

Indian Academy of Pediatrics (IAP)



# STANDARD TREATMENT GUIDELINES 2022



## Management of Fever without Focus in Office Practice

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# Management of Fever without Focus in Office Practice

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## Introduction

**Fever without focus:** Fever without a source (FWS), defined as acute fever for <7 days without a clear focus of infection after a complete examination, is challenging for physicians as children often present with nonspecific symptoms and the initial clinical presentation can vary widely.<sup>1</sup>

Most infants with fever without focus (FWF) have a good prognosis, and most of the cases are self-limited.<sup>2</sup> However, between 1–30% of the patients may have some severe bacterial infection (SBI) such as urinary tract infection, bacteremia, pneumonia, or meningitis.<sup>2</sup>

## Why important?

## Risk Factors for Serious Bacterial Infection

No single risk factor can be used in isolation, but certain children are at a greater risk of SBI.

- ☑ Age <3 months<sup>3</sup>
- ☑ Those with ill appearance
- ☑ Children with comorbidities such as chronic medical conditions and intellectual disability
- ☑ Immunocompromised children

**Causes**

Although the differential diagnosis of fever is quite broad and includes both infectious and non-infectious causes, many febrile children have underlying infectious causes of fever. The etiology might vary with age and the risk of invasive bacterial infection is more common in children <3 months of age.

- ☑ Most children between 3–36 months of age, who are well-appearing and have no identifiable source of infection have a self-limited viral illness.
- ☑ Other common causes are UTI, occult bacteremia, and clinically occult pneumonia.
- ☑ Postvaccination fever is common, with a typical onset within 24 hours of immunization and duration up to 2–3 days; however, in an unwell child, fever should not be attributed to vaccination alone.
- ☑ **Urinary tract infection:** With a prevalence of about 8–10% in young children with a fever  $\geq 39^{\circ}\text{C}$  ( $102.2^{\circ}\text{F}$ ), urinary tract infection (UTI) is the most common occult bacterial infection among febrile infants and young children.<sup>4</sup> In children <2–3 years, UTI may present with nonspecific symptoms; fever may be the sole manifestation.
- ☑ **Bacteremia:** Occult bacteremia is defined as the isolation of a bacterial pathogen in a blood culture taken from an otherwise well-appearing febrile child. The risk of occult bacteremia in these patients depends upon their immunization status. The incidence of occult bacteremia in completely immunized children who have FWS is <1%.<sup>3</sup> However, the frequency of occult bacteremia in well-appearing 3–36-month-old children with temperatures  $>39^{\circ}\text{C}$  ( $102.2^{\circ}\text{F}$ ) prior to the availability of PCV7 or PCV13 and Hib conjugate vaccines was 3–11%.<sup>5</sup>
- ☑ **Pneumonia:** Most children with fever and pneumonia have some abnormality on physical examination. However, a reliable physical examination in a young child can be a challenge, and pneumonia may not be apparent.
- ☑ **Rare and uncommon causes:** Septic arthritis or osteomyelitis is often missed.

The goal of the evaluation of the young, well-appearing, febrile child without an apparent source of infection on examination is to determine the risk of a clinically occult bacterial infection and the need for further investigation and/or antibiotic therapy **Table 1**.

**Historical Findings**

- These findings suggest an occult source of infection may be subtle.
- ☑ Was there documented fever? If so, how was it documented? “Fever Phobia” has to be ruled out.
  - ☑ A response (or lack thereof) to antipyretic medications does not predict whether the underlying cause is bacterial or viral.
  - ☑ The provider should ask about the child’s functional status, including oral intake, presence of irritability or lethargy, change in activity, and associated symptoms and immunization history. Decreased walking, crawling, or movement of an extremity may indicate a deep soft tissue or bone infection. In older children, dysuria, foul-smelling urine, and frequency may point to a UTI.
  - ☑ The clinician should also identify any underlying medical condition that increases the child’s risk for serious infection such as the presence of underlying immunosuppressed state.

