**American College of Radiology**
**ACR Appropriateness Criteria®**

# Fever Without Source or Unknown Origin-Child

## Variant: 1 Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.

| Procedure | Appropriateness Category | Peds Relative Radiation Level |
|---|---|---|
| Radiography chest | May Be Appropriate | ☢ |
| US chest | Usually Not Appropriate | O |
| MRI chest without and with IV contrast | Usually Not Appropriate | O |
| MRI chest without IV contrast | Usually Not Appropriate | O |
| MRI whole body without and with IV contrast | Usually Not Appropriate | O |
| MRI whole body without IV contrast | Usually Not Appropriate | O |
| CT abdomen and pelvis with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| FDG-PET/MRI whole body | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without and with IV contrast | Usually Not Appropriate | ☢☢☢☢☢ |
| FDG-PET/CT whole body | Usually Not Appropriate | ☢☢☢☢ |

## Variant: 2 Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.

| Procedure | Appropriateness Category | Peds Relative Radiation Level |
|---|---|---|
| Radiography chest | May Be Appropriate | ☢ |
| US abdomen | Usually Not Appropriate | O |
| US kidneys and bladder | Usually Not Appropriate | O |
| MRI chest without and with IV contrast | Usually Not Appropriate | O |
| MRI chest without IV contrast | Usually Not Appropriate | O |
| MRI whole body without and with IV contrast | Usually Not Appropriate | O |
| MRI whole body without IV contrast | Usually Not Appropriate | O |
| CT paranasal sinuses with IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT paranasal sinuses without IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT abdomen and pelvis with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck with IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT neck without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck without IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT paranasal sinuses without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |

| | | |
|---|---|---|
| FDG-PET/MRI whole body | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without and with IV contrast | Usually Not Appropriate | ☢☢☢☢☢ |
| FDG-PET/CT whole body | Usually Not Appropriate | ☢☢☢☢ |

## Variant: 3 Child. Fever without source and neutropenia. Initial imaging.

| Procedure | Appropriateness Category | Peds Relative Radiation Level |
|---|---|---|
| Radiography chest | May Be Appropriate (Disagreement) | ☢ |
| CT paranasal sinuses with IV contrast | May Be Appropriate | ☢☢☢ |
| CT paranasal sinuses without IV contrast | May Be Appropriate | ☢☢☢ |
| CT abdomen and pelvis with IV contrast | May Be Appropriate | ☢☢☢☢ |
| CT chest with IV contrast | May Be Appropriate | ☢☢☢☢ |
| CT chest without IV contrast | May Be Appropriate | ☢☢☢☢ |
| FDG-PET/MRI whole body | May Be Appropriate | ☢☢☢☢ |
| FDG-PET/CT whole body | May Be Appropriate | ☢☢☢☢ |
| US abdomen | Usually Not Appropriate | O |
| 3-phase bone scan whole body | Usually Not Appropriate | ☢☢☢☢ |
| Bone scan and WBC scan whole body | Usually Not Appropriate | ☢☢☢☢ |
| MRI abdomen and pelvis without and with IV contrast | Usually Not Appropriate | O |
| MRI abdomen and pelvis without IV contrast | Usually Not Appropriate | O |
| MRI chest without and with IV contrast | Usually Not Appropriate | O |
| MRI chest without IV contrast | Usually Not Appropriate | O |
| MRI whole body without and with IV contrast | Usually Not Appropriate | O |
| MRI whole body without IV contrast | Usually Not Appropriate | O |
| CT abdomen and pelvis without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck with IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT neck without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck without IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT paranasal sinuses without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without and with IV contrast | Usually Not Appropriate | ☢☢☢☢☢ |
| Fluoride PET/CT whole body | Usually Not Appropriate | ☢☢☢☢ |

## Variant: 4 Child. Fever of unknown origin. Initial Imaging.

| Procedure | Appropriateness Category | Peds Relative Radiation Level |
|---|---|---|
| Radiography chest | May Be Appropriate | ☢ |
| MRI whole body without and with IV contrast | May Be Appropriate | O |
| MRI whole body without IV contrast | May Be Appropriate | O |
| FDG-PET/MRI whole body | May Be Appropriate | ☢☢☢☢ |
| FDG-PET/CT whole body | May Be Appropriate | ☢☢☢☢ |
| US abdomen | Usually Not Appropriate | O |
| 3-phase bone scan whole body | Usually Not Appropriate | ☢☢☢☢ |
| Bone scan and WBC scan whole body | Usually Not Appropriate | ☢☢☢☢ |
| MRI chest without and with IV contrast | Usually Not Appropriate | O |
| MRI chest without IV contrast | Usually Not Appropriate | O |

| | | |
|---|---|---|
| CT paranasal sinuses with IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT paranasal sinuses without IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT abdomen and pelvis with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT chest without IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck with IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT neck without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT neck without IV contrast | Usually Not Appropriate | ☢☢☢ |
| CT paranasal sinuses without and with IV contrast | Usually Not Appropriate | ☢☢☢☢ |
| CT abdomen and pelvis without and with IV contrast | Usually Not Appropriate | ☢☢☢☢☢ |
| Fluoride PET/CT whole body | Usually Not Appropriate | ☢☢☢☢ |

