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PEDIATRIC
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Evidence-Based Education • Practical Application

CLINICAL CHALLENGES

- **What are the most common causes of prolonged fever in children?**
- **What features of the history and examination can be used to develop a strategy for evaluating children presenting with prolonged fever?**
- **Which children with prolonged fever are at higher risk for deterioration?**

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Prior to beginning this activity, see the "CME Information" on page 2.

Management of Prolonged Pediatric Fever in the Emergency Department

Abstract

Prolonged pediatric fever is most often due to a self-limiting infectious illness, but can sometimes be a sign of much more serious disease. The care of children with prolonged fever can be challenging, since there is significant variation in the definition of prolonged pediatric fever, and evidence-based decision support tools to guide evaluation and management of children with prolonged fever are limited. This issue constructs a framework for initial emergency department evaluation and management of children with fever lasting ≥5 days and fever of unknown origin lasting ≥8 days.

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Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) identify areas in practice that require modification to be consistent with current evidence in order to improve competence and performance; (2) develop strategies to accurately diagnose and treat both common and critical ED presentations; and (3) demonstrate informed medical decision-making based on the strongest clinical evidence.

CME Objectives: Upon completion of this activity, you should be able to: (1) define *prolonged fever* in children; (2) identify the most common causes of prolonged fever in children who may present to the emergency department for evaluation; (3) develop a strategy for evaluating children presenting with prolonged fever, based on the history and examination; and (4) differentiate which children presenting with prolonged fever are at higher risk for deterioration or may require admission for further management.

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Case Presentations

CASE 1

An 18-month-old boy presents with 14 days of fever...

- The child's parents tell you he has been sick with cough, congestion, and rhinorrhea for at least 2 weeks, and he has had tactile fevers "every night."
- He is fully vaccinated, well hydrated, and playful in the examination room, with clear nasal rhinorrhea and an occasional cough.
- Your leading diagnosis is viral illness, but you wonder whether you should investigate further, due to the family's report of fever for 2 weeks...

CASE 2

A 3-year-old girl presents with 6 days of fever, red eyes, and rash...

- Her mother says she has had daily fevers to a maximum temperature of 103.8°F, with low energy, red eyes without discharge, and a rash of small red bumps on her chest and back.
- The family thought it was "just a cold" and have been treating her with antipyretics, rest, and fluids, but tell you her symptoms are not getting better.
- You consider that this could still be a viral infection, but also wonder whether you should investigate for bacterial infection or other conditions, since the girl has had a fever for more than 5 days...

CASE 3

An 8-year-old boy with autism presents for 10 days of true fever and no localizing symptoms...

- The boy's parents report that he has had fever to at least 101°F each day for 10 days and that he seems less active than usual, with poor appetite and not wanting to run and play as he normally does. The boy's parents say he speaks only a few words and does not often express pain, so they have a hard time knowing whether anything specific has been bothering him.
- The boy is febrile and tired-appearing, with a nonfocal examination.
- You consider what further workup you should pursue or if he needs further monitoring, given his difficulty communicating and his inability to clearly indicate pain.

Introduction

Fever is one of the most common reasons for pediatric emergency department (ED) visits, leading to billions of dollars in healthcare costs in the United States each year.[1,2] The majority of these patients present with self-resolving infectious illnesses. The duration of fever is an important feature in distinguishing potentially serious causes of illness, but when a fever is considered "prolonged" is not well defined, and there is wide variation in the evaluation and management of prolonged fever in children in the ED. This issue of *Pediatric Emergency Medicine Practice* constructs a framework for initial ED evaluation and management of pediatric prolonged fever. This issue does not cover fever in infants aged <60 days, for which there are specific evidence-based guidelines,[3] nor does it cover in-depth prolonged fever in high-risk populations, including patients with immune compromise, pregnancy, complex medical conditions, or rare travel-related infections.

Critical Appraisal of the Literature

A literature search was performed using PubMed, the Web of Science, and Embase, with the search terms: *fever of unknown origin*, *FUO*, *prolonged fever*, *unexplained fever*, *unknown origin fever*, AND *neonate*, *newborn*, *infant*, *child*, *teenager*, *adolescent*, *youth*, and *pediatric*. The Cochrane Database was searched for systematic reviews using the key terms *prolonged fever* and *fever of unknown origin* but did not yield any relevant reviews. The search term *pediatric fever* yielded 555 results, some of which were deemed relevant, but none of which specifically addressed duration of fever as a diagnostic indicator.

Guidelines from the American College of Emergency Physicians (ACEP) in 2016[4] and the American Academy of Family Physicians (AAFP) in 2020[5] were reviewed. These guidelines contained recommendations based on the only available weak evidence or expert consensus.

Using standard evidence-level scales for evaluation, most evidence on prolonged pediatric fever is weak. There are multiple explanations for this. First, there is a lack of standard definitions of prolonged pediatric fever, as well as variations in the definition of fever itself. Second, advances in diagnostic testing such as the widespread availability of polymerase chain reaction (PCR) testing for common infectious pathogens has made it possible to identify many patients who are likely to have self-resolving illnesses, leading to changes in both the definition and recommended

evaluation of prolonged fever. In addition, most of the existing literature does not focus on ED evaluation and management of prolonged fever, but rather on inpatient management or outpatient follow-up.

The biggest contributor to the weakness of evidence may be that fever, including prolonged fever, has many heterogeneous causes, and the appropriate evaluation and treatment of prolonged fever must consider factors that include patient demographics, personal and family medical history, history of the current illness, physical examination findings, and travel and environmental exposures, among others. There is no one-size-fits-all approach to prolonged pediatric fever. This issue will give evidence-based recommendations wherever possible, and will note when evidence is consensus-based.

Etiology and Pathophysiology

Fever is a common complaint in children and, in most cases, it is due to self-limited viral infections or, less often, common bacterial infections that may or may not require antibiotic treatment.[6] Fever as a response to infection or inflammation is the result of a complex cascade of thermoregulatory signaling molecules (sometimes called *pyrogens*) acting on the hypothalamus, which regulates body temperature.[7]

Normal human body temperature is usually considered to be 37°C, but individual median temperature may vary by up to 1°C in healthy individuals, and is affected by many variables. Children, especially those aged <1 year, have higher metabolic rates at baseline, and therefore, have a slightly higher range of normal body temperatures. There is also a circadian rhythm to body temperature, with the peak typically occurring between 5:00 PM and 7:00 PM.[8]

The gold-standard method of measuring core body temperature in children is by rectal thermometer, with a meta-analysis suggesting that peripheral measurements including oral (sublingual), axillary, temporal artery, and tympanic thermometers can vary from rectal temperature by >0.5°C (limits of agreement from -1.49°C to 0.43°C) in febrile children.[9] Tactile temperature (when a caregiver assesses for fever by placing a hand on the patient's forehead or body) has been found to have sensitivity ranging from 71% to 89% and specificity <55%.[10,11] Subjective fever, in which patients themselves report feeling hot, chilled, or both, has been less well studied, though shaking chills have been reported to have a specificity of 87% in predicting bacteremia in adult patients.[12] There is no evidence comparing the risk for serious outcomes with prolonged fever in children with fevers measured using these different methods. We therefore recommend that clinicians consider a prolonged fever to carry the same risk, regardless of measurement method, including subjective or tactile fevers.

Relevant definitions of fever include:

- *Fever* is typically defined as a core body temperature of ≥38°C (≥100.4°F).
- *Fever without a source* is fever of any duration with no identifiable etiology.
- *Prolonged fever* usually refers to fever for 5 days or more with or without a source.[8] This issue uses this 5-day definition.
- *Fever of unknown origin* (FUO) does not have a single agreed-upon definition. Historically, the definition of FUO for both adults and children was a fever, without a source, lasting at least 3 weeks,[13,14] but this time frame has decreased to ≥8 days,[8,15] due in part to the increasing availability of more rapid diagnostic tools such as PCR.[16] In this issue, fever without a clear source (eg, with only mild or vague symptoms) for ≥8 days is also considered to be an FUO.
- *Pseudo-FUO* is a term used to describe successive benign, self-limited infections with fever that patients or families perceive as 1 prolonged episode of fever.[8]
- *Tactile fever* describes a caregiver's assessment of fever by placing a hand on the patient's forehead or body.[10]
- *Subjective fever* describes when the patient reports feeling hot, chilled, or both.[12]

Differential Diagnosis

The differential diagnosis for prolonged fever is broad. Infectious etiologies are most common, though reported frequencies have varied over time from as low as 20% to as high as 50% of cases.[17-21] The general categories of pathology responsible for most of the remaining cases include oncologic, inflammatory/autoimmune, and idiopathic conditions.[17,18] It is likely that as diagnostic technologies have improved, more children are diagnosed with a specific condition earlier in their course of illness. A thorough history and physical examination can narrow down the differential greatly, taking care to determine additional risk factors for less common diagnoses, such as exposures and travel history.

When formulating a differential diagnosis for prolonged fever, it is also important to consider diagnoses specific to pediatric patients. After 5 days of fever, clinicians should consider Kawasaki disease, a vasculitis associated with widespread inflammation that can lead to coronary artery aneurysms, which permanently increase a patient's risk for cardiovascular disease and death.[22] Certain infections are seen more commonly in children, such as retropharyngeal abscess.[23] Other conditions may have a different presentation than in adults, such as urinary tract infections, which often present with fever as the only sign of illness in infants and young toddlers.[24] Septic joints, most commonly in the hip or knee, may cause

a young child to stop crawling or walking but can be very difficult to localize.[25]

It is helpful to break down the differential into the general categories of pathophysiology most associated with prolonged fever. **Table 1** provides examples of potential sources of prolonged fever in children that may not be apparent from the initial history and physical examination.

Prehospital Care

Families or referring clinicians in the community may use emergency medical services (EMS) to provide transportation or initial stabilization for children with prolonged fever, particularly in cases in which the child may be more severely ill. EMS personnel should take care to wear the appropriate personal protective equipment based on the risk for certain infections and mode of transmission (eg, airborne precautions for tuberculosis, contact for diarrheal disease) and reduce the number of personnel having contact with patients suspected of easily transmissible or rare infections.

Prehospital clinicians should focus on the ABCs (airway, breathing, circulation) and consider antipyretics for the febrile state, depending on the degree of discomfort, with avoidance of rectal medications for any patient with suspected neutropenia. Oxygen or respiratory support should be considered for children with signs of respiratory distress, hypoxia, altered mental status, or shock (compensated or uncompensated). It is rare that antimicrobials or other targeted treatments would be administered in the field before further workup, except in the case of patients undergoing interfacility transport.

Emergency Department Evaluation

Initial Evaluation

Initial ED evaluation of patients with prolonged fever should focus on rapid identification and treatment of unstable patients, including their ABCs, obtaining intravenous (IV) access, respiratory support, and empiric administration of IV crystalloid fluid boluses, antibiotics, and vasopressors for patients with signs of shock.

