

## 1.13 FEVER OF UNKNOWN ORIGIN

### Introduction

Fever is the most common presenting complaint in the pediatric outpatient and emergency room setting. In most cases, the etiology of acute fever is readily discernable. In contrast, fever of unknown origin (FUO) is typically defined as fever of 38.3° C (101° F) or greater for 14 days duration (range 8-21 days) with no apparent cause after a thorough history, physical examination, and initial laboratory evaluation. The differential diagnosis of FUO is very broad. Infection is the most common cause of prolonged fever; other major etiologic categories include malignancy, rheumatologic conditions, inflammatory bowel disease, drug fever, and miscellaneous causes. When children require hospitalization for prolonged fever with concern for FUO, pediatric hospitalists should develop a thoughtful, stepwise, and cost-effective approach to diagnosis and management.

### Knowledge

Pediatric hospitalists should be able to:

- Discuss the pathophysiologic mechanisms that result in fever.
- List the different methods available for obtaining a temperature and explain common errors associated with each.
- Differentiate FUO from disorders known to present with serial or prolonged fevers.
- Describe the differential diagnosis of FUO for children of varying chronological and developmental ages and state the relative prevalence of each etiologic category.
- Identify the common infectious causes of FUO, particularly as they differ by geographic region.
- Describe the key features of the history, including details of the fever pattern and course of illness, immunization status, travel and exposure history, and family history.
- Discuss areas of specific focus when performing the physical examination, including those related to occult infection and/or underlying single or multiple organ-system pathology, such as skin and eye findings, lymph nodes, sinuses, liver and spleen size, bone and joint exam, neurologic exam, and neurobehavioral state.
- Describe the indications for and goals of hospitalization, including the role of close observation without treatment and daily physical examination.
- List common initial laboratory tests for FUO, recognizing the utility, sensitivity, and specificity of diagnostic tests, as well as local availability and processing times.
- Summarize the diagnostic value of advanced testing (such as bone scan, bone marrow aspiration/biopsy, repeated blood cultures with fever, and others) when initial testing and observation is non-diagnostic.
- Recognize indications for subspecialty consultation, such as infectious disease, rheumatology, hematology/oncology, and others.
- Discuss the benefits, risks, and potential complications of empiric antibiotic treatment.
- Compare and contrast the mechanisms of action and modi-

fyng effect on systemic symptoms of antipyretics versus anti-inflammatory agents, noting common side effects.

- Discuss reasons for patient transfer to a referral center in cases requiring pediatric-specific services not available at the local facility.
- Explain goals for hospital discharge, including specific measures of clinical stability and a post-discharge care plan for safe transition.

### Skills

Pediatric hospitalists should be able to:

- Obtain a thorough fever history, including method obtained, duration, height, pattern, associated signs and symptoms.
- Obtain a complete medical history, including signs and symptoms, immunization status, travel history, exposure history (such as animals, tick bites, consumption of raw foods or contaminated water, sick contacts, and others), and family history.
- Perform a comprehensive physical examination, assessing for manifestations of infection and/or underlying single or multiple organ system pathology.
- Access and comprehensively review all relevant prior records.
- Perform careful reassessments daily and as needed, note changes in clinical status and test results, and respond with appropriate actions.
- Interpret basic tests and identify abnormal findings that require further testing or consultation with a subspecialist.
- Engage consultants (such as infectious disease physicians, rheumatologists, and others) efficiently and appropriately when indicated.
- Perform a cost-effective, sequential, evidence-based evaluation, avoiding unnecessary repeat testing.
- Demonstrate the ability to order laboratory studies with appropriate detail to ensure specimens are correctly collected, stored, handled, and processed.
- Determine when to continue inpatient versus outpatient diagnostic evaluation, considering factors including persistence of fever and pending test results.
- Formulate appropriate treatment plans for the presumptive or confirmed diagnosis when indicated.
- Create an effective discharge plan, including specific expectations for home observation of fever and other symptoms.
- Coordinate care with the primary care provider and subspecialists if indicated, arranging an appropriate transition plan for hospital discharge.

### Attitudes

Pediatric hospitalists should be able to:

- Recognize the importance of effective collaboration with the primary care provider and consultants regarding the evaluation and treatment conducted in and out of the hospital, along with discharge and follow up needs.
- Acknowledge the significant stress placed on the family/caregivers when the diagnosis is unclear and multiple healthcare providers are involved in care, assist the family

through periods of uncertainty, and mobilize other family support resources.

- Realize responsibility for educating patients and the family/caregivers regarding the importance of observation and the need for a thoughtful, stepwise approach to the diagnosis and potential treatment plan.

### Systems Organization and Improvement

In order to improve efficiency and quality within their organizations, pediatric hospitalists should:

- Lead, coordinate, or participate in multidisciplinary initiatives to develop and implement evidence-based clinical

guidelines to effectively use hospital resources, promote a targeted stepwise clinical approach, and improve quality of care for children with FUO.

### References

1. Chien YL, Huang FL, Huang CM, Chen PY. Clinical approach to fever of unknown origin in children. *J Microbiol Immunol Infect*. 2015;50(6):893-898. <https://doi.org/10.1016/j.jmii.2015.08.007>.
2. Tolan RW Jr. Fever of unknown origin: a diagnostic approach to this vexing problem. *Clin Pediatr (Phila)* 2010;49:207-213. <https://doi.org/0.1177/0009922809347799>.
3. Chusid MJ. Fever of Unknown Origin in Childhood. *Pediatr Clin North Am*. 2017; 64:205-230. <https://doi.org/10.1016/j.pcl.2016.08.014>.