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**Summary of Literature Review**

**Introduction/Background**

Fever is the most common reason for the evaluation of pediatric patients in acute care settings and accounts for 10% to 20% of all pediatric emergency department visits annually [1,2]. Fever is defined as a temperature of 38 °C/100.4 °F or greater. Rectal temperature is the most accurate method and closest to core temperature and is used in neonates and young children to be as sensitive as possible to detect fever due to the increased risk of serious bacterial infection in those patients. Obtaining temperature orally is preferred in older, cooperative patients. A viral or bacterial cause of fever is identified in slightly more than half of pediatric patients after a thorough history, physical examination, and laboratory evaluation. Patients for whom no source of infection is identified are classified as having fever without source (FWS). FWS is therefore defined as an acute illness in which the origin of the fever is not apparent after initial careful history and physical examination and laboratory evaluation. About 75% of children who are well appearing and without an identified source of infection will have a self-limited viral infection.

Special considerations should be taken in the evaluation of neonates and neutropenic patients because they are at a higher risk of serious bacterial infection. Patients with prolonged fever lasting >3 weeks who have no identifiable source of fever are classified with fever of unknown origin (FUO) and represent an additional subset of febrile pediatric patients who also require special consideration.

The purpose of this document is to describe the most common clinical scenarios of FWS and FUO in childhood and to provide the clinician with guidance based on the existing literature so that they can choose the most appropriate initial imaging. All scenarios described herein relate to the

initial imaging encounter. For appropriate care, patients with fever and the appropriate localizing symptoms should also have imaging guided by the ACR Appropriateness Criteria® topics on "Pneumonia in the Immunocompetent Child" [3], "Urinary Tract Infection-Child" [4], and "Suspected Appendicitis–Child" [5].

**Initial Imaging Definition**

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

· There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

· There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

**Discussion of Procedures by Variant**

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**

This scenario addresses a febrile neonate without respiratory signs or symptoms. Although febrile illnesses in children are most commonly self-limited viral infections, approximately 8% to 13% of young febrile infants have a bacterial infection, predominantly urinary tract infections [6,7]. Additionally, 1% to 2% of young febrile infants have an invasive bacterial infection, such as bacteremia and/or bacterial meningitis [8-10]. Infants who are 90 days of age or younger are at high risk of bacterial infections due to exposure to bacterial pathogens in the perinatal period and lack of vaccine-based immunity [1,11]. Fever is often the only sign of illness in young infants, making it clinically difficult to differentiate infants with a benign self-limiting illness from those with invasive bacterial infections. Delayed diagnosis of invasive bacterial infection is associated with increased morbidity and mortality. Infants <28 days of age are at higher risk than older infants [12]. The prevalence of pneumonia in febrile infants <3 months of age is low, approximately 1% to 3% [13,14]. The evaluation of febrile young infants includes urinalysis, laboratory testing for inflammatory markers and blood culture and may include lumbar puncture [15], and hospital admission. Empiric antibiotic therapy is used in these patients [15]. The decision to perform a lumbar puncture to exclude meningitis is based upon clinical factors that categorize the patient as high or low risk. Several clinical practice guidelines have been developed by various groups to decrease practice variation in the diagnosis and treatment of febrile young infants to decrease unnecessary lumbar punctures, antibiotic administration, and hospitalizations [8-10,16-20].

For appropriate care, patients with fever and the appropriate localizing symptoms should also have imaging guided by the ACR Appropriateness Criteria® topics on "Pneumonia in the Immunocompetent Child" [3], "Urinary Tract Infection-Child" [4], and "Suspected Appendicitis–Child" [5].

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**A. CT abdomen and pelvis with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with intravenous (IV) contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**B. CT abdomen and pelvis without and with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**C. CT abdomen and pelvis without IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**D. CT chest with IV contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**E. CT chest without and with IV contrast**

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**F. CT chest without IV contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**G. FDG-PET/CT whole body**

There is no relevant literature to support the use fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**H. FDG-PET/MRI whole body**

There is no relevant literature to support the use of FDG-PET/MRI whole body in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**I. MRI chest without and with IV contrast**

There is no relevant literature to support the use of MRI chest without and with contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**J. MRI chest without IV contrast**

There is no relevant literature to support the use of MRI chest without IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**K. MRI whole body without and with IV contrast**

There is no relevant literature to support the use of MRI whole body without and with IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**L. MRI whole body without IV contrast**

There is no relevant literature to support the use MRI whole body without IV contrast in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**M. Radiography chest**

Multiple prospective studies show that the yield of chest radiography is low in children <3 months of age, who are judged to be low clinical risk for pneumonia. Although chest radiographs are not indicated for febrile neonates without respiratory symptoms, chest radiography can help exclude congenital or cardiac disease in a neonate who is febrile and ill-appearing.