Table 1. Differential Diagnosis of Prolonged Fever Without Obvious Source in Children

Category	Examples	

Bacterial infection	• Head and neck
	  ○ Sinusitis +/- extension (eg, Pott puffy tumor)
	  ○ Dental infection
	• Chest
	  ○ Pneumonia
	  ○ Tuberculosis (may also be extrapulmonary)
	  ○ Endocarditis
	• Abdomen
	  ○ Ruptured appendicitis
	  ○ Intra-abdominal abscess
		• Genitourinary
		  ○ Pyelonephritis
		  ○ Disseminated gonococcal disease
		• Musculoskeletal
		  ○ Osteomyelitis
		  ○ Septic joint
		  ○ Discitis
		• Bacteremia
		• Lyme disease
		• Cat scratch disease (*Bartonella henselae* infection)
		• Travel-associated infections (eg, typhoid)

Viral infection	• Adenovirus • Influenza • COVID-19 • Epstein-Barr virus • Cytomegalovirus	• Herpes simplex virus • Human immunodeficiency virus • Common upper respiratory viruses (eg, rhinovirus, parainfluenza, human metapneumovirus, coronavirus) • Travel-associated infections (eg, dengue)
Parasitic infection	• Malaria • Toxoplasmosis • Cryptosporidiosis	• Cysticercosis • Schistosomiasis • Leishmaniasis
Fungal infection	• Valley fever (*Coccidioides*) • Blastomycosis	• Histoplasmosis • Cryptococcosis
Oncologic and hematologic	• Leukemia • Lymphoma	• Solid organ tumors • Hemophagocytic lymphohistiocytosis
Autoimmune/inflammatory	• Kawasaki disease • Systemic lupus erythematosus	• Juvenile idiopathic arthritis • Inflammatory bowel disease
Other	• Drug fever/reaction • Iatrogenic (eg, vaccine reaction) • Retained foreign body (eg, sinus, lung) • Genetic syndrome (eg, familial Mediterranean fever syndrome)	• Dysautonomia (eg, after traumatic brain injury, stroke) • Endocrine causes (eg, hyperthyroidism, diabetes insipidus, Addison disease) • Factitious

The following steps describe the evaluation of stable patients with prolonged fever:

- Confirm the onset date, method of measurement, and that a daily fever has been present.
- Obtain a complete history and review of systems.
- Perform a head-to-toe physical examination.
- Consider signs, symptoms, and risk factors for common bacterial infections including urinary tract infection; pneumonia; or bone, joint, or soft tissue infection.
- For patients with fever for ≥5 days, consider Kawasaki disease. **(See the Clinical Pathway for Management of Fever ≥5 Days, page 21.)**
- For patients with fever for ≥8 days, perform the evaluation steps as noted, plus the following: obtain additional history (if not yet gathered), including past medical and surgical history, medication history, travel history, exposures (eg, animals, insects, diet, sexual history, illicit drug use), sick contacts, and oncologic risk factors.

History

For stable patients, evaluation of prolonged fever should begin with a thorough history, starting with confirmation of a true prolonged fever. Ask whether fever has been measured with a thermometer or is tactile (by caregiver) or subjective (by patient), and the height of any measured fevers. Confirm that the patient has been experiencing a daily fever of at least 38°C, and ask the date of fever onset to calculate the number of consecutive days of fever. This will help to distinguish a true FUO from a pseudo-FUO.

Perform a review of systems to elicit any potential localizing symptoms that may point to the etiology of fever, such as congestion, cough, and pharyngitis suggestive of a viral upper respiratory infection or respiratory distress; otalgia suggestive of otitis media; or dysuria suggestive of a urinary tract infection. Ask about red-flag symptoms (also commonly referred to as *B-symptoms*) including weight loss, night sweats, and bone or joint pains that can point to a neoplastic etiology of prolonged fever.

Criteria for Kawasaki Disease

Kawasaki disease is an important diagnosis to consider in any pediatric patient with ≥5 days of fever. "Typical" or "classic" Kawasaki disease is diagnosed after at least 4 days of fever when ≥4 clinical criteria are present. Incomplete Kawasaki disease can be diagnosed after ≥5 days of fever when only 2 or 3 clinical criteria are present, and specific, additional laboratory criteria are met.[22] (See the "Laboratory Studies" section on page 8.) A mnemonic sometimes used for the clinical criteria for Kawasaki disease is "CRASH and Burn:"

- **C**onjunctivitis: nonexudative and limbal sparing (a small area of white sclera visible around the iris)
- **R**ash: often maculopapular or polymorphic
- **A**denopathy: classically, unilateral cervical lymphadenopathy
- **S**trawberry tongue: tongue or other oral symptoms including lip swelling, erythema, or oropharynx hyperemia
- **H**ands and feet: erythema and edema followed by later periungual desquamation
- **Burn**: fever lasting 5 or more days

Specific Risk Factors

In addition to the patient's symptoms, it is important to gather information about their exposures, including sick contacts, history of travel within the past year (as some infections may have prolonged incubation periods),[26] contact with animals, insect bites, and dietary exposures to raw or unpasteurized foods. Ask about recent surgeries, procedures including dental surgery, and presence of indwelling devices such as central lines, intraventricular shunts, or orthopedic hardware that could be a source of local infection. Because of the risk for drug reactions and drug fevers, it is important to ask about current and recent use of medications, vitamins, and supplements, including complementary medications.[8]

Other important history questions include immunization history, since being unvaccinated or undervaccinated leaves patients susceptible to vaccine-preventable diseases. Ask older children and teens confidentially about specific high-risk behaviors and exposures including sexual activity, which increases the risk for sexually transmitted infections, and IV drug use, which increases the risk for abscess, cellulitis, infectious endocarditis, and bacteremia.[8,21] A history of incarceration or being unhoused, travel to endemic areas, or exposure to infected contacts can increase the risk for tuberculosis exposure.

Physical Examination

A complete physical examination, with special attention paid to a full-body skin and mucosal examination, is recommended, given the broad differential for these cases. A lack of specific examination findings may be reassuring for a relatively benign cause of fever; however, a subset of patients may develop findings later, so serial examinations may be necessary, depending on the results of the initial workup and the child's general appearance.[8,12]

Begin with obtaining vital signs, noting any signs of instability, and whether the child has a fever at the time of ED evaluation. Vital signs alone may provide early clues into the cause of fever, such as elevated respiratory rate and/or hypoxia in cases of pneumonia.[27] The child's general appearance should be noted: whether they are energetic and alert despite the fever versus lethargic and/or ill-appearing, especially after appropriate doses of antipyretics have been given.

Fever is typically associated with tachycardia, with an expected increase in heart rate of 10 to 15 beats

per minute for every 1°C increase in temperature.[28] Repeating vital signs after antipyretics can identify persistent tachycardia that may indicate dehydration or serious infection such as myocarditis or bacterial sepsis.[29] A thorough routine physical examination should then be performed. **Table 2, pages 8 and 9,** lists some key findings, by system, and their commonly associated etiologies.

Head, Ears, Eyes, Nose, and Throat Examination

A head, ears, eyes, nose, and throat examination should be performed, with attention paid to the presence of conjunctivitis, oral lesions, or signs of dental infection. A neck examination should include palpation for lymphadenopathy or other masses. Given the risk for leukemia, lymphoma, or other oncologic processes, patients with prolonged fever should also be examined for the presence of axillary and inguinal nodes.[40] Tenderness on sinus palpation may suggest sinusitis, though this finding alone is not very reliable.[41] The neck and submandibular areas should also be evaluated for signs of meningismus; Kernig and Brudzinki signs are late findings for meningitis.[36] Stiffness or unwillingness to extend the neck may indicate a retropharyngeal abscess.[23]

Chest Examination

Cardiac examination should include auscultation for murmurs, gallops, or rubs. Consider the addition of point-of-care ultrasound (POCUS) if any abnormalities are present or there is high concern for endocarditis, rheumatologic conditions that may cause pericardial effusion, or another cardiac source of fever, particularly in children with a history of congenital cardiac disease, surgery, or valve replacement.[42] Faint or muffled heart sounds may suggest pericardial effusion. Note any sternotomy scars or signs of instrumentation. A careful lung examination should be performed, taking care to note any asymmetry that may indicate a focal infection or lung mass, although a meta-analysis in adult patients demonstrated that lung auscultation has poor inter-rater reliability.[43] Signs of increased work of breathing (eg, retractions) and tachypnea may be more reliable than auscultatory findings for the diagnosis of community-acquired pneumonia.[27,44]

Abdominal Examination

Careful palpation of the abdomen should be performed, including both the right and left upper quadrants, to assess for abdominal masses or hepatomegaly or splenomegaly that can result from viral infections such as Epstein-Barr virus or cytomegalovirus, or from hematologic and other malignancy. Serious intra-abdominal infection including perforated appendicitis should be suspected if the patient demonstrates signs of peritoneal inflammation, including rebound tenderness, guarding, or pain with movement (movement of the patient's bed, having patients stand and hop up and down at the bedside).[45] Directly visualize incision sites for any children with history of recent surgery.

Musculoskeletal Examination

A complete musculoskeletal examination should be performed to evaluate for bony tenderness, arthralgia or arthritis, or areas of edema or erythema. These may indicate a localized orthopedic infection such as osteomyelitis or septic arthritis or suggest a rheumatologic etiology such as juvenile idiopathic arthritis, if more diffuse. Evaluate the position of comfort, particularly at the hip joint, if there is concern for septic arthritis, as patients with a septic hip will prefer to hold the hip abducted, externally rotated, and slightly flexed.[46] Passively range all joints to note whether joint movement elicits tenderness. Evaluation for joint effusions, particularly of the hip, may also be performed with POCUS by skilled users.[47]

Skin Examination

A full skin examination should include checking for any rashes and evaluating for blanching, to identify petechiae and purpura that may indicate more serious infection or a hematologic process. Other lesions may include insect bites, wounds, areas of erythema, or skin breakdown, including areas that are often overlooked, such as the sacrum or genitourinary areas. The differential for rash is broad, so it is important to obtain a thorough examination and consider photo documentation to track progression or for facilitation of discussion with subspecialty clinicians.

Genitourinary Examination

For patients with female anatomy who are sexually active or when there is high concern for possible genitourinary infection such as disseminated gonococcal disease, a pelvic examination, including a bimanual examination, should be performed and any discharge, cervical motion tenderness, or skin lesions present noted.[39] For patients with male anatomy, perform a penile and testicular examination to evaluate for signs of scrotal infection or testicular mass.

Neurologic Examination

Perform a complete neurologic examination, looking for deficits that may be associated with infections (eg, encephalitis, meningitis, intracranial abscess), brain mass, or other inflammatory conditions (eg, post-infectious, autoimmune).

Diagnostic Studies

Given the breadth of diagnostic testing available for this broad differential, it is essential to take a tiered approach. Testing should begin by focusing on the most likely or most common etiologies, while also considering early evaluation for life-threatening or serious causes that may lead to significant morbidity and mortality if not identified and treated emergently.

