Acute Fever Without Source: 3-36 Months

Background

1. Definition
    - Core body temp >102.2°F [39°C]
        - Some sources suggest 100.4°F [38°C]
    - No identifiable source by H&P
    - Duration of fever usually defined as 7 days or less
2. General information
    - Risk of serious dz, incr risk of:
        - Occult bacteremia
        - UTI
        - Pneumonia
        - Meningitis
        - Other serious bacterial infection
    - Impact of vaccines and vaccination status
        - Pneumococcal conjugate vaccine (PCV7) has significantly decr incidence of pneumococcal pneumonia and bacteremia
        - Hib conjugate vaccine has significantly decr incidence of Hib related illnesses and bacteremia
        - One study:
            - E. coli is now the most prevalent pathogen isolated in blood cultures

Pathophysiology

1. Pathology of disease
    - Pathophysiology/ mechanism of fever (brief)
        - Infection, inflammation, and trauma can all induce phagocytes to release cytokines into blood stream
        - These cytokines are then carried to anterior hypothalamus triggering an incr in synthesis of prostaglandins
        - Prostaglandins elevate set-point of hypothalamic thermostat
        - Result is an incr in body temp through elevated metabolic rate and muscle activity
    - Possible advantages of fever
        - Multiplication and survival of some bacteria and viruses is inhibited at temperatures of 104°F [40°C] or higher
        - Decr in serum iron
            - Some pathological bacteria need iron for multiplication
        - Incr lymphocyte and polymorphonuclear leukocyte activity
        - Incr interferon levels
    - Possible disadvantages of fever
        - Incr metabolic rate
        - Incr oxygen consumption
        - Incr carbon dioxide production
        - May precipitate febrile convulsions
        - Physical discomfort for pt
2. Incidence/ prevalence
    - Almost 1/3 of pediatric visits are for fever

- Almost all children will be evaluated for fever before their 3rd birthday
- From 0–2 yrs:
  - 65% of children visit a physician because of a febrile illness
  - In 75% of these visits, temperature is <102.2°F [39°C]
  - In 14%, fever has no apparent source

3. Morbidity/ mortality
   - Depends upon etiology of fever
   - Generally very low risk of morbidity/ mortality
     - Most illnesses viral or mild bacterial infections (i.e., AOM, sinusitis) that are self-limited

Diagnostics

1. History
   - Associated S/S
     - Nasal discharge
     - Cough
     - Dyspnea
     - HA
     - Ear pain
     - Sore throat
     - Diarrhea
     - Vomiting
     - Strong-smelling urine
     - Abdominal or flank pain
     - New onset urinary incontinence
     - Dysuria
     - Failure to thrive
     - Rash
   - Past medical hx
     - Previous urinary tract infections
     - Recurrent otitis media
     - Recurrent other infections/ immunodeficiency
   - Medications
     - Chronic medications
     - Antipyretic use
     - Note that response to antipyretics is not a reliable predictor of etiology or severity of illness
   - Family hx
   - Social hx
     - Exposures to known infective agents
     - Sick contacts
     - Pets in home
       - Dogs
       - Cats
       - Reptiles
       - Birds
       - Fish
     - Recent travel

- Immunization hx
  - Are immunizations up to date?
  - Unimmunized w/conjugate (Hib and Pneumococcus) vaccines incr risk of occult Hib and Pneumococcal bacteremia

