM	NUMBER[1]	NUMBER[2]	NUMBER[3]
S pneumoniae	130	23	164
H influenzae type b	29	2	9
Neisseria meningitidis	5	0	2
Salmonella sp	0	2	7
Others	0	0	10

From McCarthy PL. Occult bacteremia in infants and young children. In: Jenson HB, Baltimore RS, eds.* **Pediatric Infectious Diseases: Principles and Practice. *Norwalk, Conn: Appleton and Lange; 1995:336.*
[1]Data from Alario AJ, Nelson EW, Shapiro ED. Blood cultures in the management of febrile outpatients later found to have bacteremia. **J Pediatr.** *1989;115:195–199.*
[2]Data from Jaffe DM, Fleisher GR. Temperature and total white blood cell count as indicators of bacteremia. **Pediatrics.** *1991;87:670–674.*
[3]Data from Fleisher GR, Rosenberg N, Vinci R, et al. Intramuscular versus oral antibiotic therapy for the prevention of meningitis and other bacterial sequelae in young, febrile children at risk for bacteremia. **J Pediatr.** *1994;124:504–512.*

in detecting serious illnesses, that is, the percentage of significant illnesses that are identified by those maneuvers. Most notable is the limitation of observation, history, and physical examination alone to diagnose serious illness in infants younger than 90 days of age who have fever.

The age of the child is an important item in the history because this has implications for the possible etiology (Table 6). The degree of fever is related to the occurrence of bacteremia. Previous underlying illnesses or problems (such as an immunologic deficiency) may make the child more prone to serious illness. For the infant, this would include problems in the perinatal period such as perinatal antimicrobial therapy, being hospitalized longer than the mother, or prematurity. It is important to ask about ill contacts, such as family members who may have similar illnesses, and to be aware of the types of infectious agents that are circulating in the community. For infants and younger children, the parents or caretakers need to provide two types of information: how the child has been acting, such as playing, smiling, and eating; and specific symptoms that might indicate the etiology of the illnesses (eg, a high-pitched cry may indicate CNS disease or prolonged fever and significant abdominal pain may indicate inflammatory bowel disease). Finally, in children who have FUO it is important to document that fever is, in fact, present. Studies have demonstrated that up to 20% of patients who have purported FUO have no fever. This is usually due to incorrect temperature taking or to fabrication of temperature data.

While taking the history and performing the physical examination, it is important to observe not only any specific evidence of disease, such as increased work of breathing with nasal flaring, intercostal retractions, and grunting, but also the child's state of well-being. This often is assessed through interaction with the child. Although the efficacy of observation in children who have prolonged FUO has not been studied formally, it is difficult to believe that such data are not vitally important for assessing these patients.

During the physical examination (Table 7), it is important to make the child as comfortable as possible to obtain optimal data. Hence, in children up to 36 months of age, significant portions of the examination (eg, the chest and cardiac areas) may be performed with the child seated on a parent's lap. Keeping in mind potential serious illnesses, less noxious portions of the examination are undertaken initially

TABLE 4. Etiology of FUO in 100 Children

PATIENTS <6 Y			PATIENTS ≥6 Y		
Infectious disease		34	Infectious disease		18
Viral	14		Viral	4	
Bacterial	20		Bacterial	14	
Collagen vascular disease		4	Collagen vascular disease		16
Juvenile rheumatoid arthritis	3		Juvenile rheumatoid arthritis	7	
Henoch-Schönlein purpura	1		Systemic lupus erythematosis	3	
			Other	6	
Malignancy		4	Malignancy		2
Leukemia	3		Leukemia	1	
Sarcoma	1		Lymphosarcoma	1	
Miscellaneous		7	Miscellaneous		3
Central nervous system fever	2		Behçet syndrome	1	
Dehydration	1		Hepatitis	1	
Other	4		Ruptured appendix	1	
Undiagnosed		3	Undiagnosed		9
Total		52	Total		48

From McCarthy PL. Fever of unknown origin. In: Jenson HB, Baltimore RS, eds.* Pediatric Infectious Diseases: Principles and Practice. *Norwalk, CT: Appleton and Lange; 1995:342.