In a retrospective review of febrile infants <3 months of age [13], of the 173 patients without signs of respiratory distress, 5 patients had positive findings on chest radiograph, giving a prevalence of clinically occult pneumonia in this population of <3%. Of those 5 patients without respiratory signs, 3 were interpreted by 1 radiologist as having slight findings, whereas the other radiologist reported negative findings. The authors stated that this emphasized the mild and often equivocal degree of radiographic changes seen in these patients. The authors concluded that a chest radiograph should only be obtained in febrile infants if respiratory signs are present.

In a retrospective review of the usefulness of chest radiographs in febrile infants ≤8 weeks of age, of the 148 asymptomatic patients in the study, 2 (1%) had chest radiographs identified as abnormal. In both cases, the interpretation was a mild diffuse pattern (mild peribronchial thickening), and the study radiologists originally differed as to whether the abnormality was

present or not. Medical management of these 2 patients was not affected by the chest radiograph reading, because both patients were treated as if the chest radiograph was negative [21].
In a retrospective cohort study of febrile infants 7 to 60 days of age at a tertiary children's hospital, 0 of the 58 patients in the study who had no respiratory symptoms and had a chest radiograph performed had abnormal chest radiograph findings [14].

In a retrospective study, which included meta-analysis of additional research totaling 361 febrile infants ≤3 months of age implied that the probability of a normal chest radiograph in an infant with no clinical evidence of pulmonary disease is ≥98.98% [22].

**Variant 1: Child up to 3 months of age. Fever without source and clinical concern for occult pneumonia. Initial imaging.**
**N. US chest**

There is no relevant literature to support the use of ultrasound (US) chest in the initial evaluation of a child up to 3 months of age with FWS and clinical concern for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**

The majority of febrile children will have a benign, self-limited viral infection [23]. The risk of serious bacterial infection decreases with age and increases with the height and duration of fever [1,23]. The evaluation of febrile older infants (>3 months of age) and children who are ill-appearing or have an evident focus of infection is straightforward. The otherwise well-appearing, previously healthy children presenting without an obvious source of infection after an outpatient or hospital evaluation that includes a careful history and physical examination and initial laboratory evaluation receive a diagnosis of FWS. There is often confusion about the terms FUO and FWS. Distinguishing between FUO and FWS is based on the duration of the fever. A duration of <1 week has been listed as a criterion for FWS [13]. There is much variability in published studies of FUO, with a required duration of fever ranging from 1 to 3 weeks [24,25]. In the absence of a "toxic" appearance, respiratory distress, poor peripheral perfusion, high fever, and leukocytosis, the risk for serious bacterial infection is low in children with FWS. Since the introduction of conjugate vaccines against Streptococcus pneumoniae and Haemophilus influenzae type b, the prevalence of occult bacteremia in febrile children has decreased to 0.5%, and the prevalence of pathogens has changed [26]. In the postconjugate vaccine era, the most common serious bacterial infection in febrile children <24 months of age is Escherichia coli secondary to urinary tract infections with a prevalence of 5% to 7% [23]. The initial diagnostic evaluation of lower-risk young patients between 3 to 36 months of age with fever and without signs of respiratory illness may include urinalysis and urine culture, rapid influenza testing, and close outpatient monitoring [27]. Previous studies on febrile children have mainly focused on infants and young children and literature regarding febrile adolescents is scarce [28], and thus a separate variant in an older age group was not pursued.

For appropriate care, patients with fever and the appropriate localizing symptoms should also have imaging guided by the ACR Appropriateness Criteria® topics on "Pneumonia in the Immunocompetent Child" [3], "Urinary Tract Infection-Child" [4], and "Suspected Appendicitis–Child" [5].