2. Physical exam
   - Must be thorough
   - General (toxic vs. non-toxic)
     - Well vs. unwell appearing
     - Hydration status
     - Not able to elicit smile from pt
   - Temperature
     - Tympanic thermometry has very low sensitivity compared to rectal
   - VS: eval for
     - Tachycardia
     - Tachypnea
     - Pulse oximetry
       - Should be >95%
   - HEENT
     - Eye injection/ discharge
     - Nasal flaring
     - Appearance of tympanic membranes
     - Lesions in oropharynx
   - Neck
     - Palpable cervical lymph nodes
     - Position of trachea
     - Size of thyroid
   - Lungs
     - Intercostal retractions
     - Accessory muscle use
     - Decr breath sounds
     - Rales or rhonchi
   - Heart
     - Peripheral or central cyanosis
     - Cardiac murmurs
   - Abdomen
     - Distention
     - Visible hernias
     - Tenderness
     - Peritoneal signs such as guarding or rebound
   - GU
     - CVA tenderness
     - Urethral or vaginal discharge
     - Scrotal swelling or tenderness
   - Musculoskeletal
     - Joint tenderness, redness, or swelling
     - Bone tenderness or swelling

- Neuro
  - Lethargy
  - Uninterested in surroundings
  - Decr general tone
- Skin
  - Rash
  - Petechiae
  - Cellulitis

3. Diagnostic testing
   - CBC and blood culture
     - WBC >15,000: incr risk of occult bacteremia
       - CBC alone is not sensitive / specific enough to tell bacterial from viral infections
       - ANC has been proposed as a superior marker of serious bacterial infection
     - Manual differential results not highly sensitive or specific for serious bacterial infection
     - Waiting for cultures may delay tx
   - Urinalysis (UA) and urine culture
     - Bag specimen:
       - Ok for UA, but inadequate for urine culture
       - Often contaminated, such that specificity for UTI is poor
     - Cath specimen:
       - Preferred if clean catch is not possible
     - Suprapubic tap specimen:
       - If clean catch and catheterization are not possible
     - Normal UA:
       - Nitrite negative, WBC <10/hpf, RBC <10/hpf
     - Urine culture on all urine samples:
       - <2 yo
         - 15% of UTIs have normal UAs
       - For all abnormal UA results
       - When UTI is highly suspected
   - CSF studies
     - Consider if
       - <12–18 mos (meningeal exam not reliable at this age)
       - Meningeal signs present
       - Severe illness
     - Cultures
     - Gram stain
     - Cell count and differential
     - Protein
     - Glucose
   - Stool studies
     - Perform if bloody or chronic diarrhea
     - Can screen w/guaiac and fecal leukocytes
     - Consider culture, O&P, C. diff toxin, rotavirus Ag

- CRP
  - Not specific: thus generally not helpful
  - Elevates w/bacterial and viral infections
  - May help in evaluating progress of known dz
- Rapid Dx testing depending on clinical presentation and season
  - Influenza
  - Respiratory syncytial virus (RSV)
  - Enteroviruses
  - Severe bacterial infection is less likely if a viral etiology of fever is identified
- Procalcitonin
  - Rises more rapidly in bacterial infections than CRP
  - Clinical usefulness is currently uncertain and under investigation

4. Diagnostic imaging
   - Chest X-ray
     - Respiratory symptoms
     - Decr oximetry
     - Elevated WBC (esp. if WBC >20,000)
   - Sinus imaging (X-rays/ CT)
     - Sinus tenderness or discharge
     - Facial/ periorbital swelling
     - Significant purulent nasal discharge w/cough
     - Often unnecessary
   - Rarely, other imaging studies based upon clinical concern
     - Bone scan or MRI to assess for osteomyelitis
     - U/S or CT to assess for appendicitis

Differential Diagnosis

1. Key DDx
   - Bacterial
     - Streptococcal pharyngitis
     - Pneumonia
     - UTI
     - Meningitis
     - Bacteremia
   - Viral
     - Upper respiratory infection
     - Viral exanthems
     - Cytomegalovirus
     - Epstein-Barr virus
2. Extensive DDx
   - Infectious
     - Bacterial: generalized
       - Brucellosis
       - Cat scratch dz
       - Tuberculosis
       - Leptospirosis
       - Malaria
       - Salmonellosis

- Toxoplasmosis
- Tularemia

▪ Bacterial: localized
- Bone and joint infections
- Infective endocarditis
- Abdominal abscess/ appendicitis