**Evaluation**

On careful evaluation, some children initially felt to have fever without a source may demonstrate subtle findings that suggest an infectious focus. Specific features to note include:

- ☑ Lesions in the oropharynx that may identify a recognizable viral illness, such as herpetic gingivostomatitis (anterior ulcers) or Coxsackie virus infection (pharyngeal vesicles).
- ☑ Pain with bone palpation or passive joint range of motion
- ☑ Skin findings, such as petechiae, cellulitis, or viral exanthem
- ☑ Tachypnea

**TABLE 1: NICE traffic light system for assessment of children with fever.**

	<b>Green—Low-risk</b>	<b>Amber—Intermediate</b>	<b>Red—High-risk</b>
Color	Normal color	Pallor reported by parent	Pale/mottled/blue
Activity	<ul style="list-style-type: none"> <li>☑ Responds normally to social cue</li> <li>☑ Stays awake or quickly awakes</li> <li>☑ Strong normal cry/not crying</li> </ul>	<ul style="list-style-type: none"> <li>☑ Not responding normally to social cue</li> <li>☑ Wakes only with prolonged stimulation</li> <li>☑ Decreased activity</li> </ul>	<ul style="list-style-type: none"> <li>☑ No response to social cue</li> <li>☑ Does not wake or stay roused if awoken</li> <li>☑ Weak cry or continuous cry</li> </ul>
Respiratory		<ul style="list-style-type: none"> <li>☑ Nasal flare</li> <li>☑ <i>Tachypnea</i>: Respiratory rate &gt;50/min; 6–12 months &gt;40/min; &gt;12 months SpO<sub>2</sub> ≤95% in air</li> <li>☑ Crackles in chest</li> </ul>	<ul style="list-style-type: none"> <li>☑ Grunting</li> <li>☑ <i>Tachypnea</i>: Respiratory rate &gt;60/min</li> <li>☑ Moderate-to-severe chest indrawing</li> </ul>
Circulation and hydration	<ul style="list-style-type: none"> <li>☑ Normal skin and eyes</li> <li>☑ Moist mucous membranes</li> </ul>	<ul style="list-style-type: none"> <li>☑ <i>Tachycardia</i>: Heart rate &gt;160/min; &lt;12 months &gt;150/min; 12–24 months &gt;140/min; 2–5 years CRT ≥3s</li> <li>☑ Dry mucous membrane</li> <li>☑ Poor feeding in infants</li> <li>☑ Reduced urine output</li> </ul>	Reduced skin turgor
Others	None of amber or red symptoms	<ul style="list-style-type: none"> <li>☑ Age 3–6 months; Temperature ≥39°F</li> <li>☑ Fever ≥5 days</li> <li>☑ Rigors</li> <li>☑ Swelling of a limb or joint</li> <li>☑ Non weight-bearing limb/ not using a extremity</li> </ul>	<ul style="list-style-type: none"> <li>☑ Age &lt;3 months Temperature ≥ 38°F</li> <li>☑ Non-blanching rash</li> <li>☑ Bulging fontanelles</li> <li>☑ Neck stiffness</li> <li>☑ Status epilepticus</li> <li>☑ Focal neurological signs</li> <li>☑ Focal seizures</li> </ul>

Source: NICE, National Institute for Health and Care Excellence 2019.

