

Diagnosis and Management of Infants and Children ≤ 36 Months Old with Fever of Unknown Etiology

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A fever without localizing signs or symptoms is a common diagnostic dilemma for pediatricians, emergency physicians, and family physicians who care for infants or children ≤ 36 months old. Fever is defined as a temperature $>100.4^{\circ}\text{F}$ (38°C), and fever is usually of acute onset and present for less than 1 week. Clinical appearance is the most sensitive and specific indicator for predicting whether or not a febrile infant ≤ 36 months is at risk for serious bacterial disease.

Evaluation, Diagnosis, and Treatment

Age-group-specific criteria are helpful in the evaluation, diagnosis, and treatment of infants and children under the age of 36 months who have a fever of unknown etiology. For example, a temperature $>100.4^{\circ}\text{F}$ is significant in a 0-2 months old child. In a child who is between 2 and 36 months old, temperatures $>102.2^{\circ}\text{F}$ ($>39^{\circ}\text{C}$) may be associated with bacteremia with unknown etiology. The following are criteria specific for previously healthy neonates who are ≤ 1 month old, 1-2 months old, and 2-36 months old, respectively.

A Previously Healthy Neonate, ≤ 1 month old with temperature $>100.4^{\circ}\text{F}$

Infants who are ≤ 1 month old may acquire community pathogens. They may also manifest late-onset bacterial diseases characteristic of neonatal sepsis.

Investigation:

- a. History
- b. Physical
- c. White-blood-cell (WBC) count (look for $<5,000/\text{mm}^3$ or $>15,000/\text{mm}^3$)
- d. Blood cultures; urine cultures
- e. Chest X-ray
- f. Lumbar puncture

Diagnostic considerations (serious):

- a. Group B streptococcus
- b. *Escherichia coli*
- c. *Listeria monocytogenes*
- d. Herpes simplex virus

Treatment:

- a. Hospitalize the patient.
- b. Consider treatment with ceftriaxone or cefotaxime/ampicillin while investigations continue.

A Previously Healthy Infant, 1-2 months old with temperature >100.4 ° F

Fever and suspected sepsis among infants ≤ 2 months of age are particularly difficult to evaluate. Fever in such infants always suggests the possibility of serious bacterial disease, particularly bacteremia and bacterial meningitis. An infectious agent is identified in 70% of these infants, and the remainder are presumed to have had self-limiting, nonspecific viral infections.

Investigation:

- a. History
- b. Physical
- c. WBC count
- d. Blood cultures; urine cultures
- e. Chest X-ray
- f. Lumbar puncture

Diagnostic considerations (serious):

- a. Serious bacterial disease: 10% to 15% of cases
- b. Bacteremia: 5% of cases

Diagnostic considerations (non-serious):

Seasonal viral illness:

Respiratory Syncytial Virus (RSV; fall, winter)

Enterovirus (summer)

Treatment

- a. Hospitalize the patient if any one of the following is positive:

Ill appearing or lethargic
The child is not eating or drinking well
WBC: $<5000/\text{mm}^3$ or $>15,000/\text{mm}^3$
Exposure history

- b. If the patient is hospitalized, consider using the same antibiotics listed above (ceftriaxone or cefotaxime/ampicillin) until a diagnosis is made.
- c. A daily report from the mother is mandatory if the patient is sent home.

To determine which infants (0-2 months old) can be managed as outpatients, investigators from the University of Rochester have developed a combination of clinical assessments and laboratory tests that can be used as a comprehensive screening model (Figure 1).

Figure 1: Rochester Criteria

Physical Exam:

1. Not acutely ill.
2. No findings consistent with a soft-tissue, skeletal or ear infection.

Laboratory Evaluation:

1. WBC between 5,000-15,000
2. Absolute band count $< 1,500$
3. Urinalysis with < 10 WBC/HPF spun
4. If diarrhea, < 5 leukocytes/HPF

Also, middle ear infections have been removed as a source of serious bacterial infection by some (17).

