

Fever of Unknown Origin in PEDs

Background

1. Definition

- Fever >101.1°F [38.4° C] in a child
 - Lasting >7–14 days
 - H&P and preliminary lab eval fail to reveal a probable cause for fever
- In contrast, fever w/o source (FWS) is =< 7 days

2. General information

- Most children w/FUO have uncommon presentations of common illnesses, rather than rare or exotic dz
- 3 most commonly identified causes of FUO are:
 - Infectious dz
 - Rheumatologic disorders
 - Malignancies

Pathophysiology

1. Pathology of dz

- Dependent upon underlying etiology

2. Incidence/ prevalence

- No data available on frequency of FUO in children

3. Risk factors

- Immunodeficiency
- Chronic medical conditions/ challenges
 - "Children w/Special Healthcare Needs"
- Exposures to infectious dz
- Travel to developing countries

4. Morbidity/ mortality

- 40% of children w/FUO have serious, long-lasting sequelae
- Cause-related mortality ranges from 9-17%

Diagnostics

1. History

- Clinical approach to any child w/FUO should be individualized
- Fever: method of measurement, duration, height and pattern
 - Is fever real or not?
 - Is fever persistent or are there periods of complete cessation between episodes?
- Other associated symptoms
 - Location
 - Length of time involved
- Contacts
 - People: ill contacts, carriers
 - Animal: dog, cat, rodent, exotic pets, others
 - Insect: mosquitoes, ticks, others
- Travel hx
 - Especially foreign, w/in past 12 mos

- Medications
 - Current medications
 - Consider any meds which could cause drug fever
 - Consider herbal and OTCs
 - Ethnicity/ family hx
 - Past medical hx
 - Immunization status
 - Transfusion hx
2. Physical exam
- General assessment
 - Documented fever? Oral, tympanic or rectal?
 - Growth curves: poor wt gain or wt loss? Decr linear growth?
 - Thorough and complete PE
 - Specific PE areas to focus on
 - Skin lesions, rashes
 - Eyes
 - Sinuses
 - Oropharynx
 - Chest
 - Heart
 - Abdomen
 - Bone/ joint exam
 - Rectal, genital exam, pelvic exam if sexually active
3. Diagnostic testing
- Laboratory eval
 - 1st tier
 - (Ordered together, as a group)
 - CBC and peripheral smear
 - Blood cultures
 - Urinalysis and urine culture
 - Chem-12
 - ESR
 - PPD
 - HIV serology
 - ANA
 - Stool culture and O&P if diarrhea present
 - 2nd tier
 - (Considered individually, if 1st tier labs and H&P do not reveal etiology)
 - CRP
 - Quantitative immunoglobulins
 - Stool culture and O&P (if not already done)
 - EBV/ CMV serologies, and other appropriate serologies
 - LP, if indicated
 - Diagnostic imaging
 - 1st tier
 - CXR
 - Sinus imaging

- 2nd tier
 - Bone scan
 - Nuclear tagged WBC scan
 - Echocardiogram
 - U/S vs. CT vs. MRI
- Other studies
 - Bone marrow biopsy
 - Other biopsies
 - Liver
 - Lymph node, etc.

Differential Diagnosis

1. Infectious, Systemic

- Benign "nonspecific" viral syndrome
- EBV
- CMV
- Viral hepatitis
- HIV
- Spirochete infections
 - Lyme
 - Cat Scratch
 - Leptospirosis
- Rickettsial infections
- Tuberculosis
- Salmonellosis
- Brucellosis
- Tularemia
- Malaria
- Toxoplasmosis
- Fungal infections

2. Infectious, localized

- Sinusitis
- Otitis media
- Pneumonia
- Bacteremia
- Tonsillitis
- UTI
- Meningitis
- Osteomyelitis
- Septic arthritis
- Endocarditis
- Occult abscesses
- Other focal bacterial infection

3. Connective tissue dz

- JRA
- SLE
- Acute rheumatic fever
- Vasculitis

4. Malignancies

- Leukemia
- Lymphoma
- Neuroblastoma
- Hepatoma
- Rhabdomyosarcoma
- Atrial myxoma

5. Miscellaneous

- Factitious fever
- Kawasaki Dz
- Familial Mediterranean fever
- Behcet syndrome
- Drug fever
- CNS dysfunction ("central")
- Immunodeficiency
- Inflammatory bowel dz
- Sarcoidosis
- Subdural hematoma/ effusion
- Thyroiditis
- Diabetes insipidus
- Idiopathic

Therapeutics

1. Acute tx

- ABCs
- Supplemental oxygen if hypoxic
- Empiric antibiotics not recommended until dx established, unless pt critically ill

2. Further mgmt

- See dx above
- Based upon specific etiology of fever

Follow-Up

1. Return to office

- Time frame for return visit
 - At least every 2-3 days until dx found, or fever resolves
- Recommendations for earlier follow-up
 - Sooner, if any clinical change.
 - Worsening clinical status
 - New complaint

2. Refer to specialist

- Consider ID consultation
- Consider Hematology/ Oncology consultation

3. Admit to hospital

- No formal recommendations exist on when to admit
 - However if pt is unstable or there is concern for factitious fever, consider admission

Prognosis

1. Most causes of FUO self-limited or treatable
2. 10 - 20% of FUO cases spontaneously resolve
3. 40% w/long-term morbidity
4. Cause-related mortality ranges from 9-17%

References

1. Approach to the child with fever of unknown origin. Up-To-Date [database online]. Updated October 2005. Available at <http://www.uptodateonline.com>. Accessed on August 3, 2007.
2. Powell K. Fever without a Focus. In: Behrman RE, Kliegman RM, Jenson HB, eds. Behrman: Nelson's Textbook of Pediatrics; 17th Ed. Philadelphia, PA: Saunders 2004; 843-846.
3. Kline MW, Lorin MI. Fever without Source. In: McMillan JA, DeAngelis CD, Feigin RD, Warshaw JB, eds. Oski's Pediatrics: Principles and Practice, 3rd Ed. Philadelphia, PA: Lippincott Williams & Wilkins 1999; 842-848.

Author: Elizabeth Rulon, MD, *FMR of Idaho*

Editor: Perry Brown, MD, *Idaho State University FPR*