Laboratory Studies

Fever of at Least 38°C for 5 Days or More

If the patient has had fever for ≥5 days and at least 2 clinical criteria for Kawasaki disease, laboratory evaluation should be performed. Clinical Kawasaki disease may be diagnosed without laboratory testing if ≥4 clinical criteria are present. Laboratory diagnostic criteria for incomplete Kawasaki disease include elevation of erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) plus 3 or more of the following additional laboratory criteria:[22,31]

- Leukocytosis ≥15,000/mcL
- Anemia for age
- Albumin ≤3 g/dL
- Platelet count ≥450,000/mcL after the seventh day of fever
- Elevated alanine aminotransferase level
- Urinalysis with ≥10 white blood cells (WBC)/high-power field

OR

- A concerning echocardiogram

Evaluation for suspected incomplete Kawasaki disease is detailed further in the **Clinical Pathway for Management of Fever ≥5 Days, page 21**.

Urinalysis and/or urine culture should be obtained for patients in higher-risk groups, including neonates and children in diapers, children who are

Table 2. Diagnoses to Consider From Physical Examination Findings in Pediatric Patients With Prolonged Fever (Continued on page 9)

Examination Findings, by Region	Conditions to Consider
General	
Unexplained weight loss, cachexia	Malignancy, tuberculosis
Generalized (cervical, axillary, inguinal) lymphadenopathy	Malignancy, HIV, Epstein-Barr virus, cytomegalovirus, toxoplasmosis
Localized lymphadenopathy, especially with history of exposure to cats	*Bartonella henselae* infection (cat scratch disease)[30]
Head, Eyes, Ears, Nose, and Throat	
Pain with extraocular movements, proptosis, +/- periorbital edema, erythema	Orbital cellulitis
Mastoid tenderness and unilateral ear proptosis	Mastoiditis
Neck stiffness and pain, especially with neck extension, muffled voice, drooling	Retropharyngeal abscess[17]
Unilateral bulging of soft palate, uvular deviation	Peritonsillar abscess
Dental pain, pain with tapping or biting tongue depressor, gum swelling and fluctuance, localized facial swelling	Dental abscess
Painful, tender lymphadenopathy or anterior neck mass	Lymphadenitis
Firm, nonmobile, nontender lymphadenopathy	Lymphoma, other malignancies
Nonexudative conjunctivitis, lip and tongue inflammation ("strawberry tongue"), cervical lymphadenopathy, truncal rash, hand and foot erythema and/or edema (periungual desquamation as a late finding)	Kawasaki disease[31]
Oral, labial, and gum ulcerations; gingival swelling	Herpes gingivostomatitis
Posterior pharyngeal ulcerations	Coxsackievirus ("herpangina") with or without hand, foot, and mouth rash
Chest and Abdomen	
Tachypnea, hypoxemia (room air saturations <96%),[32] even in the absence of crackles or asymmetric breath sounds	Pneumonia
Tachycardia disproportionate to fever or pain	Myocarditis
Upper abdominal pain	Pneumonia, cholecystitis, sexually transmitted infections (Fitz-Hugh-Curtis syndrome or perihepatitis due to chlamydia or gonorrhea)[33]
Peritoneal signs (pain with jumping or shaking the bed)	Appendicitis including ruptured, intra-abdominal abscess, spontaneous bacterial peritonitis
Suprapubic tenderness	Urinary tract infection, sexually transmitted infection
Costovertebral angle tenderness	Pyelonephritis
Hepatomegaly and/or splenomegaly	Epstein-Barr virus or cytomegalovirus infection, malaria if history of travel, malignancy[34,35]
Generalized abdominal pain with history of weight loss and/or bloody stool	Inflammatory bowel disease

nonverbal or nonambulatory, those with a history of urologic or renal disease, and those with urinary symptoms.[48] A predictive tool, such as the University of Pittsburgh UTI calculator (https://uticalc.pitt.edu/), can be used to assist with calculation of the predicted probability of a urinary tract infection in children aged 2 to 23 months. Urine culture should be sent for infants aged <1 year and any other high-risk group for whom urinalysis alone is less reliable. A catheterized urine specimen is the most reliable in diapered children. If a bagged urine sample is positive for pyuria or nitrites, a catheterized specimen should be obtained for culture. Sterile pyuria is also helpful in the diagnosis of Kawasaki disease.[31]

A nasal swab for viral panel testing may be a useful adjunct, but these tests should be used with caution, because they contain only a subset of viral pathogens and do not rule out bacterial infections or other serious pathology.

Viral panel testing can be helpful if it identifies an infection more commonly associated with a longer course of fever or symptomatology (eg, adenovirus) or if the institution's respiratory pathogen panel also includes treatable conditions such as pertussis or mycoplasma. Turnaround times may also be delayed in many settings, depending on laboratory capacity.

Table 2. Diagnoses to Consider From Physical Examination Findings in Pediatric Patients With Prolonged Fever (Continued from page 8)

Examination Findings, by Region	Conditions to Consider
Musculoskeletal	
Refusal to bear weight (includes not crawling or walking in young patients who previously did these activities)	Septic joint, osteomyelitis, discitis
Hip held in abduction, flexion, and external rotation	Septic hip joint vs transient synovitis
Bony tenderness with or without overlying signs of skin/soft tissue infection	Osteomyelitis
Joint pain, swelling, redness, warmth	Rheumatologic disease (juvenile idiopathic arthritis and others), serum sickness and serum sickness-like reaction, septic joint (usually single joint involved)
Skin	
Diffuse macular, papular, or maculopapular rash, typically sparing palms, soles, and mucosal surfaces	Viral exanthem in many common viruses, drug eruption, Kawasaki disease
Polymorphic rash of macules, papules, vesicles, and ulcers including palms, soles, intraoral, and genitourinary lesions	Coxsackievirus infection
Generalized vesicular rash	Varicella, eczema herpeticum, eczema coxsackium
Localized vesicular rash	Herpes simplex virus, impetigo
Sandpaper rash of fine papules, circumoral pallor	Scarlet fever (group A streptococcal infection)[37]
Petechiae, purpura, ecchymoses	Malignancy, hemolytic uremic syndrome, Rocky Mountain spotted fever[38]
Evanescent "rose spot" rash	Salmonella bacteremia
Erythematous rash in skin folds with blistering, desquamation	Staphylococcal scalded skin syndrome
Gottron papules (digits), erythema nodosum (anterior tibia)	Rheumatologic disease
Genitourinary	
Urethral or cervical discharge	Sexually transmitted infection
Cervical motion tenderness	Moderate sensitivity but low specificity for pelvic inflammatory disease[39]
Sharply demarcated perianal erythema	Perianal streptococcal infection
Painful ulcerations	Herpes simplex virus
Painless ulceration	Syphilis
Neurologic	
Seizure, focal neurologic deficit	Meningitis, encephalitis, brain abscess, neurocysticercosis, intracranial malignancy
Headache, neck pain especially with flexion	Meningitis[36]

Fever of at Least 38°C for 8 Days or More Without a Clear Source

For patients with fever lasting ≥8 days, testing (including CBC and blood cultures) is recommended, regardless of whether it was performed recently. CBC with differential is overall nonspecific, but specific elements may be useful in the evaluation of FUO.

- White blood cell count: Leukocytosis may indicate a bacterial infection, including appendicitis or pneumonia, and is used in some predictive algorithms (eg, Kocher criteria for septic arthritis of the hip). Leukopenia can be due to viral bone marrow suppression, but if it is associated with other cytopenias (eg, anemia, thrombocytopenia), it may indicate malignancy.
- Absolute neutrophil count: High or low absolute neutrophil count is used in some algorithms (including the Pediatric Appendicitis Score and neonatal fever guidelines) that are used for predicting bacterial infections.
- Red blood cell count: Anemia, by itself or with thrombocytosis, can indicate inflammation from Kawasaki disease or rheumatologic conditions.
- Platelet count: Thrombocytosis may indicate inflammation, while thrombocytopenia can indicate viral bone marrow suppression, malignancy, or a consumptive disorder such as hemolytic uremic syndrome.

Blood cultures should also be obtained if no focal source of fever can be identified.[22] False-positive results are common, with some studies finding that between 13% and 56% of all positive blood cultures are contaminated.[49] Care should be taken not to send this test for children when another possible source of infection is identified or likely.

Risk-Factor–Based Testing

A comprehensive metabolic panel (CMP) including liver enzymes is part of the diagnostic evaluation for incomplete Kawasaki disease.[31] It can indicate hepatitis, renal disease, or dehydration but is otherwise nonspecific. It is also a widely accessible test in most ED settings.

CRP is a nonspecific marker of inflammation and can be useful if there is concern for orthopedic infection, an inflammatory process, or an autoimmune process (eg, Kawasaki disease). CRP is relatively quick to rise and fall in response to inflammation, and thus can be useful in identification of inflammatory processes or used to trend response to therapy.[50]

ESR is another nonspecific marker of inflammation. It is slower to rise and fall in comparison to CRP, and may thus be more useful if there is concern for more chronic infectious (eg, osteomyelitis), inflammatory, autoimmune, or oncologic processes.[51]

In comparison to other inflammatory markers, procalcitonin is more specific for bacterial infection and has the highest supporting evidence for use in pediatric patients for the evaluation of the febrile neonate or children with concern for lower respiratory tract infection.[52] It is less sensitive for diagnosing or ruling out suspected sepsis.[53] A 2004 meta-analysis found that procalcitonin is more sensitive and specific than CRP for detection of bacterial infections versus inflammatory processes, and is more sensitive but not more specific than CRP for detection of bacterial versus viral infections.[54] Procalcitonin is less reliable in patients with renal disease, oncologic conditions, and recent major physiologic stressors such as trauma, severe burns, or major surgery.[55] It may be less widely available or have a slow turnaround time in the ED setting. **See Table 3, page 11** for potential uses and cautions for using procalcitonin.

Testing Recommended for Specific Circumstances

Additional autoimmune testing, including antinuclear antibodies, anti–double-stranded DNA antibody, and other specific antibody tests, should be ordered only in consultation with a rheumatologist, given the delays in turnaround time, high false-negative rate, and need for nuanced interpretation.

Lactate dehydrogenase and uric acid are recommended if there is moderate to high suspicion for malignancy or in consultation with oncology, as these tests are nonspecific, nondiagnostic, and must be interpreted within a larger evaluation. Specific tumor markers may also be considered in consultation with oncology. Serum ferritin can be elevated in cases of infection or inflammation, but is markedly high (>10,000 mcg/L) in association with hemophagocytic lymphohistiocytosis and macrophage activation syndrome,[62,63] and should be considered if these are on the differential.

Stool studies may be considered if gastrointestinal symptoms accompany prolonged fever. Fecal calprotectin is a marker of intestinal inflammation seen in inflammatory bowel disease but may be slow to result and difficult to interpret without experience. Additional stool studies, such infectious pathogen panels (eg, stool PCR, ova and parasite, viral panel), stool cultures, and *Clostridioides difficile* toxin testing should also be considered if the child is having diarrhea, bloody stool, or other chronic gastrointestinal symptoms, often in consultation with gastroenterology or the patient's primary care provider, since these tests may take days to result.