The "Rochester Criteria" is useful in identifying a subgroup of infants (0-2 months old) that could be managed as outpatients. Other considerations to the "Rochester Criteria" include parental reliability, parental access to a telephone and transportation, distance of home to the medical facility, and possession of a thermometer.

A Previously Healthy Infant, 2-36 months old with temperature $>102.2^\circ\text{F}$

Investigation:

- a. History
- b. Physical (see Yale Observation Score)
- c. WBC count
- d. Blood cultures

- e. Chest X-ray (if indicated)
- f. Lumbar puncture (if indicated)

Table 1: The Yale Observation Scale

Clinical Observation	Normal Score Value: 1	Moderate Impairment Score Value: 3	Severe Impairment Score Value: 5
Cry Quality	Strong, normal tone; or infant is content and not crying.	Whimpering or sobbing.	Weak or high-pitched moaning.
Reaction to Parent Stimulation	Cries briefly, then stops; or, infant is content and not crying.	Cries intermittently.	Cries continuously or hardly responds.
State Variation	If awake, stays awake. If asleep, woken up quickly.	Eyes close briefly if awake; wakes if asleep and stimulated.	Falls asleep or will not rouse; awakes with prolonged stimulation.
Color	Pink	Pale extremities or acrocyanosis	Pale, cyanotic, mottled, or ashen
Hydration	Normal skin and eyes, moist mucus membranes	Normal skin and eyes, mouth slightly dry	Skin doughy or tinted, dry mucus membranes or sunken eyes
Response to social overtures	Smiles or is alert.	Smiles or alerts briefly.	No smile; face is anxious, dull, expressionless or not alert.

A patient score is derived by adding the scores of each observation, resulting in a total score of 6 to 30. Whereas only 2.7 % of patients with a score < 10 have a serious illness, 92.3% of patients with a score > 16 have a serious illness. (Adapted from McCarthy PL, Sharp MR, Spiese SC, et al. Observation scales to identify serious illness in febrile children. *Pediatrics*. 1982;70:802-809.) McCarthy et al. have shown that the Yale Observation Score has a specificity of 88% and a sensitivity of 77% for identifying serious illnesses such as bacteremia. Assessment of the scoring system's sensitivity and specificity was based largely on observations of experienced pediatricians. It has not been tested extensively in the hands of emergency medicine physicians and residents.

Diagnostic Considerations

- a. Bacteremia: 3% of cases
- b. The risk of occult bacteremia is increased by the following:

Temperature $>104^{\circ}\text{F}$ or increasing temperature
WBC count $<5000/\text{mm}^3$ or $>15,000/\text{mm}^3$
A positive exposure history
An ill-appearing (lethargic) infant or child

- c. A temperature $>105^{\circ}\text{F}$ suggests the following:

Meningitis, bacteremia, pneumonia, heat stroke, or hemorrhagic shock-encephalopathy syndrome

- d. A fever with petechiae suggests the following:

Bacteremia, meningococcus, *Haemophilus influenzae* type B, or pneumococcus

Treatment

- a. Hospitalize the child if:

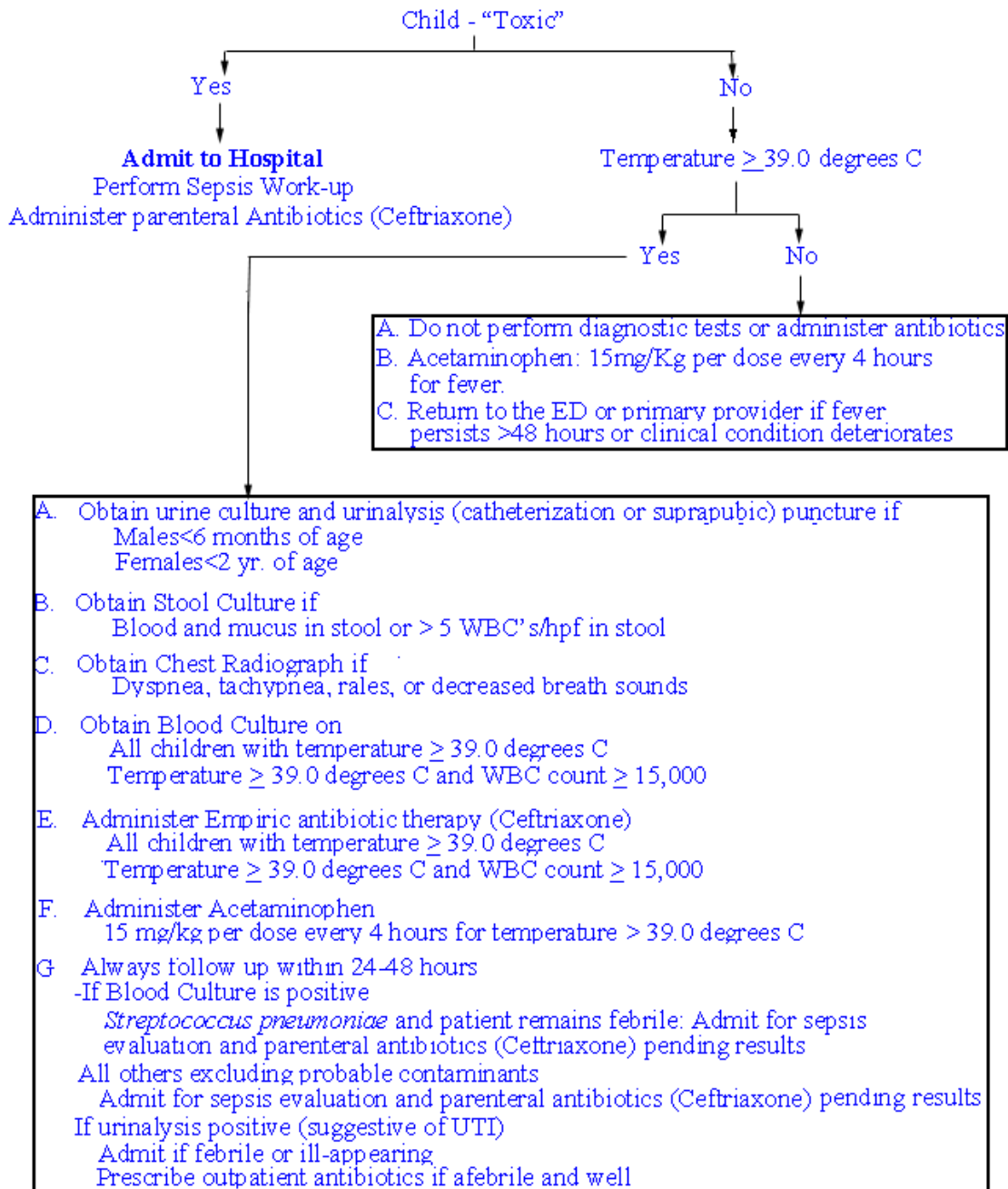
One or more of above diagnostic considerations present
Ill appearing or lethargic

- b. Also consider hospitalization if:

Child is not eating or drinking well
WBC count $<5000/\text{mm}^3$ or $>15,000/\text{mm}^3$
Temperature $>104^{\circ}\text{F}$

- c. Use the same initial antibiotics as above (ceftriaxone or cefotaxime/ampicillin) until a diagnosis made.
- d. If the child has been sent home, continue to monitor him or her daily until fever decreases to $<104^{\circ}\text{F}$ and the child is clinically better.

Management Strategy for the healthy child 3 months to 36 months, presenting with fever and no source.



Adapted from Baraff LJ, Bass JW, Fleisher GR et al. Practice Guideline for the Management of Infants and Children 0-36 months of age with fever without source. Pediatrics 1993, 92-9