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**A. CT abdomen and pelvis with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**B. CT abdomen and pelvis without and with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**C. CT abdomen and pelvis without IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**D. CT chest with IV contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**E. CT chest without and with IV contrast**

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**F. CT chest without IV contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**G. CT neck with IV contrast**

There is no relevant literature to support the use of CT neck with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**H. CT neck without and with IV contrast**

There is no relevant literature to support the use of CT neck without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**I. CT neck without IV contrast**

There is no relevant literature to support the use of CT neck without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**J. CT paranasal sinuses with IV contrast**

There is no relevant literature to support the use of CT paranasal sinuses with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**K. CT paranasal sinuses without and with IV contrast**

There is no relevant literature to support the use of chest CT paranasal sinuses without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**L. CT paranasal sinuses without IV contrast**

There is no relevant literature to support the use of CT paranasal sinuses without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**M. FDG-PET/CT whole body**

There is no relevant literature to support the use of FDG-PET/CT whole body in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**N. FDG-PET/MRI whole body**

There is no relevant literature to support the use of FDG-PET/MRI whole body in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**O. MRI chest without and with IV contrast**

There is no relevant literature to support the use of MRI chest without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**P. MRI chest without IV contrast**

There is no relevant literature to support the use of MRI chest without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**

**Q. MRI whole body without and with IV contrast**

There is no relevant literature to support the use of MRI whole body without and with IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**R. MRI whole body without IV contrast**

There is no relevant literature to support the use of MRI whole body without IV contrast in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**S. Radiography chest**

Multiple prospective studies show that the yield of chest radiography is low in infants and toddlers who are judged to be low clinical risk for pneumonia. Although chest radiographs are not indicated for febrile infants and toddlers without respiratory symptoms, chest radiography can help exclude congenital or cardiac disease in a young child who is febrile and ill.

In a prospective study of 121 infants and toddlers between 1 week and 22 months of age (mean age 5.3 months) without signs and symptoms of lower respiratory tract infection, the positive yield of chest radiography was 0% to 3% with a 95% confidence interval [29].

In a prospective study of 1,181 children 3 months to 18 years of age, a clinical evaluation that suggested a low risk of pneumonia had a negative predictive value (NPV) of 95.6% (95% confidence interval, 88.5%-98.6%) for radiographic pneumonia [30].

In a prospective study of 1,142 children aged 3 months to 18 years of age, a clinical evaluation that predicted a low risk of pneumonia (<6.2%) had a NPV of 95.3% for radiographic pneumonia [31].

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**T. US abdomen**

There is no relevant literature to support the use of US abdomen in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 2: Child aged 3 to 36 months. Fever without source and with low risk for occult pneumonia. Initial imaging.**
**U. US kidneys and bladder**

There is no relevant literature to support the use of US kidneys and bladder in the initial evaluation of a child with FWS and low risk for occult pneumonia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**

Special considerations must be taken for febrile patients with neutropenia, because fever may indicate the presence of a life-threatening infection and prompt recognition is critical. Patients at risk of febrile neutropenia include patients who have been administered chemotherapy or immune modulators, as well as those with congenital or acquired immunodeficient states. Serious bacterial infection is a significant cause of morbidity and mortality to neutropenic patients [32]. These patients must be rapidly evaluated and are administered empiric systemic antibiotics to avoid sepsis and death [33]. When febrile neutropenia does not respond to broad-spectrum antibiotics,

current pediatric-specific guidelines recommend initiation of empirical antifungal therapy in high-risk patients to decrease the morbidity and mortality related to invasive fungal disease [34].

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**A. 3-phase bone scan whole body**

There is no relevant literature to support the use of 3-phase bone scan whole body in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**B. Bone scan and WBC scan whole body**

There is no relevant literature to support the use of bone scan and white blood cell (WBC) scan whole body in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**C. CT abdomen and pelvis with IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to obtain a CT of the abdomen for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], even without localizing symptoms. The guideline does not specify if IV contrast is to be used for the CT scan.

In a retrospective study of pediatric (≤21 years of age) febrile neutropenic patients that included 36 patients who received a CT scan of the abdomen and pelvis alone, 14 scans (39%) identified a potential source of infection [35]. The study did not specify if IV contrast was or was not used on the CT scans.

In a retrospective review of pediatric patients with neutropenic fever, 65 patients had an abdomen CT performed [36]. The study did not specify if IV contrast was or was not used on the CT scans. Although 12% of the abdomen CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**D. CT abdomen and pelvis without and with IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to obtain a CT of the abdomen for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], even without localizing symptoms. The guideline does not specify if IV contrast is to be used for the CT scan.

In a retrospective study of pediatric (≤21 years of age) febrile neutropenic patients that included 36 patients who received a CT scan of the abdomen and pelvis alone, 14 scans (39%) identified a potential source of infection [35]. The study did not specify if IV contrast was or was not used on the CT scans.

In a retrospective review of pediatric patients with neutropenic fever, 65 patients had an abdomen CT performed [36]. The study did not specify if IV contrast was or was not used on the CT scans. Although 12% of the abdomen CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**E. CT abdomen and pelvis without IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to obtain a CT of the abdomen for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], even without localizing symptoms. The guideline does not specify if IV contrast is to be used for the CT scan.

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In a retrospective review of pediatric patients with neutropenic fever, 65 patients had an abdomen CT performed [36]. The study did not specify if IV contrast was or was not used on the CT scans. Although 12% of the abdomen CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**F. CT chest with IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a strong recommendation to obtain a chest CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], as the lungs are the most commonly affected site. The guideline does not specify if IV contrast is to be used for the CT scan.