Cerebrospinal fluid (CSF) testing, including, but not limited to, culture, protein, glucose, cell counts, and specific pathogen testing (eg, herpes simplex virus, Epstein-Barr virus, other infectious panels), is recommended if there is altered mental status or any suspicion for meningitis or encephalitis. Additional specific infectious pathogen testing from CSF, serum, or other samples may be sent, including but not limited to: fungal testing, specific viral serologies (eg,

Epstein-Barr virus, cytomegalovirus, arboviruses), thick and thin smear for malaria, and Lyme titers, based on potential exposures and/or in consultation with infectious disease specialists.

Imaging Studies

Common imaging modalities can be used to evaluate for focal sources of infection or other pathology, based on symptomatology and examination. Imaging should be focused based on the history and examination, as unfocused testing is less likely to yield meaningful results.[20]

X-Ray

Common x-rays include chest x-ray to evaluate for pneumonia or chest masses (eg, lymphoma). Other x-rays of specific areas of pain can be considered, given that they are easily obtained in the ED setting and use relatively low doses of radiation, although x-rays can be normal in cases of osteomyelitis.[64] Soft tissue neck x-rays are indicated to evaluate for deep space infections such as retropharyngeal abscess, but must be obtained with the neck in extension to reduce the likelihood of false-positive interpretation.[23]

Ultrasound

Ultrasound can be used to evaluate for areas of superficial soft tissue infection, and it can be performed at the bedside by most ED clinicians. Abdominal ultrasound can be used as the initial step in evaluation for appendicitis or gallbladder disease, though this requires an experienced user.

Bedside or formal echocardiogram should be considered for children with concern for endocarditis or other cardiac etiology of infection or inflammatory process. For patients with suspected Kawasaki disease, formal echocardiogram is necessary to evaluate the coronary arteries for possible aneurysm; however, this is not necessary to make the diagnosis, and appropriate treatment should not be delayed for this testing.

Computed Tomography and Magnetic Resonance Imaging

Cross-sectional imaging is useful to evaluate for focal areas of infection or abscess. Computed tomography (CT) is faster and often more accessible to obtain in many ED settings versus magnetic resonance imaging (MRI), which may require sedation for children who are more active or less cooperative, given the longer duration of these studies. Some centers have the capacity to perform focused, quick MRI for certain conditions, though this is typically limited to pediatric hospitals. There is some overlap in the utility of CT versus MRI, but CT is generally considered more useful for infections or abscesses that are nonmusculoskeletal in nature (eg, intra-abdominal, intrathoracic, head and neck) while MRI is more sensitive to soft tissue and bony inflammation (eg, osteomyelitis, myositis, septic arthritis).

Table 3. Procalcitonin Uses and Cautions

Recommendations/Considerations:	Supporting Evidence
PCT testing is recommended: • Neonatal fever • Lower respiratory tract infection	• Meta-analyses and reviews of literature find that PCT is sensitive in detection of bacterial infections in neonates, with variable specificity.[54] • Multiple prospective trials have found PCT to have a high negative predictive value for bacterial pneumonia in pediatric patients.[56-58]
Conditions in which PCT may be low despite bacterial infection: • Localized bacterial infections • Atypical bacterial pathogens • Preceding antibiotic therapy	• A meta-analysis found that sensitivity of PCT for osteomyelitis in pediatric patients was moderate; for septic arthritis, it was low.[59] • PCT levels are known to fall after initiation of antimicrobial therapy, either due to decreased microbial burden or a direct effect of antibiotics on PCT production.[60]
Conditions in which PCT may be high (unrelated to invasive bacterial infection): • Physiologic stressors ○ Newborns during first 48-72 hr of life ○ Trauma ○ Severe burns ○ Cardiac shock ○ Major surgery ○ Pancreatitis ○ Intestinal ischemia/necrosis • Nonbacterial cytokine activation ○ Chronic kidney disease ○ Malaria and some fungal infections ○ Some vasculitis and graft vs host disease • Dysregulated PCT production ○ Paraneoplastic syndromes ○ Medullary thyroid and small-cell lung cancer ○ Treatment with agents that stimulate cytokines	• A literature review found that in pediatric trauma and burn patients, PCT levels were markedly elevated up to 72 hr after the event, regardless of the presence or absence of infection, but once initial values were determined, rising PCT levels were associated with worse outcomes.[61] • In patients with chronic kidney disease, PCT is not eliminated at the usual rate and baseline levels can be twice normal; however, elevation above baseline can still be a clinically useful indicator.[54]

Abbreviation: PCT, procalcitonin.

Use of CT must also be balanced with radiation exposure and the risk for subsequent malignancy in children and young adults.[65] Contrast should be added whenever possible, since this increases sensitivity for visualizing abscesses or inflammatory processes. MRI can also be used to evaluate for intracranial inflammation or infection, such as encephalitis.

Electroencephalogram

Electroencephalogram should be performed only in consultation with a pediatric neurologist, since it is unlikely to assist in diagnosis for patients presenting with prolonged fever.

Electrocardiogram

Other testing modalities include electrocardiogram (ECG), which may provide insight into cardiac causes or associated symptoms of certain disease manifestations. Myocarditis can cause ECG changes, such as ST-segment elevation; however, a normal ECG does not exclude this diagnosis. ECG may also assist in identifying pericarditis or structural disease that may be more highly associated with certain infections or inflammatory conditions.[66]

Treatment

Treatment depends on the most likely source of fever. **Table 4** summarizes some common treatment modalities based on the likely cause of fever.

Due to the risk for drug fever or other reactions to medication as a possible cause of prolonged fever, it is recommended to discontinue any nonessential medications, including antipyretics or other remedies for fever as a symptom.

For patients presenting with concern for sepsis and/or septic shock, timely administration of IV crystalloid fluids and empiric antibiotics is critical.[72] In contrast, for overall well-appearing patients with subacute, stable presentations, empiric treatment with antibiotics or other anti-inflammatory medications (eg, corticosteroids) is not routinely recommended, given the risk for masking symptoms and delaying diagnosis or, in the case of antibiotics, potentially leading to antibiotic resistance.[73] A large observational study demonstrated that children with fever ≥5 days are more likely to have a bacterial infection than those with fever for <5 days (8.4% vs 5.7%). However, most children with bacterial infections demonstrated clinical warning signs and/or elevated inflammatory markers, with UTI being the most common source.[74]

Table 4. General Treatment Principles for Pediatric Prolonged Fever, by Suspected or Identified Cause of Fever

Cause of Fever	Treatment Considerations
Bacterial infection	• Broad-spectrum antibiotic therapy for septic or high-risk patients (see the "Special Populations" section, page 13) • Targeted antibiotic therapy for most bacterial infections • Infectious disease consultation for drug-resistant, uncommon, or reportable diseases (eg, tuberculosis) • Other pediatric specialty consultation as indicated (eg, orthopedics for osteomyelitis or septic joint, otolaryngology for mastoiditis or head and neck abscess)
Viral infection	• Supportive care for most cases • Antiviral therapy is recommended only for specific infections in high-risk pediatric patients ○ Oseltamivir for influenza in severe, complicated, or progressive illness; hospitalized patients; or those at increased risk for complications[67] ○ Antiviral treatment of COVID-19 only for those with severe symptoms (oxygen requirement) or those who are critical (mechanical ventilation, multiorgan failure)[68] ○ Infectious disease consultation and parenteral antiviral therapy for immunocompromised patients with herpes simplex virus or varicella infection[69-71] ○ Infectious disease consultation for antiretroviral therapy in new diagnosis of HIV
Other infections (parasitic, fungal)	• Targeted therapy such as antiparasitic (eg, antimalarial) or antifungal treatment • Infectious disease consultation
Autoimmune/inflammatory	• Consultation of appropriate pediatric specialist(s) to guide further workup and to initiate treatment ○ Kawasaki disease: treatment with intravenous immunoglobulin and aspirin; infectious disease, rheumatology, and cardiology may all be involved in the care of patients with Kawasaki disease[31] ○ Systemic autoimmune diseases: rheumatology alone or with other consultants as needed ○ Inflammatory bowel disease: gastroenterology
Drug reaction	• Cessation of any unnecessary medications or suspected causes • Consultation with dermatology and/or burn unit for severe skin reactions (eg, Stevens-Johnson syndrome)
Other causes of prolonged fever (malignancy, endocrine, neurologic, or genetic disease)	• Consultation with appropriate specialist • Most periodic fever syndromes are diagnosed in consultation with a genetic specialist; may be managed by a pediatric rheumatologist • Treatment varies depending on suspected diagnosis

Special Populations

For patients who are in an immunocompromised state and/or at high risk for invasive bacterial infections, clinicians should have a lower threshold to perform diagnostic tests, treat empirically, consult specialists, and admit. For these individuals, testing is usually indicated on the first day of presentation for fever. A nonexhaustive list of such disease states and patient characteristics follows:[1]

- Neutropenia
- Immunosuppression (eg, post-transplant, chemotherapy)
- Age <60 days
- Chronic pulmonary disease (eg, oxygen or ventilator-dependent)
- Limited mobility (eg, cerebral palsy, neuromuscular disorders)
- High risk for aspiration
- End-stage renal disease/dialysis-dependent
- Urologic anomalies (including indwelling Foley catheter or use of intermittent catheterization)
- Cardiac disease
- Short bowel syndrome
- Sickle cell disease
- Presence of central venous catheter
- Pregnancy

These patients may require more intensive infectious workup even in the absence of specific clinical signs or evidence of laboratory changes, given their impaired ability to mount an immune response to certain pathogens. We recommend consulting the relevant subspecialists for the child's underlying condition and/or consultation with infectious disease to ensure adequate workup and treatment. This may require more urgent transfer to a pediatric hospital.

Controversies and Cutting Edge

Whole-Body Imaging

Targeted imaging is frequently used in the evaluation of pediatric patients with prolonged fever, such as a chest radiograph to evaluate for focal lung disease or mediastinal masses, or ultrasound of the abdomen, joint spaces, or skin and soft tissues to look for an abscess or another focus of infection. Whole-body imaging, including positron emission tomography (PET) scans, combined PET/CT scans, and whole-body MRI scans have been evaluated in a few small studies but are not widely used. These studies may be considered in critically ill children without a source of fever or in consultation with pediatric specialists. These patients may require transfer to a pediatric facility.

Positron Emission Tomography/Computed Tomography

A 2023 consensus guideline from the Society of Nuclear Medicine and Molecular Imaging included members from the Infectious Diseases Society of America and supported the use of 18F-fluorodeoxyglucose (FDG) PET/CT (FDG PET/CT), a protocol that detects foci of hypermetabolism that can indicate inflammation, infection, or neoplasm, for use in certain cases.[75] For pediatric patients, evidence was limited, but the guideline supports the use of FDG PET/CT in children with FUO requiring intensive care support, and possibly those with immunocompromise. A separate review article concluded that FDG PET/CT may be useful for localizing possible FUO lesions and guiding further management of pediatric patients after an extensive initial workup has failed to identify a diagnosis and if fevers continue.[76]

Magnetic Resonance Imaging

There is less evidence for the use of whole-body MRI than for the use of FDG PET/CT. A 2021 retrospective study demonstrated that whole-body MRI was helpful in determining appropriate treatment in only 67% of cases of prolonged fever, was 10.2 times less likely to be helpful in immunosuppressed children, and almost 5.7 times less likely to be helpful when fever was present for >3 weeks at the time of MRI.[77] Given this and the associated time and costs, whole-body MRI is rarely appropriate in the ED, but may be considered in the inpatient setting.