TABLE 5. Sensitivity of Observation, History, and Physical Examination in Detecting Serious Illnesses

AGE	SENSITIVITY OF CLINICAL EVALUATION
<3 mo	78%[1]
3 to 36 mo	89% to 92%[2]
Prolonged fever*	62%[3] 81%[4] 87%[5]

[1]Based on the author's review of five studies published from 1981 to 1985 encompassing 1,251 patients.
[2]From McCarthy PL, Sharpe MR, Spiesel SZ, et al. Observation scales to identify serious illness in febrile children.* Pediatrics. *1982;70: 802–809 and McCarthy PL, Lembo RM, Fink HD, Baron MA, Cicchetti DV. Observation, history and physical examination in the diagnosis of serious illnesses in febrile children ≤24 months.* J Pediatr. *1987;110:26–30.
****For references 3–5 below, history and physical examination findings suggested the diagnosis:***
[3]Pizzo PA, Lovejoy FH Jr, Smith DH. Prolonged fever in children: review of 100 cases.* Pediatrics. *1975;55:468–473.
[4]Lohr JA, Hendley JO. Prolonged fever of unknown origin: a record of experiences with 54 childhood patients.* Clin Pediatr. *1977;16:768–773.
[5]McClung HJ. Prolonged fever of unknown origin in children.* Am J Dis Child. *1972;124: 544–550.

before proceeding to those portions that may be more upsetting to the child. Thus, the chest, cardiac, eye, extremity, and neurologic examination are performed before the abdominal examination. Finally, the ears and throat are examined. If the febrile child is fussy and uncooperative and optimal data cannot be obtained during the initial observation and physical examination, the child should be made more comfortable by feeding and/or administering an antipyretic.

It is important to note that data from certain portions of history-taking, observational assessment, and the physical examination have developmental dimensions. Diagnoses such as UTI may present with fever and few other symptoms because the infant cannot convey historical information about, for example, dysuria. Although pulmonary findings are highly accurate for detecting pneumonia in infants and children, meningeal signs are not highly sensitive in the first 12 to 16 months of life (especially in the infant) for detecting meningitis. Meningitis may be present in these younger patients without causing nuchal rigidity or the Kernig or Brudzinski signs.

Laboratory Evaluation (Table 8)

For the febrile infant who is younger than 90 days of age, a full sepsis evaluation generally is indicated. This includes a complete blood count (CBC) with white blood cell (WBC) differential count, urinalysis, lumbar puncture, and cultures of cerebrospinal fluid, blood, and urine (obtained by bladder catheterization). Chest roentgenograms and stool cultures usually are obtained only on clinical indication. Although some have advocated a "modified" sepsis evaluation in this age group, its sensitivity for bacterial infections is not as great as that of the full evaluation.

For the child who is 3 to 36 months of age, decisions about obtaining a lumbar puncture and chest roentgenograms can be based on results of observation, history, and physical examination. A great deal of controversy has focused on the necessity of performing blood and urine cultures in children in this age group who have no clinical evidence of serious illnesses. In various studies, three indicators of occult bacteremia have been found: the child's appearance, the height of the fever, and the height of the WBC count (or height of the absolute neutrophil count). Some have recommended obtaining blood cultures in all children who have fevers greater than 39˚C (102.2˚F), but other recent data indicate that 40˚C (104˚F) is a more reasonable cutoff. Certainly, children who have higher grades of fever and, while not appearing seriously ill, are fussy and less consolable are candidates for blood cultures. Approximately 1 in 11 (9%) of children who have WBC counts of 15,000/mm^3 or greater with a predominance of polymorphonuclear leukocytes, absolute neutrophil counts of 10,000/mm^3 and greater, and temperatures of at least 40˚C (104˚F) will have bacteremia.

Urine cultures should be considered for children who have fever without source, such as those who have no cough or rhinorrhea. This is especially important in young females, in whom the occurrence of UTI is common. Indirect indicators of UTI are the child's appearance and the height of the WBC count. If clinical and/or screening laboratory data suggest this diagnostic possibility, a urine culture should be obtained by bladder catheterization. Urinalysis via microscopic examination may indicate an increased risk for a UTI, but urine culture is the definitive test.

For the child who has prolonged fever, it is important to ascertain that fever is, in fact, present. This may necessitate admission to the hospital for careful measurement of temperatures. If prolonged fever is docu mented, studies to investigate specific findings are warranted. For example, the child who has severe headaches should receive appropriate CNS imaging studies. If no source of fever is apparent by observation, history, and physical examination, then a CBC; urinalysis; cultures of blood, urine, and stool; and a chest radiograph should be obtained and a lumbar puncture considered. Both studies to investigate the possibility of autoimmune disease and tuberculin skin testing are appropriate. If these studies prove nondiagnostic, bone marrow examination or an upper gastrointestinal

TABLE 6.
Important Domains to Explore in History Taking in Children Who Have Fever

• Age
• Height of fever*
• Underlying illnesses (eg, immunocompromised status)
• Epidemiologic factors – Ill contacts – Community epidemics
• Caretaker's report of well-being (eg, playing, smiling, eating)
• Caretaker's report of specific symptoms (eg, high-pitched cry, abdominal pain)

For children who have prolonged fever, it is important to document that fever is, in fact, present and is not factitious.