▪ Viral
- Hepatitis viruses
- HIV
- Arbovirus

o Non-infectious

▪ Drug fever
- Allergic reaction
- Atropine
- Phenothiazines
- Anticholinergics
- Epinephrine

▪ Malignancy/ neoplasm
▪ Inflammatory bowel dz
▪ Juvenile rheumatoid arthritis
▪ CNS dysfunction
- Brain damage

▪ Factitious fever
- Absence of S/S w/high temperature
- Extreme temps
- No diaphoresis as fever resolves
- Failure of normal diurnal variation
- Discrepancies in reported vs. measured
- Consider measuring temp of freshly voided urine

▪ Diabetes insipidus
▪ Familial dysautonomia
▪ Infantile cortical hyperostosis

Therapeutics

1. Acute Tx

o Low risk

▪ Well appearing
▪ No co-morbid conditions
▪ Stable social situation
▪ Fully immunized
▪ WBC <15,000, normal UA, normal CXR if obtained
- If WBC >15, 000, consider
  - Parenteral ceftriaxone, or
  - PO high-dose amoxicillin or clindamycin or macrolide

▪ Recheck in 24 hrs

o High risk

▪ Ill appearing
▪ Co-morbid conditions
▪ Unstable social situation

        - Incompletely immunized
        - Consider admission to hospital, supportive care
        - Parenteral ceftriaxone
    2. Further mgmt (24 hrs)
        - Watch for
            - Lethargy
            - Incr fever
            - Decr appetite
            - Tachycardia
            - Tachypnea
        - Follow pending cultures daily
        - Consider admission to hospital if sx persist or worsen

Follow-Up

1. Return to office
    - 24 hrs after initial eval
    - Every one to three days thereafter until resolution
        - Depending on clinical progress
    - Ensure parents'
        - Telephone number is accurate
        - Know after hrs access options
        - Know worrisome S/S
    - Return sooner or go to ED if worsening of Sx:
        - VS
        - Appetite
        - Activity
2. Refer to specialist
    - Depends upon comfort level of PCP and capabilities of tx facility
3. Admit to hospital
    - Toxic appearance
    - Dehydration
    - Lethargy
    - Significant tachycardia or tachypnea
    - Positive culture w/o significant clinical improvement

Prognosis

1. Generally excellent w/close follow-up and appropriate interventions

References

1. Fever without a source in children 3 to 36 months of age. UpToDate Online 14.3; July 20, 2006. Available from: http://www.uptodateonline.com/utd/content/topic.do?topicKey=ped_emer/4803&;type=P&selectedTitle=3~8 Accessed August 30, 2007.
2. Evidence based clinical practice guideline for fever of uncertain source in children in 2 to 36 months of age, Cincinnati Children's Hospital Medical Center. National Guideline Clearinghouse. Available from: http://www.ngc.gov/summary/summary.aspx?doc_id=5613&;nbr=003783&string=fever+AND+children Accessed August 30, 2007

3. Clinical Policy for Children Younger than Three Years Presenting to the Emergency Department with Fever. Annals of Emergency Medicine Volume 42, Issue 4. American College of Emergency Phyisians; October 2003. Available from: http://www.mdconsult.com/das/article/body/79118619-3/jorg=guideline&;source=MI&sp=14100867&sid=629006770/N/382378/1.html. Accessed October 3, 2007.
4. Ishimine P. Fever Without a Source in Children 0 to 36 Months of Age. Pediatric Clinics of North America Volume 53, Issue 2. W.B. Saunders Company; 2006. Available from: http://www.mdconsult.com/das/article/body/79118619-4/jorg=clinics&;source=MI&sp=16115327&sid=629011985/N/527330/1.html. Accessed October 3, 2007.

Evidence-Based Inquiry

1. How accurate is ear thermometry for diagnosing fever in children?
2. Can you differentiate bacterial from viral pediatric infections based on the CBC?

Author: Ronald Healy, MD, *University of Washington Medical Center FMR-Harborview*

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