Biomarkers

Multiple biomarkers are used in the evaluation of prolonged pediatric fever. Some, including WBC count, ESR, CRP, and procalcitonin are frequently used in the evaluation of pediatric fevers when the goal is to ascertain risk for bacterial infection or autoimmune/inflammatory disease.[21]

Other biomarkers are not commonly used in routine evaluation of pediatric fevers, but may have utility in evaluation of FUO, particularly when used by specialists for confirmation or to rule out specific diagnoses. Ferritin may be useful in distinguishing infectious and noninfectious causes, especially when values are highly elevated. One study found that a cutoff of 10,000 mcg/L was more sensitive in detection of hemophagocytic lymphohistiocytosis, though not specific.[78] Another study cited a cutoff of 5 times the upper limit of normal as useful in diagnosing rheumatologic diseases such as juvenile idiopathic arthritis.[63] A 2022 cohort study demonstrated that serum calprotectin (also called myeloid-related protein 8/14 [MRP8/14]) was elevated in systemic juvenile idiopathic arthritis compared with other diagnoses, including infections and autoinflammatory diseases, and showed the best accuracy when compared with ferritin, interleukin-18, ESR, soluble IL-2 receptor, and procalcitonin.[79] Among other laboratory tests, D-dimer, fibrinogen, and troponin have been proposed for evaluating for multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, though

the incidence of MIS-C has decreased significantly since the initial years of the COVID-19 pandemic.[21]

Additional experimental biomarkers are being explored, including other inflammatory markers or indicators of endothelial cell damage; however, these are not yet approved by the United States Food and Drug Administration nor are they available routinely in the clinical laboratory setting.

Diagnostic Pathogen Panels

Broad PCR-based pathogen panels including those that test for gastrointestinal pathogens in stool or for meningitis or encephalitis in CSF have become more accessible due to improved turnaround times and ability to evaluate for multiple infections from a single sample. These may be considered in children with ongoing fever and suspected infectious source after initial workup is inconclusive. Consultation with infectious disease is recommended, as these tests are not commonly available in many general hospital laboratories and may require sending samples to public health or other specialized laboratory facilities.

Disposition

Pediatric patients with prolonged fever who present with severe or critical illness should be admitted to a pediatric hospital with the appropriate resources to meet their needs. These patients should be stabilized, and empiric broad-spectrum antibiotics should be given to those with high concern for possible sepsis from a bacterial infection. Admission or transfer to a pediatric facility is also indicated in the following cases:

- The patient is unstable and/or requires parenteral treatments, respiratory support, or other services unavailable in the outpatient setting.
- There is rapid or concerning progression of symptoms or a high-risk diagnosis that requires emergent treatment.
- Outpatient workup and diagnostics have not been successful, and the child has worsening symptoms.
- Access to outpatient pediatric services is limited or hindered by social circumstances preventing adequate workup.
- Admission or transport will facilitate access to more timely subspecialist evaluation, testing, or imaging.

For well-appearing patients with prolonged fever, including those who are febrile at the time of ED arrival but whose vital signs and behavior normalize within a few hours of appropriately dosed antipyretics, the decision to admit or discharge can be challenging. In general, conditions that should prompt admission include the need for specialized evaluation or treatment that cannot be completed as an outpatient, intolerance of oral fluids or medications, limited access to outpatient follow-up, or lack of understanding or agreement of the patient's caregiver to continue outpatient management.

Patients with prolonged fever—even one that is ongoing—can be discharged if they are stable, well-appearing, tolerating oral liquids and necessary medications (eg, antibiotics to treat a urinary tract infection), have access to follow-up, and a caregiver who understands and agrees with the outpatient management plan. Patients without a diagnosis can still be discharged, especially in cases in which a self-limited viral infection is the most likely diagnosis or in which outpatient management is indicated by consulting subspecialists. These patients should be instructed to follow up with a primary care clinician and given resources to follow up with an appropriate specialist, such as a pediatric infectious disease specialist, if fevers continue for an additional 1 to 2 days after ED discharge.

Summary

Prolonged fever in children is most often due to self-limiting infectious illness but can sometimes be a sign of much more serious disease. Specific testing should be directed by the patient's history, including travel, exposures, personal and family medical history, and physical examination findings. Kawasaki disease and cancer may mimic infectious disease. Common occult infections are urinary tract infections and pneumonia.

5 Things That Will Change Your Practice

1. For well-appearing children without risk factors with fever duration <8 days, laboratory workup is not always necessary.
2. Without specialist guidance, empiric antibiotics and corticosteroids are not indicated for stable pediatric patients with prolonged fever of any duration.
3. For pediatric patients with FUO (≥8 days), a thorough history, including specific risk factors and physical examination, should be used to guide initial workup.
4. For pediatric FUO without a diagnosis on initial workup, subspecialist guidance should be sought prior to ordering more than basic laboratory and imaging tests.
5. Consider outpatient follow-up for stable patients with prolonged fever who can access appropriate care.

Case Conclusions

CASE 1

For the 18-month-old boy with 14 days of fever...

You took a detailed history from his family and discovered that he had low-grade fevers for a few days, briefly improved and was fever-free for a few days, then had recurrence of fever 4 days ago, with a max temperature of 38.3°C. You diagnosed him with back-to-back viral infections and determined that no further testing was indicated at this time. You empathized with the family about the challenges of winter virus season, counseled them on supportive care measures, and discharged the patient home to follow up with his pediatrician.

CASE 2

For the 3-year-old girl with 6 days of fever, red eyes, and rash...

A rapid group A streptococcus swab of her throat was negative. You remembered that Kawasaki disease can present with prolonged fever along with conjunctivitis and rash, and found that on examination, your patient also had cervical lymphadenopathy, swelling of her fingers and toes, and an inflamed red tongue (strawberry tongue). You performed basic laboratory evaluations, which revealed leukocytosis, mild anemia, and elevated alanine aminotransferase, as well pyuria without nitrites or bacteria. You diagnosed the girl with Kawasaki disease and arranged for transfer to a pediatric center where she was treated with IVIG and aspirin, in consultation with pediatric cardiology and rheumatology.

CASE 3

For the 8-year-old boy with autism with 10 days of true fever and no localizing symptoms...

You decided to perform a basic evaluation for pediatric FUO, given the lack of focal signs and symptoms and the patient's inability to express or localize discomfort. Basic laboratory studies, including a CBC, CMP, ESR, CRP, and procalcitonin were notable for nonspecific signs of inflammation. A urinalysis, chest radiograph, and complete abdominal ultrasound were all unremarkable, and a respiratory viral swab was negative. You discussed with the family the option of continued outpatient care versus hospitalization. His parents shared that they had no vehicle and would have difficulty attending multiple follow-up appointments, and they preferred admission for ongoing monitoring and workup. You arranged for transfer to a pediatric center for observation, serial examination, and consultation with pediatric infectious disease and rheumatology to guide further diagnostic workup.

Management and disposition should be based on the duration of fever and on features of the history and physical examination.

For daily fever for ≥5 days:

- Confirm that a true fever has been present daily for ≥5 days.
- Obtain a complete history and review of systems.
- Consider signs and symptoms that may indicate Kawasaki disease.
- Consider signs, symptoms, and risk factors for common bacterial infections including urinary tract infection; pneumonia; or bone, joint, or soft tissue infection.
- Perform a thorough physical examination.
- If the child is well-appearing and there is low concern for Kawasaki disease or bacterial infection, consider discharge with close outpatient follow-up.

For daily fever for ≥8 days:

- Confirm that a true fever has been present daily for ≥8 days.
- Obtain additional history if not yet gathered, including thorough review of systems, past medical and surgical history, medication history, travel history, exposures (eg, animals, insects, diet, sexual history, illicit drug use), and sick contacts.
- Perform a thorough physical examination.
- Begin initial workup:
  - Urinalysis
  - Laboratory studies: CBC, CMP, ESR, CRP, procalcitonin, blood culture
  - Imaging: chest x-ray
  - PCR testing for common respiratory viruses: influenza, COVID-19, others if available
- Obtain additional specialist consultation (eg, rheumatology, oncology, or infectious disease) based on the history and examination findings.
- Treat identified bacterial infections with antibiotics.

Patients with prolonged fever may be appropriate for discharge if they are well-appearing and stable; hydrated; have access to prompt follow-up care, including specialists and necessary outpatient laboratory and imaging tests; and their caregiver understands and agrees to the plan. Patients who are critically ill, not tolerating oral hydration or medications, or have limited access to follow-up care should be admitted, as should those who need further diagnostic evaluation or treatment at a pediatric center.

Risk Management Pitfalls for Emergency Department Management of Pediatric Patients With Prolonged Fever

1. **"The girl looked well, but has had 7 days of low-grade fever up to 37.8°C, so I decided to get labs and a blood culture."** Patients and families often confuse temperatures below 38°C for fever, but in otherwise healthy children, this may be normal and does not generally require diagnostic workup.

2. **"His parents said he's had a cold and fever for 4 weeks straight, so I thought I should get labs and a chest x-ray."** It is common for young children to get back-to-back viral infections, so it is especially important to gather careful history about the duration of daily fevers to distinguish a truly prolonged fever from 2 or more distinct episodes of illness.

3. **"I didn't get a confidential history from my teenaged patient with prolonged fever, but that's okay, because it's probably just the flu."** Detailed history, including specific risk factors such as sexual activity, IV drug use, travel within the past 12 months, insect bites, and animal exposures can save time and guide specific diagnostic testing. A brief confidential history should be taken from all adolescent patients.

4. **"My patient wasn't fully undressed, but I was pretty sure she didn't have a rash or lymphadenopathy."** For evaluation of prolonged fever, clinicians should perform a thorough physical examination, including a complete skin examination, and check for cervical, axillary, and inguinal lymphadenopathy. It is best to have patients undress or change into a gown to ensure no important sign is missed.

5. **"The boy looked fine, but he'd had 6 days of fever, so I did labs, blood cultures, urine testing, and a chest x-ray just to be safe."** While patients are typically told to seek care after 5 days of fever, in the well-appearing child without signs or symptoms of focal bacterial infection, Kawasaki disease, or other serious illness, it is not always necessary to perform extensive evaluation. Overtesting may cause harm through unnecessary radiation and false-positive test results.

6. **"He'd had 6 days of fever with a rash, red eyes, and lymphadenopathy. A rapid strep was negative, so I thought it was probably a virus."** After 5 days of fever, it is important to evaluate patients for signs and symptoms of Kawasaki disease. This patient should have laboratory and urine testing in addition to a thorough physical examination.