In a retrospective review of 141 pediatric patients 0 to 14 years of age with febrile neutropenia, chest CT with IV contrast for the diagnosis of invasive pulmonary aspergillosis was reported to have a sensitivity of 79%, a specificity of 85%, a positive predictive value (PPV) of 76%, and an NPV of 87% [37].

In a retrospective study of pediatric (≤21 years of age) febrile neutropenic patients, 26 of whom received a CT scan of the chest alone, 15 scans (58%) identified a possible source of infection [35]. Commonly detected likely infectious etiologies included pulmonary opacities and pulmonary lesions suspicious for fungal infection. The study did not specify if IV contrast was or was not used on the CT scans.

In a retrospective review of pediatric patients with neutropenic fever, 66 patients had a chest CT performed [36]. Although 18% of the chest CTs had positive signs for possible infection, only 2 of these scans with positive findings (2/66; 3%) led to an alteration of therapy. The study did not specify if IV contrast was or was not used on the CT scans. The authors suggested that if there is concern for occult fungal disease in a patient with persisting fever and neutropenia and no localizing signs or symptoms, only a chest CT should be performed, and CT examinations of other parts of the body should not be performed.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**G. CT chest without and with IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and

Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a strong recommendation to obtain a chest CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], because the lungs are the most commonly affected site. The guideline does not specify if IV contrast is to be used for the CT scan.

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**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**H. CT chest without IV contrast**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a strong recommendation to obtain a chest CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], because the lungs are the most commonly affected site. The guideline does not specify if IV contrast is to be used for the CT scan.

In a retrospective study of pediatric (≤21 years of age) febrile neutropenic patients, 26 of whom received a CT scan of the chest alone, 15 scans (58%) identified a possible source of infection [35]. Commonly detected likely infectious etiologies included pulmonary opacities and pulmonary lesions suspicious for fungal infection. The study did not specify if IV contrast was or was not used on the CT scans.

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**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**

**I. CT neck with IV contrast**

There is no relevant literature to support the use of CT neck with IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**J. CT neck without and with IV contrast**

There is no relevant literature to support the use of CT neck without and with IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**K. CT neck without IV contrast**

There is no relevant literature to support the use of CT neck without IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**L. CT paranasal sinuses with IV contrast**

Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to consider not routinely obtaining a sinus CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], but no localizing symptoms, because abnormalities on these examinations are common but do not seem to distinguish between those with and without invasive fungal disease. The recommendation is weak due to the lack of studies directly addressing the usefulness of sinus CT in this population.

In a retrospective study of pediatric (≤21 years of age) febrile neutropenic patients, 23 of whom received a CT scan of the head and sinuses alone, 13 scans (57%) identified a possible source of infection [35]. The study did not specify if IV contrast was or was not used on the CT scans. The most commonly detected infectious etiology was sinusitis.

In a retrospective review of pediatric patients with neutropenic fever, 44 patients had a sinus CT performed [36]. Although 25% of the sinus CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy. The study did not specify if IV contrast was or was not used on the CT scans.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**M. CT paranasal sinuses without and with IV contrast**

Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to consider not routinely obtaining a sinus CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], but no localizing symptoms, because abnormalities on these examinations are common but do not seem to distinguish between those with and without invasive fungal disease. The recommendation is

weak because of the lack of studies directly addressing the usefulness of sinus CT in this population.

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In a retrospective review of pediatric patients with neutropenic fever, 44 patients had a sinus CT performed [36]. Although 25% of the sinus CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy. The study did not specify if IV contrast was or was not used on the CT scans.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**N. CT paranasal sinuses without IV contrast**

Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a weak recommendation to consider not routinely obtaining a sinus CT for patients with prolonged (>96 hours) febrile neutropenia when there is a concern for invasive fungal disease [34], but no localizing symptoms, because abnormalities on these examinations are common but do not seem to distinguish between those with and without invasive fungal disease. The recommendation is weak due to the lack of studies directly addressing the usefulness of sinus CT in this population.

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In a retrospective review of pediatric patients with neutropenic fever, 44 patients had a sinus CT performed [36]. Although 25% of the sinus CTs had positive signs for possible infection, none of these positive findings lead to an alteration of therapy. The study did not specify if IV contrast was or was not used on the CT scans.
FDG-PET/CT Whole Body

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**O. FDG-PET/CT whole body**

The Children's Oncology Group Diagnostic Imaging Committee/SPR Oncology Committee White Paper recommends FDG-PET/CT in hematopoietic stem cell transplant patients in the early posttransplant period who are immunosuppressed and neutropenic as the test has high sensitivity and specificity for infections in the chest, abdomen, and pelvis [38].