- ☑ **Blood investigations:** Blood tests in well children early in their febrile illness play a limited role as they have not been shown to be reliable predictors of SBI.
- ☑ An elevated total peripheral white cell count (WCC), or leukocytosis, can occur with infection but also with other conditions such as chronic inflammation, medications, and malignancy.
- ☑ A “left shift” refers to the release of immature neutrophils into the circulation and the subsequent rise in absolute neutrophil count (ANC), but this is usually delayed until approximately 24 hours after clinical infection.
- ☑ Andreola et al.<sup>7</sup> report that CRP and procalcitonin are useful markers in predicting SBI in children with fever without source and that they perform better than WCC and ANC.
- ☑ Procalcitonin is the most cost-effective strategy for the detection of SBI in infants with FWS.<sup>8</sup> However, these results should be interpreted within the clinical context of the patient and not as a single method for therapeutic decision-making.
- ☑ **Urine test:** The risk of a UTI remains substantial in some fully immunized children and supports rapid testing by urine dipstick or microscopic urinalysis and a urine culture in selected patients. In children who are not toilet-trained, urine should be collected by catheterization. Bag specimens should not be sent for culture because they are frequently contaminated. A clean-voided urine specimen is preferred in toilet-trained children.
- ☑ **Chest X-ray:** The decision to obtain a chest radiograph must be balanced against the potential harms, such as radiation exposure and cost. In a well-child, the high likelihood of benign viral illnesses producing respiratory symptoms must be considered and chest X-ray is often unnecessary. However, in an ill-appearing child where no focus can be identified, a chest X-ray is often beneficial.

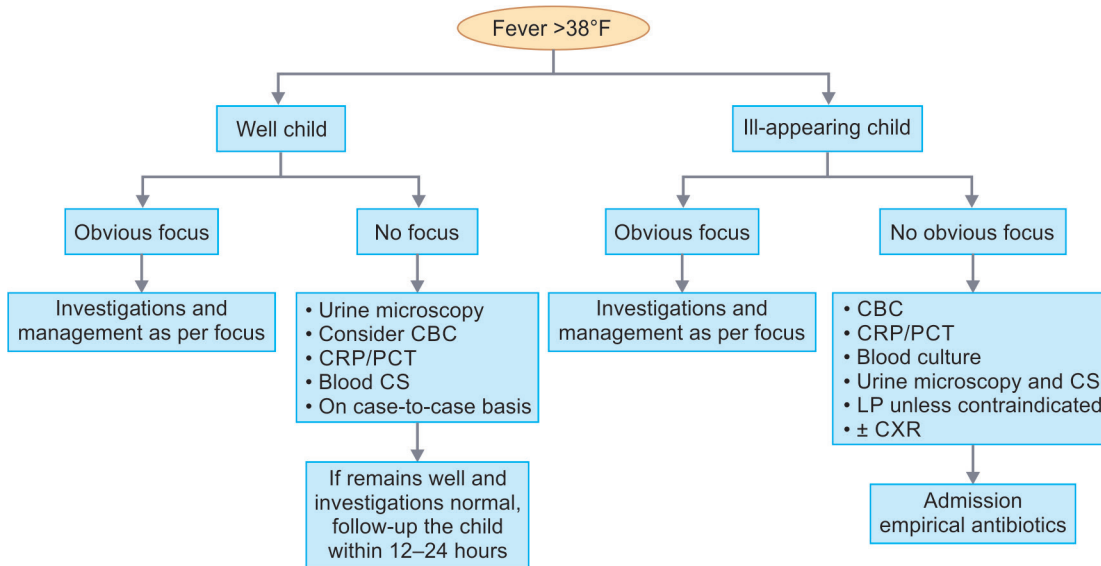
**TABLE 2:** Management based on NICE traffic light system.

<b>Red</b>	<b>Amber</b>	<b>Green</b>
<ul style="list-style-type: none"> <li>☑ CBC</li> <li>☑ Blood culture</li> <li>☑ C-reactive protein or Procalcitonin</li> </ul>	All the investigations under “red” should be organized unless considered to be unnecessary by an experienced pediatrician	Urine testing
Urine testing	Lumbar puncture should be considered for children <1 year	
Following investigation guided by clinical assessment: <ul style="list-style-type: none"> <li>☑ Lumbar puncture</li> <li>☑ Chest X-ray</li> <li>☑ Serum electrolytes</li> <li>☑ Blood gas</li> </ul>	Chest X-ray for a child with fever >39°F and WBC >20 × 10 <sup>9</sup> /L even in absence of respiratory symptoms	

(CBC: complete blood count)