7. **"We were drawing blood, so I decided to send an antinuclear antibody, ferritin, lactate dehydrogenase, and uric acid just in case they wanted them later."** Ordering tests without a specific indication increases cost and may cause harm if false-positive testing leads to additional follow-up. Clinicians should not order tests that they do not feel comfortable interpreting, except in consultation with a specialist.

8. **"My patient had 8 days of fever, and the labs and urine looked okay. I decided to give a dose of ceftriaxone just in case of bacterial infection."** Empiric use of antibiotics is not recommended for prolonged pediatric fever for otherwise healthy children with stable vital signs. Antibiotics may cause side effects, allergic reactions, and can complicate later diagnostic evaluation.

9. **"I prescribed prednisone to decrease inflammation for my patient with 10 days of fever and joint pains."** Empiric use of corticosteroids without a specific diagnosis is not recommended for prolonged pediatric fever. Corticosteroids may cause side effects and can complicate later diagnostic evaluation, particularly for rheumatologic and oncologic diseases.

10. **"She'd had 11 days of fever and was finishing a course of amoxicillin for acute otitis media. Her ears looked fine, but I didn't want to stop the medication early."** For cases of prolonged pediatric fever, patients and families should be counseled to stop nonessential medications, since reaction to medication is a potential cause of prolonged fever.

Time- and Cost-Effective Strategies

- Use the history and physical examination to evaluate risk and guide evaluation in well-appearing patients with <8 days of fever.
- Avoid overtesting for less-common etiologies of fever in patients without specific risk factors. For most patients with uncomplicated infectious illnesses, laboratory tests and imaging are not necessary or useful, even if their fever extends past 5 days.
- For those who can access appropriate outpatient follow-up care, avoid admission or transfer of well-appearing patients with prolonged fever of >5 or even 8 days. Stable patients with a plan for close follow-up (including primary care and/or specialist care) can be safely discharged with ED return precautions.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

1. Williams RM. The costs of visits to emergency departments. *N Engl J Med.* 1996;334(10):642-646. **(Retrospective analysis; 24,010 emergency department visits)**
2. Piller S, Herzog D. The burden of visits for fever at a paediatric emergency room: a retrospective study on patients presenting at the Cantons Hospital of Fribourg, a peripheral public hospital of Switzerland. *PHMT.* 2019;10:147-152. **(Retrospective analysis; 4936 visits)**
3.* Leazer RC. Evaluation and management of young febrile infants: an overview of the new AAP guideline. *Pediatr Rev.* 2023;44(3):127-138. **(Review)** **DOI: 10.1542/pir.2022-005624**
4. Mace SE, Gemme SR, Valente JH, et al. Clinical policy for well-appearing infants and children younger than 2 years of age presenting to the emergency department with fever. *Ann Emerg Med.* 2016;67(5):625-639.E13. **(Clinical practice guideline)**
5. Hamilton JL, Evans SG, Bakshi M. Management of fever in infants and young children. *Am Fam Physician.* 2020;101(12):721-729. **(Review)**
6. El-Radhi AS. Fever in common infectious diseases. In: El-Radhi AS, ed. *Clinical Manual of Fever in Children.* 2nd ed. Springer; 2018:85-140. **(Book chapter)**
7. Cimpello LB, Goldman DL, Khine H. Fever pathophysiology. *Clin Pediatr Emerg Med.* 2000;1(2):84-93. **(Review)**
8.* Antoon JW, Potisek NM, Lohr JA. Pediatric fever of unknown origin. *Pediatr Rev.* 2015;36(9):380-391. **(Review)** **DOI: 10.1542/pir.36-9-380**
9. Niven DJ, Gaudet JE, Laupland KB, et al. Accuracy of peripheral thermometers for estimating temperature: a systematic review and meta-analysis. *Ann Intern Med.* 2015;163(10):768-777. **(Meta-analysis; 75 studies; 8682 patients)**
10. Li YW, Zhou LS, Li X. Accuracy of tactile assessment of fever in children by caregivers: a systematic review and meta-analysis. *Indian Pediatr.* 2017;54(3):215-221. **(Meta-analysis; 11 studies, 3625 children)**
11. Avner JR. Acute fever. *Pediatr Rev.* 2009;30(1):5-13. **(Review)**
12. Aita T, Nakagawa H, Takahashi S, et al. Utility of shaking chills as a diagnostic sign for bacteremia in adults: a systematic review and meta-analysis. *BMC Med.* 2024;22(1):240. **(Meta-analysis; 19 studies; 14,641 patients)**
13. David A, Quinlan JD. Fever of unknown origin in adults. *Am Fam Physician.* 2022;105(2):137-143. **(Review)**
14. Seashore CJ, Lohr JA. Fever of unknown origin in children. *Pediatr Ann.* 2011;40(1):26-30. **(Review)**
15. McCarthy PL. Fever. *Pediatr Rev.* 1998;19(12):401-407. **(Review)**
16. Wright WF, Auwaerter PG. Fever and fever of unknown origin: review, recent advances, and lingering dogma. *Open Forum Infect Dis.* 2020;7(5):ofaa132. **(Review)**
17. Lohr JA, Hendley OJ. Diagnostic review: prolonged fever of unknown origin: a record of experiences with 54 childhood patients. *Clin Pediatr* (Phila). 1977;16(9):768-773. **(Retrospective cohort study; 54 patients)**
18. McClung HJ. Prolonged fever of unknown origin in children. *Am J Dis Child.* 1972;124(4):544-550. **(Retrospective chart review; 99 patients)**
19. Pizzo PA, Lovejoy FH Jr, Smith DH. Prolonged fever in children: review of 100 cases. *Pediatrics.* 1975;55(4):468-473. **(Retrospective cohort study; 100 patients)**
20. Steele RW, Jones SM, Lowe BA, et al. Usefulness of scanning procedures for diagnosis of fever of unknown origin in children. *J Pediatr.* 1991;119(4):526-530. **(Retrospective cohort study; 109 patients)**
21.* Trapani S, Fiordelisi A, Stinco M, et al. Update on fever of unknown origin in children: focus on etiologies and clinical approach. *Children.* 2024;11(1):20. **(Review)** **DOI: 10.3390/children11010020**
22.* McCrindle BW, Rowley AH, Jane WN, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation.* 2017;135(17):e927-e999. **(Scientific statement)** **DOI: 10.1161/CIR.0000000000000484**
23. Craig FW, Schunk JE. Retropharyngeal abscess in children: clinical presentation, utility of imaging, and current management. *Pediatrics.* 2003;111(6):1394-1398. **(Retrospective chart review; 64 cases)**
24. Robinson JL, Finlay JC, Lang ME, et al. Urinary tract infections in infants and children: diagnosis and management. *Paediatr Child Health.* 2014;19(6):315-325. **(Clinical practice guideline)**
25. QingSong T, XinLing M, Xiang R, et al. Clinical indicators for distinguishing septic arthritis from paediatric transient synovitis of the hip: a systematic review and meta-analysis. *BMC Infect Dis.* 2024;24(1):1432. **(Meta-analysis; 11 studies; 1810 cases)**
26. Abdel-Haq N, Asmar BI. Fever in the returned pediatric traveler. *Glob Pediatr Health.* 2021;8:2333794X211026188. **(Review)**
27. Neuman MI, Monuteaux MC, Scully KJ, et al. Prediction of pneumonia in a pediatric emergency department. *Pediatrics.* 2011;128(2):246-253. **(Prospective cohort study; 2574 patients)**
28. Heal C, Harvey A, Brown S, et al. The association between temperature, heart rate, and respiratory rate in children aged under 16 years attending urgent and emergency care settings. *Eur J Emerg Med.* 2022;29(6):413-416. **(Prospective cohort study; 188,635 visits)**