FDG-PET/CT has been shown to be a clinically impactful examination for adult patients with neutropenic fever [39].

In a retrospective review of 14 pediatric patients (1-17 years of age) with neutropenic fever, the

clinical impact was considered “high” in 11 patients (79%), with the FDG-PET/CT result either prompting referral of patients for specialist consults, which resulted in a diagnosis or change to management or the FDG-PET/CT result, leading to alterations to antimicrobial and/or antifungal therapy [40].

Studies on pediatric patients who are immunosuppressed but not necessarily neutropenic have been performed. A retrospective study investigating FDG-PET/CT in 31 children with pyrexia of unknown origin included 12 with immunosuppression, in which FDG-PET/CT correctly identified the source of fever in 7 patients (88%) [41]. In a retrospective study of immunosuppressed pediatric patients, which included 5 patients with FUO, FDG-PET/CT demonstrated the cause of FUO in 2 patients but did not demonstrate the cause of FUO in 2 patients. The PET/CT was false-positive in 1 FUO patient [42].

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**P. FDG-PET/MRI whole body**

Although there are insufficient data to support the use of FDG-PET/MRI in the initial evaluation of a child or adult with FWS and neutropenia, this procedure has been suggested to be of potential usefulness, and further prospective studies are needed to evaluate FDG-PET/MRI in this clinical scenario in children and adults [40,43].

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**Q. Fluoride PET/CT whole body**

There is no relevant literature to support the use of fluoride PET/CT whole body in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**R. MRI abdomen and pelvis without and with IV contrast**

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**S. MRI abdomen and pelvis without IV contrast**

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**T. MRI chest without and with IV contrast**

There is no relevant literature to support the use of MRI chest without and with IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**U. MRI chest without IV contrast**

There is no relevant literature to support the use of MRI chest without IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**V. MRI whole body without and with IV contrast**

There is no relevant literature to support the use of MRI whole body without and with IV contrast in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**W. MRI whole body without IV contrast**

There is no relevant literature to support the use of MRI whole body without IV in the initial evaluation of a child with FWS and neutropenia.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**X. Radiography chest**

The clinical Guideline for Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients by the Society of Clinical Oncology makes a strong recommendation to obtain chest radiograph only in febrile neutropenic patients with respiratory signs or symptoms [34].

In a prospective study of neutropenic children with cancer, out of 108 episodes of febrile neutropenia, 4 patients (3.7%) had pneumonia documented by radiograph [44]. The authors of the study concluded it was not necessary to obtain a chest radiograph in children with no respiratory abnormalities who were hospitalized for fever and neutropenia.

In a retrospective review of 200 chest radiographs performed in children with cancer and febrile neutropenia, 93% of the chest radiographs show no evidence of pneumonia. Of the 15 patients who had positive radiographs, 66% had symptoms. The authors concluded that chest radiography is warranted in the evaluation of the newly febrile neutropenic pediatric oncology patient only when respiratory signs and symptoms are present [45].

In a retrospective study of 81 children with hematopoietic stem cell transplantation and fever who had a chest radiograph performed as a routine part of their admission, 94% of the chest radiographs showed no evidence of pneumonia [46]. Of the 5 patients who had positive radiographs, 60% had symptoms. None of the patients had a change made in the empiric antibiotic regimen based upon the results of the chest radiograph. The authors concluded that routine radiographs are not useful in the evaluation of asymptomatic children at the time of an initial febrile event while undergoing hematopoietic stem cell transplantation.

**Variant 3: Child. Fever without source and neutropenia. Initial imaging.**
**Y. US abdomen**

There is no relevant literature to support the use of US abdomen in the initial evaluation of a child with FWS and neutropenia.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**

FUO has been defined as fever with core temperature >38 °C, lasting more than 1 to 3 weeks, and with a negative initial workup [47,48]. For children, FUO causes are characterized as 40% to 50% infection, 10% to 20% inflammatory disease, 10% to 20% malignancy, and unknown in the remainder of cases [24,49]. Evaluation of patients with FUO include a thorough history, physical examination, and laboratory evaluation for inflammatory markers, blood culture and sensitivity, urinalysis, and culture. A more targeted workup may include invasive tests such as cerebrospinal fluid analysis, bone marrow biopsy, and imaging [24].

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**A. 3-phase bone scan whole body**

There is no relevant literature to support the use of a 3-phase bone scan whole body in the initial

evaluation of a child with FUO.

WBC (gallium- or indium-111-labeled) scans have not been well studied in the diagnosis of pediatric FUO. Limited evidence in children and additional studies in adults suggest that these techniques have low sensitivity and specificity in the evaluation of FUO and should be used only if traditional imaging fails to reveal a diagnosis [24].

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**B. Bone scan and WBC scan whole body**

There is no relevant literature to support the use of bone scan and WBC scan whole body in the initial evaluation of a child with FUO.

