Clinical management of fever in children younger than three years of age

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The clinical management of febrile children continues to evolve, especially in the light of vaccines against Haemophilus influenzae type B and more recently, Streptococcus pneumoniae. These vaccines have decreased the risk of serious bacterial illness in most children, allowing for a more selective approach to investigation and empirical treatment. However, children younger than three months of age still require an aggressive approach to investigation and careful follow-up. Certain laboratory criteria can allow safe management of even young infants on an outpatient basis. The present article outlines an age-based approach to investigation and management of children with fever.

Fever is an objective sign of an infection in a child. It is produced by the action of pyrogens on the thermoregulatory centre of the hypothalamus. Except in extremely young children, it is rare to see a significant systemic infection in the absence of fever.

Fever may be accompanied by signs of cardiorespiratory instability such as tachycardia, low blood pressure, poor skin perfusion and altered level of consciousness. These ‘toxic’ children do not pose a diagnostic or a therapeutic dilemma. For these cases, the clinician can order bacterial cultures from multiple sites and then provide maximal medical support and high doses of broad-spectrum parenteral antibiotics. The present article discusses the more common presentation of the febrile child who is otherwise well (not toxic). The majority of these children have benign viral illnesses, but in a small, defined percentage the fever is the first sign of a more serious infection. The question in these otherwise well children is who should we investigate and who needs treatment? What follows is a list of questions that clinicians may pose about the management of well-appearing children with fever who do not have a defined source. While we will do our best to propose evidence-based approaches, we find that frequently the final decision rests on the particular values of the clinician and the family.

WHAT CONSTITUTES A FEVER?

It is useful to define a fever based on thresholds that would require clinical action such as consideration of blood tests or medication. In children younger than three months of age, any temperature above 38°C that is measured rectally should be considered a fever. Tympanic, axillary or oral temperatures are unreliable in this age group and should be confirmed with a rectal measurement. Any properly measured temperature reading is acted on, whether measured in the clinic or at home. Any reports of fevers associated with shaking chills or rigors should potentially prompt a more aggressive approach to investigation and treatment based on adult studies and studies of children with fever and neutropenia. While no directly relevant paediatric studies exist, studies in these related populations show that the relative risk for bacteremia in patients with chills is three to 12 times that of patients without chills.

THE HISTORY AND PHYSICAL EXAMINATION

In a child with fever, the clinician searches for an explanation. If a specific viral source is found, then the situation is unlikely to be due to an occult sepsis and only management appropriate to the viral syndrome is required. Examples of specific viral syndromes include croup and viral exanthems (eg, varicella). However, the presence of upper respiratory tract infection signs such as rhinitis or cough do not appreciably diminish the risk of occult bacteremia. Similarly, in large studies, the presence or absence of otitis media does not diminish the risk of bacteremia.

For children who do not look toxic, no historical or physical examination finding is sufficiently discriminatory to reliably predict who will have bacteremia or will develop serious bacterial illnesses (SBIs).

HOW DOES AGE DETERMINE CARE?

Children who have poor perfusion, altered level of consciousness and appear very sick should be treated as having...
Some controversy lies in the management of children in this age group. According to some investigators such as the group from Philadelphia, USA (8), these infants require the same set of laboratory tests including a lumbar puncture, but if they look well and have no pathology on examination and no laboratory abnormality (Table 1), they can be treated as outpatients. These children still require follow-up every 24 h until the fever has resolved and all cultures are negative. Significant practice variation exists in determining the need for a lumbar puncture and the need for empirical treatment while waiting for the culture results (3). Recently, a comprehensive review of the literature (9) suggested that children 29 to 90 days of age at low risk can also be investigated without a lumbar puncture and be discharged with no empirical treatment and follow-up based on the results of the blood and urine tests in the emergency department (ED). It is important to note that children in the Philadelphia study did not receive antibiotics if they were considered to be at low risk (8). Also note that in their study, low-risk criteria mandated a lumbar puncture. It has also been shown that determining the need for a lumbar puncture based on peripheral white blood cell (WBC) count is unreliable (10).