TABLE 7.
Important Considerations in the Physical Examination of the Febrile Child

• Make the child comfortable (eg, often on the parent's lap)
• Proceed from the least to the more noxious parts of the examination (eg, from chest examination to abdominal examination to ear examination)
• Seek evidence of serious illnesses
• If necessary, repeat portions of the examination after providing comfort (eg, antipyretics)
• Be aware that selected findings have developmental dimensions (eg, meningeal signs may not be present in the child <16 mo who has meningitis)

TABLE 8. Laboratory Evaluation in Infants and Children

PATIENT AGE AND CHARACTERISTICS	RECOMMENDED EVALUATION
<3 mo	Full sepsis evaluation Stool culture and chest roentgenogram by clinical indication
3 to 36 mo Fever ≥40˚C (104˚F)	Complete blood count (CBC), white blood cell (WBC) differential Blood culture
Fever of any degree, no source on examination	Consider urine culture
Prolonged fever	
Initial evaluation	CBC, WBC differential, platelet count, erythrocyte sedimentation rate, urinalysis Blood, urine, stool cultures Chest roentgenogram Consider lumbar puncture Antinuclear antibody, rheumatoid factor, C_3 complement Tuberculin skin test with anergy controls Liver and kidney function studies
Second-stage testing	Bone marrow aspiration Upper gastrointestinal contrast study with small bowel follow-through

contrast study with small bowel follow-through may be helpful. Other imaging studies, such as gallium scan or echocardiography, have a low yield without specific clinical indication.

Management

Management of the infant who has fever is related to age. Infants 30 days of age and younger should be admitted to the hospital for intravenous antibiotics while awaiting culture results. Children ages 31 to 89 days often are admitted to the hospital for observation, but recent work has indicated that they may be followed at home if results of the screening laboratory tests (CBC with differential, microscopic examination of cerebrospinal fluid, and urinalysis) are benign, the child appears well, and no findings on history or physical examination suggest serious illness. If infants are followed as outpatients, careful observation at home must be assured by physician follow-up. Some groups have recommended using ceftriaxone in febrile infants of 31 to 89 days of age who are sent home, but this recommendation is not accepted universally.

For the acutely febrile 3- to 36-month-old child in whom a urinalysis and urine culture (obtained by bladder catheterization) have been performed, pyuria of 10 or more WBC per high-power field on unspun urine and/or organisms on Gram stain is reasonably predictive of UTI. The decision to hospitalize a child who has these findings on urinalysis depends on the child's state of well-being, ability to take fluids and antibiotics orally, and assurance of careful follow-up.

Some support the expectant use of intramuscular ceftriaxone for 48 hours in the febrile child 3 to 36 months of age while awaiting blood culture results, citing the 10% to 15% occurrence of persistent bacteremia or subsequent focal complications in children who have initial occult bacteremia. However, the efficacy of such an approach in preventing focal complications has not been demonstrated unequivocally or accepted universally. Moreover, there is concern about the emergence of resistant organisms with more widespread use of ceftriaxone.

The management of children who have prolonged fever depends on the etiology. Evaluation of the well-appearing child who has normal findings on physical examination and a normal erythrocyte sedimentation rate should concentrate initially on documentation of fever. If a persistent fever is documented, the decision to hospitalize is based on an assessment of the child's degree of illness and the likelihood of diagnostic possibilities that would require more intensive inpatient evaluation (eg, CNS tumor). Often, the evaluation of a clinically stable child can be accomplished in an outpatient setting.

Prognosis

Infants younger than 90 days of age who have serious infectious illnesses should be observed carefully for selected complications, such as bacterial meningitis. Bacteremia may progress to clinical septicemia. UTI often is associated with underlying urinary tract anomalies, suggesting the need for timely diagnostic imaging of the urinary tract. *Salmonella* enteric infections result in septicemia and meningitis more frequently in infants than in older patients. Because infants have less functional pulmonary reserve than older children, pneumonia more often leads to respiratory compromise, hypoxemia, and the need for aggressive support. Nonetheless, if early and appropriate diagnostic maneuvers are initiated, circumspect judgment about admission to the hospital and/or use of antibiotics is exercised, and careful follow-up is performed, the prognosis for febrile infants younger than 3 months of age is good.