WBC (gallium- or indium-111-labeled) scans have not been well studied in the diagnosis of pediatric FUO. Limited evidence in children and additional studies in adults suggest that these techniques have low sensitivity and specificity in the evaluation of FUO and should be used only if traditional imaging fails to reveal a diagnosis [24].

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**C. CT abdomen and pelvis with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**D. CT abdomen and pelvis without and with IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**E. CT abdomen and pelvis without IV contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**F. CT chest with IV contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**G. CT chest without and with IV contrast**

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**H. CT chest without IV contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**I. CT neck with IV contrast**

There is no relevant literature to support the use of CT neck with IV contrast in the initial evaluation

of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**J. CT neck without and with IV contrast**

There is no relevant literature to support the use of CT neck without and with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**K. CT neck without IV contrast**

There is no relevant literature to support the use of CT neck without IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**L. CT paranasal sinuses with IV contrast**

There is no relevant literature to support the use of CT paranasal sinuses with IV contrast in the initial evaluation of a child with FUO. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**M. CT paranasal sinuses without and with IV contrast**

There is no relevant literature to support the use of CT paranasal sinuses without and with IV contrast in the initial evaluation of a child with FUO. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**N. CT paranasal sinuses without IV contrast**

There is no relevant literature to support the use of CT paranasal sinuses without IV contrast in the initial evaluation of a child with FUO. Paranasal sinuses may not be fully developed in infants and young children, and this must be considered before ordering a CT in this age group.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**O. FDG-PET/CT whole body**

FDG-PET/CT whole body has been used to evaluate FUO in children and adults and has been shown to be helpful in identifying the source of fever for some patients as detailed below. The limitations of the published literature on this topic include the fact that the studies are retrospective, the lack of a structured diagnostic workup may have led to the presence of selection bias [25], and the publications were limited to only pediatric patients and have a relatively small number of patients. Some authors have recommended that FDG-PET/CT whole body should be considered for initial imaging of FUO in adults [25,50], whereas others have suggested that the test is either debatable as a first-line test [39] or may be best used after initial imaging has been performed [51].

Multiple studies have been performed to evaluate the efficacy of FDG-PET/CT in adult patients with FUO and found that these examinations can be useful in identifying the source of fever in patients with FUO [25,39,48,50-56].

A retrospective study of FDG-PET/CT in children included a 16-year-old patient with FUO, who had a FDG-PET/CT examination that diagnosed splenic abscesses [57].

In a retrospective review of the diagnostic usefulness of FDG-PET/CT whole body in pediatric patients with FUO, 28 FDG-PET/CT scans were performed on patients who were not immunosuppressed [41]. In this study the sensitivity of FDG-PET/CT was 80%, the specificity was 78%, the PPV was 67%, and the NPV was 88%.

In a retrospective review of 110 pediatric patients with FUO who underwent FDG-PET/CT whole body [58], the examination identified the source of fever (true-positive result) in 48% of patients. Endocarditis (11%), systemic juvenile idiopathic arthritis (5%), and inflammatory bowel disorder (5%) were the most common causes of FUO. In 42 patients (38%), no cause of fever was found on FDG-PET/CT. In 58 out of 110 patients (53%), treatment modifications were made after FDG-PET/CT. FDG-PET/CT achieved a sensitivity of 85.5%, a specificity of 79.2%, a PPV of 84.1%, and an NPV of 80.9%. Although the number is not specified, the authors report that most of the children in this retrospective review had undergone prior diagnostic studies such as radiography and ultrasound before FDG-PET/CT.

In a review of the literature, which included several of the articles previously listed in this discussion on the usefulness of FDG-PET/CT in pediatric patients with FUO [49], the pooled reported FDG-PET/CT sensitivity was 80% to 100% and specificity was 66.7% to 79.2%.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**P. FDG-PET/MRI whole body**

FDG-PET/MRI whole body has been used to evaluate systemic diseases in several small series and has been suggested as a potentially useful tool to evaluate for FUO [59]. However, there are no relevant studies evaluating its usefulness in the initial evaluation of a child with FUO, nor is there enough FDG-PET/MRI data to show its usefulness in adult patients to evaluate FUO [60]. However, it has been suggested that this procedure may have potential usefulness for this indication in adults [43].

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**Q. Fluoride PET/CT whole body**

There is no relevant literature to support the use of fluoride PET/CT whole body in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**R. MRI chest without and with IV contrast**

There is no relevant literature to support the use of MRI chest without and with IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**S. MRI chest without IV contrast**

There is no relevant literature to support the use of MRI chest without IV contrast in the initial evaluation of a child with FUO.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**T. MRI whole body without and with IV contrast**

Although fever syndromes and unclear inflammatory constellations indicating a systemic disease, an undetected focus, or a previously unknown malignant process are indications for whole body imaging, studies on the sensitivity and specificity of this modality in children with FUO are rare [61].