Some investigators have generated recommendations specifically for children 29 to 60 days of age. Levine et al (11) looked at whether children with respiratory syncytial virus (RSV) infection needed a full septic workup. Despite an overall significant difference in the rate of SBIs between children who did not have RSV (12.5%) and those who were RSV-positive (7.0%), the latter group also had significantly higher rates of bacteremia (1.1%) and urinary tract infections (5.4%) (11). Hence, they recommended performing a lumbar puncture to rule out meningitis in this population.

### Management of three- to 36-month-old children

Even in the absence of specific signs or symptoms, fever in children in this age group can uncommonly result in SBIs. The risk can be stratified by the magnitude of the reported or measured temperature. Children with fevers lower than 39°C do not need blood tests because their risk of bacteremia is well under 1%, however, screening urine tests are generally required if the fever persists. In children whose temperatures are greater than 39°C, physicians must balance the need for invasive testing against the (low) likelihood of poor outcome (12).

### THREE- TO 36-MONTH-OLD CHILDREN: WHO SHOULD HAVE A URINE TEST?

Urinary tract infections (UTIs) affect 5% to 7% of febrile girls, 2% to 3% of uncircumcised boys younger than 24 months of age and 0.2% of circumcised boys (12). The risk of UTIs is higher in children younger than one year of age. The American Academy of Pediatrics practice parameter (13) suggests screening urine tests for girls younger than two years and boys younger than six months of age. For girls, the risk of UTI cannot be stratified by temperature because even when the temperature is less than 39°C, the risk of UTIs is between 2% and 4% (14).

In children who are not toilet-trained, a specimen should be obtained via sterile catheterization because bag specimens and dipstick tests of bag specimens are notoriously unreliable. A number of urine rapid tests have been evaluated in terms of their ability to predict positive urine cultures (Table 2) (13,15). In general, a urine dipstick showing negative leukocyte esterase and negative nitrates is sufficient to decrease the post-test probability to the point where antibiotics should not be given pending bacterial culture results. Gram stain of the urine may have an important role in the assessment of neonates (16). Positive dipstick tests should be confirmed with urine cultures obtained by catheterization.

In general, at the initial visit, pyuria is presumptively treated with an antibiotic that is effective against local

### TABLE 1

The Philadelphia criteria for low risk of serious bacterial illness in children 28 to 90 days of age

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature: &gt;38.2°C</td>
<td>1</td>
</tr>
<tr>
<td>Well appearing</td>
<td>1</td>
</tr>
<tr>
<td>Normal immunity</td>
<td>1</td>
</tr>
<tr>
<td>Nonfocal examination</td>
<td>1</td>
</tr>
<tr>
<td>White blood cell count: &lt;15×10^9/L</td>
<td>2</td>
</tr>
<tr>
<td>Band to Neutrophil ratio &lt;0.2</td>
<td>1</td>
</tr>
<tr>
<td>Urine: &lt;10 white blood cell count per high-powered field</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrospinal fluid: &lt;8 white blood cell count per high-powered field</td>
<td>1</td>
</tr>
<tr>
<td>Chest x-ray: No infiltrate</td>
<td>1</td>
</tr>
<tr>
<td>Stool: &lt;5 white blood cell count per high-powered field</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from reference 9

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strains of *E. coli*. There is increasing evidence of in vitro *E. coli* resistance to amoxicillin and trimethoprim-sulfamethoxazole, although the latter continues to provide excellent coverage in vivo (17).