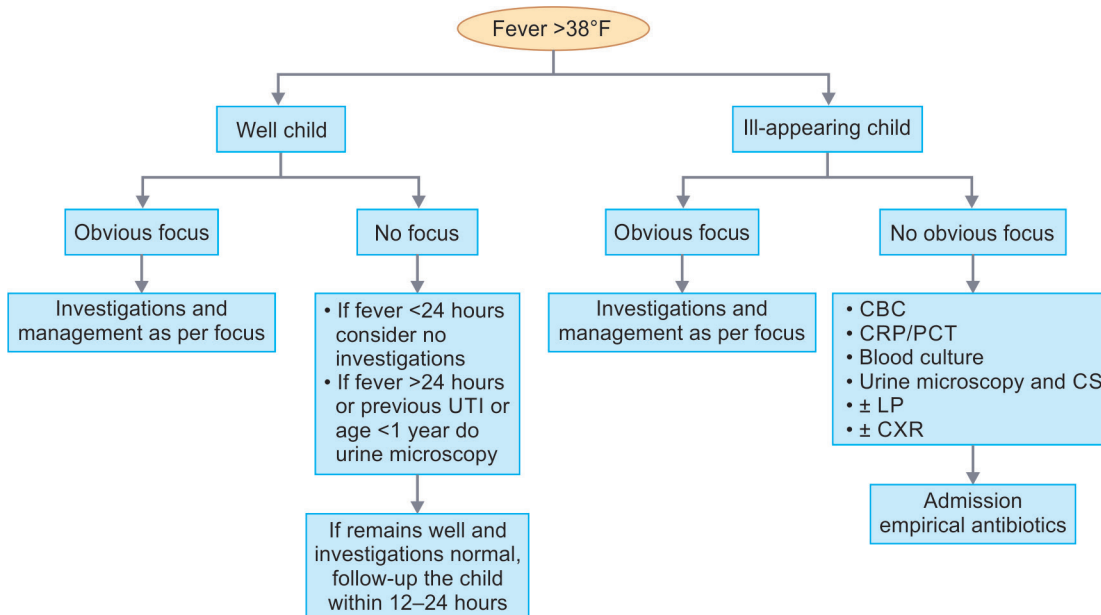
The management algorithm based on age group is shown in **Flowcharts 1 and 2:**<sup>9</sup>

**Flowchart 1:** Approach to FWF in infants 29 days–3 months corrected age.



(CBC: complete blood count; CRP: C-reactive protein; PCT: procalcitonin).

**Flowchart 2:** Approach to FWF in children >3 months corrected age.



(CBC: complete blood count; CRP: C-reactive protein; PCT: procalcitonin).

**Red Flags for Serious Illness<sup>9</sup>**

- ☑ Pale, mottled, ashen or blue skin, lips or tongue
- ☑ Ill appearance
- ☑ No response to social cues
- ☑ Respiratory rate >60 breaths per minute
- ☑ Does not wake or, if roused, does not stay awake
- ☑ Grunting
- ☑ Weak, high-pitched or continuous cry
- ☑ Moderate or severe chest indrawing
- ☑ Reduced skin turgor
- ☑ Bulging fontanelle

**Dos and Don'ts**

- ☑ Do not use the oral or rectal routes routinely to measure the body temperature in children aged 0–5 years.
- ☑ Do not use duration of fever to predict the likelihood of a serious illness.
- ☑ Response to antipyretic therapy should not be used as a clinical decision-making parameter to differentiate between a serious and non-serious illness.
- ☑ Do not prescribe oral antibiotics to children with fever without apparent source.

**Key Points**

- ☑ Presence of fever should be confirmed and documented.
- ☑ Every effort must be made to obtain a detailed history and to perform careful physical examination to identify hidden localizing clue to etiology.
- ☑ Even if febrile infant 1–3 months of age is assessed to be otherwise “well”, screening tests to rule out a serious bacterial infection are ideal beginning with urinalysis.
- ☑ In older infants and young children, a methodical clinical approach is often sufficient to guide decision making on further management.
- ☑ Counseling on further follow-up is essential until fever subsides or a definite diagnosis is made.



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