29. Law YM, Lal AK, Chen S, et al. Diagnosis and management of myocarditis in children: a scientific statement from the American Heart Association. *Circulation.* 2021;144(6):e123-e135. **(Scientific statement)**
30. United States Centers for Disease Control and Prevention. About *Bartonella henselae*. Bartonella infection. 2024. Accessed January 1, 2026. Available at: https://www.cdc.gov/bartonella/about/about-bartonella-henselae.html **(Clinical practice guideline)**
31.* Jone P-N, Tremoulet A, Choueiter N, et al. Update on diagnosis and management of Kawasaki disease: a scientific statement from the American Heart Association. *Circulation.* 2024;150(23):e481-e500. **(Scientific statement)** **DOI: 10.1161/CIR.0000000000001295**
32. Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. *J Pediatr* (Rio J). 2020;96 Suppl 1(Suppl 1):29-38. **(Review)**
33. Khine H, Wren SB, Silver EJ, et al. Fitz-Hugh-Curtis syndrome in adolescent and young adult females: utility of a decision rule. *Am J Emerg Med.* 2021;50:183-186. **(Prospective cohort study; 106 patients)**
34. Taylor GH. Cytomegalovirus. *Am Fam Physician.* 2003;67(3):519-524. **(Review)**
35. Damania B, Kenney SC, Raab-Traub N. Epstein-Barr virus: biology and clinical disease. *Cell.* 2022;185(20):3652-3670. **(Review)**
36. Tracy A, Waterfield T. How to use clinical signs of meningitis. *Arch Dis Child Educ Pract Ed.* 2020;105(1):46-49. **(Review)**
37. Wong SS, Yuen KY. *Streptococcus pyogenes* and re-emergence of scarlet fever as a public health problem. *Emerg Microbes Infect.* 2012;1(7):e2. **(Review)**
38. Biggs HM, Behravesh CB, Bradley KK, et al. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever and other spotted fever group rickettsioses, ehrlichioses, and anaplasmosis - United States. *MMWR Recomm Rep.* 2016;65(2):1-44. **(Practice guideline)**
39. Iwata H, Sugiyama Y, Satoi Y, et al. Diagnostic accuracy of pelvic examination in pelvic inflammatory disease: a meta-analysis. *J Gen Fam Med.* 2022;23(6):384-392. **(Meta-analysis; 14 studies, 2808 participants)**
40. Jayashree M, Parameswaran N, Nallasamy K, et al. Approach to fever in children. *Indian J Microbiol.* 2024;50:100650. **(Review)**
41. Shaikh N, Hoberman A, Kearney DH, et al. Signs and symptoms that differentiate acute sinusitis from viral upper respiratory tract infection. *Pediatr Infect Dis J.* 2013;32(10):1061-1065. **(Prospective study; 258 patients)**
42. Eleyan L, Khan AA, Musollari G, et al. Infective endocarditis in paediatric population. *Eur J Pediatr.* 2021;180(10):3089-3100. **(Review)**
43. Arts L, Lim EHT, van de Ven PM, et al. The diagnostic accuracy of lung auscultation in adult patients with acute pulmonary pathologies: a meta-analysis. *Sci Rep.* 2020;10(1):7347. **(Meta-analysis; 34 studies, 14,814 patients)**
44. Florin TA, Ambroggio L, Brokamp C, et al. Reliability of examination findings in suspected community-acquired pneumonia. *Pediatrics.* 2017;140(3):e20170310. **(Prospective cohort study; 128 patients)**
45. Tzortzopoulou AK, Giamarelou P, Tsolia M, et al. The jumping up (J-Up) test: making the diagnosis of acute appendicitis easier in children. *Glob Pediatr Health.* 2019;6:2333794X19884824. **(Prospective cohort study; 407 patients)**
46. Cruz AI Jr, Anari JB, Ramirez JM, et al. Distinguishing pediatric Lyme arthritis of the hip from transient synovitis and acute bacterial septic arthritis: a systematic review and meta-analysis. *Cureus.* 2018;10(1):e2112. **(Systematic review and meta-analysis; 12 studies, 88 patients)**
47. Vieira RL, Levy JA. Bedside ultrasonography to identify hip effusions in pediatric patients. *Ann Emerg Med.* 2010;55(3):284-289. **(Prospective cohort study; 28 patients)**
48. Marsh MC, Junquera GY, Stonebrook E, et al. Urinary tract infections in children. *Pediatr Rev.* 2024;45(5):260-270. **(Review)**
49. Doern GV, Carroll KC, Diekema DJ, et al. Practical guidance for clinical microbiology laboratories: a comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. *Clin Microbiol Rev.* 2019;33(1):e00009-e00019. **(Review)**
50. Jaye DL, Waites KB. Clinical applications of C-reactive protein in pediatrics. *Pediatr Infect Dis J.* 1997;16(8):735-746. **(Review)**
51. Saadeh C. The erythrocyte sedimentation rate: old and new clinical applications. *South Med J.* 1998;91(3):220-225. **(Review)**
52. Florin TA, Ambroggio L, Brokamp C, et al. Biomarkers and disease severity in children with community-acquired pneumonia. *Pediatrics.* 2020;145(6):e20193728. **(Prospective cohort study; 477 patients)**
53. Lautz AJ, Dziorny AC, Denson AR, et al. Value of procalcitonin measurement for early evidence of severe bacterial infections in the pediatric intensive care unit. *J Pediatr.* 2016;179:74-81. **(Retrospective observational study; 646 patients)**
54. Simon L, Gauvin F, Amre DK, et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis.* 2004;39(2):206-217. **(Meta-analysis; 12 studies, 1386 patients)**
55. Manzano S, Bailey B, Girodias J-B, et al. Impact of procalcitonin on the management of children aged 1 to 36 months presenting with fever without source: a randomized controlled trial. *Am J Emerg Med.* 2010;28(6):647-653. **(Randomized controlled trial; 384 patients)**
56. Baer G, Baumann P, Buettcher M, et al. Procalcitonin guidance to reduce antibiotic treatment of lower respiratory tract infection in children and adolescents (ProPAED): a randomized controlled trial. *PLOS ONE.* 2013;8(8):e68419. **(Randomized controlled trial; 337 patients)**
57. Esposito S, Tagliabue C, Picciolli I, et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. *Respir Med.* 2011;105(12):1939-1945. **(Randomized controlled trial; 319 patients)**
58. Stockmann C, Ampofo K, Killpack J, et al. Procalcitonin accurately identifies hospitalized children with low risk of bacterial community-acquired pneumonia. *J Pediatric Infect Dis Soc.* 2018;7(1):46-53. **(Retrospective convenience sample from larger epidemiologic study; 532 patients)**
59. Zhang H-T, Li C, Huang Y-Z, et al. Meta-analysis of serum procalcitonin diagnostic test accuracy for osteomyelitis and septic arthritis in children. *J Pediatr Orthop B.* **(Meta-analysis; 4 articles, 6 studies, 654 patients)**
60. Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. *BMC Med* 2011;9:107. **(Review)**
61. Koutroulis I, Loscalzo SM, Kratimenos P, et al. Clinical applications of procalcitonin in pediatrics: an advanced biomarker for inflammation and infection-can it also be used in trauma? *Int Sch Res Notices.* 2014;2014:286493. **(Review)**
62. Allen CE, Yu X, Kozinetz CA, et al. Highly elevated ferritin levels and the diagnosis of hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer.* 2008;50(6):1227-1235. **(Retrospective cohort study; 330 patients)**
63. Taylor MD, Allada V, Moritz ML, et al. Use of C-reactive protein and ferritin biomarkers in daily pediatric practice. *Pediatr Rev.* 2020;41(4):172-183. **(Review)**
64. Kothari NA, Pelchovitz DJ, Meyer JS. Imaging of musculoskeletal infections. *Radiol Clin North Am.* 2001;39(4):653-671.

(Review)

65. Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet.* 2012;380(9840):499-505. **(Retrospective cohort study; 178,604 patients)**
66. Pompa AG, Beerman LB, Feingold B, et al. Electrocardiogram changes in pediatric patients with myocarditis. *Am J Emerg Med.* 2022;59:49-53. **(Retrospective case control; 39 patients)**
67. Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2025-2026: policy statement. *Pediatrics.* 2025;156(6):e2025073620. **(Policy statement)**
68. Willis ZI, Oliveira CR, Abzug MJ, et al. Guidance for prevention and management of COVID-19 in children and adolescents: a consensus statement from the Pediatric Infectious Diseases Society Pediatric COVID-19 Therapies Taskforce. *J Pediatric Infect Dis Soc.* 2024;13(3):159-185. **(Consensus statement)**
69. Panel on Opportunistic Infections in Children With and Exposed to HIV—A Working Group of the Office of AIDS Research Advisory Council. Guidelines for the prevention and treatment of opportunistic infections in children with and exposed to HIV. 2025. Accessed January 1, 2026. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections/whats-new **(Clinical practice guideline)**
70. Lee DH, Zuckerman RA, American Society of Transplantation Infectious Diseases Community of Practice. Herpes simplex virus infections in solid organ transplantation: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant.* 2019;33(9):e13526. **(Clinical practice guideline)**
71. Pergam SA, Limaye AP, AST Infectious Diseases Community of Practice. Varicella zoster virus in solid organ transplantation. *Am J Transplant.* 2013;13 Suppl 4(Suppl 4):138-146. **(Clinical practice guideline)**
72. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med.* 2020;21(2):e52-e106. **(Clinical practice guideline)**
73. Chien Y-L, Huang F-L, Huang C-M, et al. Clinical approach to fever of unknown origin in children. *J Microbiol Immunol Infect.* 2017;50(6):893-898. **(Prospective cohort study; 93 patients)**
74. Nijman RG, Tan CD, Hagedoorn NN, et al. Are children with prolonged fever at a higher risk for serious illness? A prospective observational study. *Arch Dis Child.* 2023;108(8):632-639. **(Prospective observational study; 35,705 patients)**
75. Wright WF, Kandiah S, Brady R, et al. Nuclear medicine imaging tools in fever of unknown origin: time for a revisit and appropriate use criteria. *Clin Infect Dis.* 2024;78(5):1148-1153. **(Review)**
76. Chamroonrat W. PET/computed tomography in the evaluation of fever of unknown origin and infectious/inflammatory disease in pediatric patients. *PET Clinics.* 2020;15(3):361-369. **(Review)**
77. Delgado J, Chauvin NA, Bedoya MA, et al. Whole-body magnetic resonance imaging in the evaluation of children with fever without a focus. *Pediatr Radiol.* 2021;51(4):605-613. **(Retrospective study; 92 patients)**
78. Otrock ZK, Hock KG, Riley SB, et al. Elevated serum ferritin is not specific for hemophagocytic lymphohistiocytosis. *Ann Hematol.* 2017;96(10):1667-1672. **(Review)**
79. Park C, Miranda-Garcia M, Berendes R, et al. MRP8/14 serum levels as diagnostic markers for systemic juvenile idiopathic arthritis in children with prolonged fever. *Rheumatology* (Oxford). 2022;61(7):3082-3092. **(Cohort study; 1110 patients)**

CME Questions

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1. A stable, well-appearing 4-year-old girl presents with 2 weeks of congestion, rhinorrhea, dry cough, and nightly fevers to a maximum temperature of 37.9°C. Recommended diagnostic evaluation for this patient includes:

a. A complete blood cell count (CBC)
b. A chest radiograph
c. Inflammatory markers including erythrocyte sedimentation rate and C-reactive protein
d. No testing is indicated

2. Pain with neck extension is most often seen in which condition?

a. Peritonsillar abscess
b. Retropharyngeal abscess
c. Mediastinal mass
d. Meningitis

3. A child with a septic hip joint infection will most often position themselves with the hip joint:

a. Flexed and adducted
b. Internally rotated
c. Elevated above the knee joint
d. Flexed and abducted

4. A 3-year-old child has had 6 days of fever to at least 38°C daily. On examination, she is found to have a maculopapular rash, conjunctivitis, and cervical lymphadenopathy. Diagnostic evaluation should include:

a. A blood culture to rule out occult bacteremia
b. CBC, comprehensive metabolic panel, inflammatory markers, and urinalysis to evaluate for incomplete Kawasaki disease
c. A fine-needle aspirate of cervical lymph nodes to rule out oncologic disease
d. No evaluation is needed, since this is not a true fever of unknown origin (FUO) of ≥8 days

5. **An 18-month-old girl with 6 days of fever to a maximum temperature of 39.4°C and no localizing symptoms should have, at minimum, what diagnostic testing?**
   a. Urinalysis
   b. Chest radiograph
   c. Complete abdominal ultrasound
   d. Inflammatory markers

6. **A 16-year-old boy with recent travel to Central America presents with 3 weeks of fever, cough, shortness of breath, and weight loss. Tuberculosis testing by his outpatient clinician was negative. Which of the following statements is TRUE?**
   a. He does not need a chest radiograph since tuberculosis testing was negative.
   b. He can be managed outpatient if the family has transportation to appointments.
   c. He should have additional laboratory evaluation and a chest radiograph today.
   d. He should have repeat tuberculosis testing in 1 week if fevers continue.

7. **A 3-year-old girl presents with prolonged fever and refusal to bear weight on her right leg. You are concerned for a bone or joint infection. What diagnostic imaging test is most sensitive for this type of infection?**
   a. Computed tomography scan
   b. Ultrasound
   c. X-ray
   d. Magnetic resonance imaging

8. **You are seeing a 10-year-old boy with a penicillin allergy with 12 days of fever to at least 38.3°C each day. A few days into the illness, he was started on cefdinir for presumed group A streptococcal pharyngitis but was not tested prior to starting treatment. In addition to considering basic laboratory testing for his prolonged fever, how should you counsel the family regarding the antibiotic?**
   a. He should complete the course of cefdinir because he most likely has strep pharyngitis.
   b. He should undergo penicillin oral challenge in your ED to confirm his allergy so that he can change to a more effective therapy.
   c. He should stop the antibiotic since it may be contributing to his fever.
   d. He should receive intravenous (IV) antibiotics since he has failed outpatient therapy.