In a retrospective study of 24 adult patients with FUO, the detection rate for inflammatory foci by MRI whole body as a cause of the FUO was 71%, and 50% of patients had a change in management based on the results of the whole body MRI [47].

In a small retrospective study of children without history of an oncological process, 3 patients with FUO underwent whole body MRI without IV contrast. The examination determined the location of septic arthritis in 1 case and of pneumonia with a small pleural effusion in the second one [62], and a negative examination was useful in helping to rule out infection or other etiology in a third case. In another retrospective review of pediatric patients with FUO, whole body MRI was used in 61 patients [63], and the studies were described as useful to rule out oncologic disease and occult abscesses in patients with nonspecific and unclear clinical evaluations.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**U. MRI whole body without IV contrast**

Although fever syndromes and unclear inflammatory constellations indicating a systemic disease, an undetected focus, or a previously unknown malignant process are indications for whole body imaging, studies on the sensitivity and specificity of this modality in children with FUO are rare [61].

In a retrospective study of 24 adult patients with FUO, the detection rate for inflammatory foci by MRI whole body as a cause of the FUO was 71%, and 50% of patients had a change in management based on the results of the whole body MRI [47].

In a small retrospective study of children without history of an oncological process, 3 patients with FUO underwent whole body MRI without IV contrast. The examination determined the location of septic arthritis in 1 case and of pneumonia with a small pleural effusion in the second one [62], and a negative examination was useful in helping to rule out infection or other etiology in a third case. In another retrospective review of pediatric patients with FUO, whole body MRI was used in 61 patients [63], and the studies were described as useful to rule out oncologic disease and occult abscesses in patients with nonspecific and unclear clinical evaluations.

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**V. Radiography chest**

Radiographs and imaging may play a role in the evaluation of FUO, but research suggests that empiric imaging has limited usefulness. Radiographs can be considered if pulmonary symptoms are present or if there is concern for atypical bacterial infection, HIV, tuberculosis, or oncologic processes [24].

**Variant 4: Child. Fever of unknown origin. Initial Imaging.**
**W. US abdomen**

There is no relevant literature to support the use of US abdomen in the initial evaluation of a child with FUO.

**Summary of Highlights**

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

· Variant 1: In the setting a febrile infant >3 months of age without signs of respiratory infection, medical management only is usually appropriate. Although the usefulness of chest radiography is low in this clinical setting, a chest radiograph may be appropriate to exclude congenital or cardiac disease in a neonate who is febrile and ill-appearing.

· Variant 2: In the setting of a febrile young child 3 to 36 months of age without signs of respiratory infection, medical management only is usually appropriate. Although the usefulness of chest radiography is low in this clinical setting, a chest radiograph may be appropriate to exclude congenital or cardiac disease in a young child who is febrile and ill-appearing.

· Variant 3: In the setting of a neutropenic child with FWS, there are no imaging tests that are usually appropriate for initial imaging. Imaging tests that may be appropriate to identify sources of infection include chest radiography, CT paranasal sinuses without IV contrast or CT paranasal sinuses with IV contrast, CT chest without IV contrast or CT chest with IV contrast, CT abdomen and pelvis with IV contrast, FDG-PET/CT whole body, and FDG-PET/MRI whole body.

· Variant 4: In the setting of a child with FUO, there are no imaging tests that are usually appropriate for initial imaging. Imaging tests that may be appropriate include chest radiography, whole body MRI without IV contrast, whole body MRI without and with IV contrast, FDG-PET/CT whole body, and FDG-PET/MRI whole body.

**Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

**Gender Equality and Inclusivity Clause**

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health.

**Appropriateness Category Names and Definitions**

| Appropriateness Category Name | Appropriateness Rating | Appropriateness Category Definition |
|---|---|---|
| Usually Appropriate | 7, 8, or 9 | The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients. |
| May Be Appropriate | 4, 5, or 6 | The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with |

| | | |
|---|---|---|
| | | a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal. |
| May Be Appropriate (Disagreement) | 5 | The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned. |
| Usually Not Appropriate | 1, 2, or 3 | The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable. |

**Relative Radiation Level Information**

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

**Relative Radiation Level Designations**

| Relative Radiation Level* | Adult Effective Dose Estimate Range | Pediatric Effective Dose Estimate Range |
|---|---|---|
| O | 0 mSv | 0 mSv |
| ☢ | <0.1 mSv | <0.03 mSv |
| ☢☢ | 0.1-1 mSv | 0.03-0.3 mSv |
| ☢☢☢ | 1-10 mSv | 0.3-3 mSv |
| ☢☢☢☢ | 10-30 mSv | 3-10 mSv |
| ☢☢☢☢☢ | 30-100 mSv | 10-30 mSv |

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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