The primary concern in children 3 to 36 months of age who have fever without a known source are focal bacterial complications, such as meningitis, from bacteremia. Decision analysis by two separate investigators estimated that blood cultures on febrile children in this age group could prevent two major infections per 1,000 patients eligible for blood cultures because in some bacteremic patients the initial posi-

tive blood culture result prompts treatment before focal complications develop. The use of antibiotics while awaiting initial blood culture results would prevent an additional one focal infection in these 1,000 patients. Thus, the gain in using antibiotics while awaiting blood culture results is small and must be weighed against issues of cost, side effects of drug use, and emergence of bacterial resistance. If complications of bacteremia do occur, approximately 50% will be persistent bacteremia and the remainder will be meningitis, pneumonia, periorbital cellulitis, septic arthritis, and other soft-tissue infections.

If the organism identified in a positive blood culture from the initial evaluation is *S pneumoniae* and the child appears well, is afebrile, and has normal findings on physical examination, repeat blood culture and outpatient administration of ceftriaxone is warranted while awaiting results of a second blood culture. If the child appears ill, continues to have fever, or develops focal complications, a full sepsis evaluation and admission to the hospital for intravenous antibiotics is warranted. If the initial blood culture yields either *H influenzae* type b or *N meningitidis*, a full sepsis evaluation and admission to the hospital for intravenous antibiotics is indicated. Some have suggested obtaining a repeat blood culture and administering ceftriaxone on an outpatient basis to children in whom an initial blood culture is positive for *H influenzae* type b and who are afebrile, well-appearing, and have normal results on physican examination, but this approach is controversial.

The prognosis for children who have prolonged fever without source depends on the etiology. Because 50% have infectious illnesses, most of which are common, the outlook generally is good.

Summary

Fever is caused by a resetting of the thermoregulatory center in the hypothalamus, most often by viral or bacterial infections. The specific etiologic diagnoses vary, depending on the child's age and height and duration of fever. Fever lasting 7 days or more is termed an FUO. When evaluating children who have fever, the most critical diagnostic maneuver is the carefully performed clinical evaluation, observation, history, and physical examination. Laboratory studies may be ordered based on the results of the clinical evaluation as well as the child's age and height and duration of the fever. Recent studies have outlined the manner in which data from the clinical evaluation and laboratory test results may be integrated to formulate an effective plan of management and follow-up.

SUGGESTED READING

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PIR QUIZ

1. Which one of the following statements about fever in children is *true*?
   A. Body temperature in infants is not influenced by environmental temperature.
   B. Febrile illnesses are more common during the winter months.
   C. Most children will have a prolonged febrile illness during the first 2 years of life.
   D. Most infants will have two febrile illnesses during the first 3 months of life.
   E. Rectal temperatures are an unreliable measurement of core temperature.

2. An 8-month-old infant has a fever of 39°C (102.2°F). His immunizations are appropriate for his age. His total white blood cell count is 18,000/mm^3. Which one of the following is *most* likely?
   A. Blood culture will reveal *Haemophilus influenzae* type b.
   B. Blood culture will reveal *Streptococcus pneumoniae.*
   C. Observation, history, and physical examination will detect a serious illness if it is present.
   D. The child has bacterial meningitis.
   E. The child has a soft-tissue infection.

3. All infants younger than 90 days of age who have fever and no localizing signs routinely should have all the following evaluations *except*:
   A. Blood culture.
   B. Careful history and physical examination.
   C. Chest radiography.
   D. Complete blood count with white blood cell differential.
   E. Urine culture obtained by bladder catheterization.

4. Which one of the following statements about children who have prolonged fever (>7 days) is *true*?
   A. A cause will not be found in most.
   B. Collagen vascular diseases are more common in children younger than 6 years of age.
   C. Kawasaki disease should be considered.
   D. Malignancies are the most common cause of this condition.
   E. They are encountered commonly in private practice settings.

5. Which one of the following findings *decreases* the risk that a 1-month-old infant has a serious infection?
   A. The fever is of abrupt onset and is 40.6°C (105.1°F).
   B. The infant has not eaten for 2 days and is lethargic.
   C. The infant cries briefly and then stops.
   D. The white blood cell count is 23,000/mm^3 with an absolute neutrophil count of 18,000/mm^3.
   E. There are no meningeal signs.

Fever

Paul L. McCarthy

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