9. **You are caring for a mildly dehydrated 5-year-old boy with 6 days of fever, rash, and lymphadenopathy. Laboratory evaluation is not consistent with Kawasaki disease. What treatment should you give in the ED before discharge home with appropriate outpatient follow-up?**
   a. IV ceftriaxone in case of occult bacteremia
   b. Oral hydration
   c. Oral dexamethasone to reduce systemic inflammation
   d. IV immune globulin in case of early incomplete Kawasaki disease

10. **A well-appearing 10-year-old boy presents with 5 days of fever, a few episodes of emesis, and diarrhea. You think this is likely a viral illness and plan to discharge him with supportive care. What additional feature of his history would prompt you to perform laboratory testing?**
    a. Intermittent abdominal pain that has resolved
    b. History of autoimmune neutropenia
    c. A rash consisting of blanching red macules and papules scattered over his trunk
    d. Recent travel to Canada to visit family

Class of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

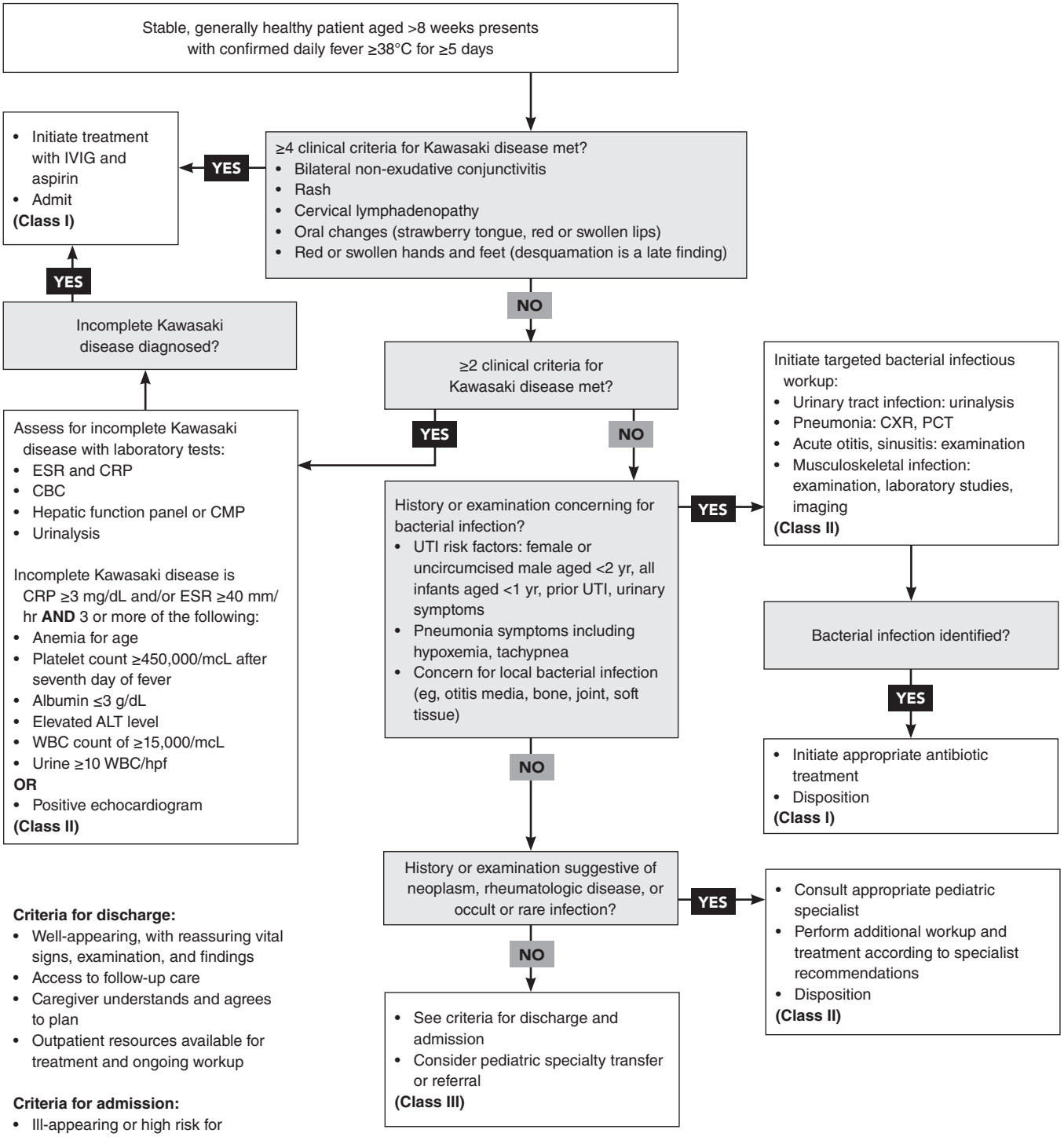
Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Clinical Pathway for Emergency Department Management of Pediatric Patients With ≥5 Days of Fever

Click or scan for interactive pathway



Criteria for discharge:

- Well-appearing, with reassuring vital signs, examination, and findings
- Access to follow-up care
- Caregiver understands and agrees to plan
- Outpatient resources available for treatment and ongoing workup

Criteria for admission:

- Ill-appearing or high risk for instability
- Limited access to follow-up care
- Caregiver does not understand/agree to plan
- Need for specialized evaluation or treatment that cannot be completed outpatient

Abbreviations: ALT, alanine aminotransferase; CBC, complete blood cell count; CMP, comprehensive metabolic panel; CRP, C-reactive protein; CXR, chest x-ray; ESR, erythrocyte sedimentation rate; hpf, high-power field; IVIG; intravenous immune globulin; PCT, procalcitonin; UTI, urinary tract infection; WBC, white blood cell.

For Class of Evidence definitions, see page 20.

Clinical Pathway for Emergency Department Management of Pediatric Patients With ≥8 Days of Fever

Click or scan for interactive pathway

Stable, generally healthy patient aged >8 weeks presents with confirmed daily fever ≥38°C for ≥8 days

Kawasaki disease diagnosed?
- ≥4 clinical criteria for Kawasaki disease

OR
- ≥2 clinical criteria plus elevated inflammatory markers and ≥3 laboratory criteria for incomplete Kawasaki disease

OR
- Infant aged <6 months with at least 7 days of fever and meets laboratory criteria for incomplete Kawasaki disease (no clinical criteria necessary)

YES
- Treat with IVIG and aspirin
- Admit

(Class I)

NO

Initiate initial infectious workup, based on suspected cause:
- Urinary tract infection: urinalysis
- Bacteremia: CBC, PCT, blood culture
- Pneumonia: CXR, PCT
- Musculoskeletal infection: examination, laboratory studies, imaging
- Viral studies: influenza, COVID-19, viral panel

(Class II)

Bacterial infection diagnosed?

YES
- Initiate appropriate antibiotic treatment
- See criteria for discharge and admission

(Class I)

NO

Concerning for drug reaction?

YES
- Stop medication
- Provide additional treatment by cause
- Disposition

(Class II)

NO

Concern for oncologic process, autoimmune disease, or occult or unusual infection?

YES
- Consult appropriate pediatric specialist
- Perform additional workup and treatment according to specialist recommendations
- Disposition

(Class II)

NO
- See criteria for discharge and admission
- Consider pediatric specialty transfer or referral

(Class III)

Criteria for discharge:
- Well-appearing, with reassuring vital signs, examination, and findings
- Access to follow-up care
- Caregiver understands and agrees to plan
- Outpatient resources available for treatment and ongoing workup

Criteria for admission:
- Ill-appearing or high risk for instability
- Limited access to follow-up care
- Caregiver does not understand/ agree to plan
- Need for specialized evaluation or treatment that cannot be completed outpatient

Abbreviations: CBC, complete blood cell count; COVID-19, coronavirus disease 2019; CXR, chest x-ray; IVIG; intravenous immune globulin; PCT, procalcitonin.

For Class of Evidence definitions, see page 20.

The *Pediatric Emergency Medicine Practice* Editorial Board

QUICK READ

Points & Pearls

FEBRUARY 2026 | VOLUME 23 | ISSUE 2

Management of Prolonged Pediatric Fever in the Emergency Department

Points

- Prolonged pediatric fever is most often due to self-limiting infectious illness but can sometimes be a sign of much more serious disease.
- The care of the child with prolonged fever should begin with confirmation of the duration of true fever.
- The gold-standard method of measuring core body temperature in children is by rectal thermometer. Peripheral measurements including oral (sublingual), axillary, temporal artery, and tympanic thermometers can vary from rectal temperature by >0.5°C (limits of agreement from -1.49°C to 0.43°C) in febrile children.[9]
- When formulating a differential diagnosis for prolonged fever, it is important to consider diagnoses specific to pediatric patients. Keep in mind that certain conditions are seen more commonly in children, and other conditions may have a different presentation than in adults.
- It is helpful to break down the differential into the general categories of pathophysiology most associated with prolonged fever **(See Table 1.)**
- If true fever has been present for ≥5 days, consider whether there are signs or symptoms of a bacterial infection or Kawasaki disease, asking about symptoms and performing a thorough examination.
- After ≥8 days of true fever, perform a basic laboratory evaluation of at least a complete blood cell count, blood culture, comprehensive metabolic panel, erythrocyte sedimentation rate, C-reactive protein, and procalcitonin. Also consider urinalysis and a chest radiograph.
- Key physical examination findings, listed by system, and commonly associated etiologies are listed in **Table 2**.
- General treatment principles for prolonged fever in pediatric patients, by suspected or identified cause of fever, are listed in **Table 4**.
- For patients with subacute, stable presentations, ensure the proper workup and evaluation have been completed before starting empiric therapy.
- It is recommended to discontinue any nonessential medications, including antipyretics.

Pearls

- Laboratory workup for children with fever lasting <8 days is not always necessary if the child is well-appearing and without risk factors.
- Empiric treatment with antibiotics or other anti-inflammatory medications (eg, corticosteroids) is not routinely recommended for stable children, given the risk of masking symptoms and delaying diagnosis, or in the case of antibiotics, potentially leading to antibiotic resistance.
- Subspecialist guidance should be sought for pediatric fever of unknown origin without a diagnosis on initial workup prior to ordering more than basic laboratory and imaging tests.
- Outpatient follow-up should be considered for stable patients with prolonged fever who can access appropriate care.

- Pediatric patients with prolonged fever who present with severe or critical illness should be admitted to a pediatric hospital with the appropriate resources to meet their needs.
- In general, conditions that should prompt admission include the need for specialized evaluation or treatment that cannot be completed as an outpatient, intolerance of oral fluids or medications, limited access to outpatient follow-up, or lack of understanding or agreement of the patient's caregiver to continue outpatient management.
- Patients without a diagnosis who do not meet the criteria for admission can be discharged, especially in cases in which a self-limited viral infection is the most likely diagnosis or in which outpatient management is indicated by consulting subspecialists.
- Patients to be discharged should be instructed to follow up with a primary care clinician and given resources to follow up with an appropriate specialist, such as a pediatric infectious disease specialist, if fevers continue for an additional 1 to 2 days after discharge.