When culture results are available, therapy can be tailored to the results of antibiotic sensitivity testing. Well-appearing children three months of age or older who can tolerate oral feeding can usually be treated as outpatients. However, with the introduction of *Haemophilus influenzae* type B and pneumococcal vaccines, the risk of bacteremia is lower (1% to 1.5%) (19,20). This means a risk of approximately one in 4000 to develop sequelae from meningitis, even if fever is higher than 39°C (21). It is likely that testing all febrile children may not be a good use of health care resources (22). Of interest, a recent prospective study by Trautner et al (23) reported that of 103 children presenting over a two-year period to their ED with temperatures higher than 41°C, in children without pre-existing conditions, the rate of SBI was 15.5% (13 of 84 children).

**WHO SHOULD HAVE BLOOD TESTS?**

The risk of bacteremia, especially with *Pneumococcus* species, is higher in three- to 36-month-old children compared with older children and adults. Considerable research has been performed to determine the appropriate approach to balance invasive testing with the low risk of bacteremia resulting in sepsis or meningitis. Based on an occult bacteremia rate of greater than 5%, a landmark guideline from 1993 (18) suggested measuring WBC count in all children with temperatures higher than 39°C. Antibiotic treatment was suggested if the WBC count was greater than 15×10^9/L or if the absolute band count was greater than 2×10^9/L. However, with the introduction of *Haemophilus influenzae* type B and pneumococcal vaccines, the risk of bacteremia is lower (1% to 1.5%) (19,20). This means a risk of approximately one in 4000 to develop sequelae from meningitis, even if fever is higher than 39°C (21). It is likely that testing all febrile children may not be a good use of health care resources (22). Of interest, a recent prospective study by Trautner et al (23) reported that of 103 children presenting over a two-year period to their ED with temperatures higher than 41°C, in children without pre-existing conditions, the rate of SBI was 15.5% (13 of 84 children).

**WHO SHOULD HAVE FOLLOW-UP?**

Children at high risk need follow-up within 24 h. This allows review of clinical status, review of cultures taken and a second dose of antibiotics if needed. Children at low risk may also warrant eventual follow-up to rule out conditions such as infective endocarditis, malaria, brucellosis, osteomyelitis, septic arthritis, occult sinusitis and enteritis. Fever that persists beyond five to seven days should prompt investigation including careful consideration of typical or atypical Kawasaki disease (26).

**CONCLUSIONS**

The management of fever in children depends on the knowledge of the inherent risks of SBI. For toxic-appearing children, antibiotic therapy is recommended if the WBC count is greater than 15×10^9/L (if a complete blood count is taken) (Table 3).
children, this risk is high and requires investigation, admission, broad-spectrum antibiotic coverage and intensive medical support. Well-appearing children with an apparent source of fever are treated with specific therapy according to the source. Children without a source who are younger than three months of age require investigation and either hospitalization or meticulous follow-up according to the criteria outlined above. Children without a source who are older than three months of age with fever are not as vulnerable to occult infections, but need careful assessment to decide on the extent of investigation and treatment needed.

PARENTAL ‘FEVER PHOIA’
Schmitt coined the term ‘fever phobia’ (27) over 25 years ago because fever can result in considerable anxiety in families who are fearful that its effects could be deleterious and permanent. Several Canadian surveys (28,29) demonstrate that parents worry a great deal about their febrile child. For over 500 parents surveyed by Karwowska et al (28), the main concern was that fever might directly harm their child due to seizures (68% of respondents), dehydration (76%) or brain damage (47%). Interestingly, only 29 parents (6%) listed ‘missing an infection’ or ‘not knowing the cause for the fever’ as a concern. These concerns should be explicitly addressed in addition to a separate discussion of the possibility of SBI. Goldman and Scolnik (29) had shown that parents utilize the ED due to fever phobia, and that many visits could have been avoided if the temperature would have been dealt with at home.

In one of the surveys (28), physicians were the most frequent (70% of parents) source for information on fever. Randomized controlled trials of parent educational programs in clinics and ED have shown that they can be effective in decreasing calls to paediatricians and ED visits (30). Thus, while our understanding of the determinants of fever phobia is incomplete, clinicians appear to be well placed to educate parents on how to deal with this common symptom.

REFERENCES