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
o 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
  o Must be thorough
  o General (toxic vs. non-toxic)
    ▪ Well vs. unwell appearing
    ▪ Hydration status
    ▪ Not able to elicit smile from pt
  o Temperature
    ▪ Tympanic thermometry has very low sensitivity compared to rectal
  o VS: eval for
    ▪ Tachycardia
    ▪ Tachypnea
    ▪ Pulse oximetry
      ▪ Should be >95%
  o HEENT
    ▪ Eye injection/ discharge
    ▪ Nasal flaring
    ▪ Appearance of tympanic membranes
    ▪ Lesions in oropharynx
  o Neck
    ▪ Palpable cervical lymph nodes
    ▪ Position of trachea
    ▪ Size of thyroid
  o Lungs
    ▪ Intercostal retractions
    ▪ Accessory muscle use
    ▪ Decr breath sounds
    ▪ Rales or rhonchi
  o Heart
    ▪ Peripheral or central cyanosis
    ▪ Cardiac murmurs
  o Abdomen
    ▪ Distention
    ▪ Visible hernias
    ▪ Tenderness
    ▪ Peritoneal signs such as guarding or rebound
  o GU
    ▪ CVA tenderness
    ▪ Urethral or vaginal discharge
    ▪ Scrotal swelling or tenderness
  o Musculoskeletal
    ▪ Joint tenderness, redness, or swelling
    ▪ Bone tenderness or swelling
Fever Without Source 3-36 Months

- Neuro
  - Lethargy
  - Uninterested in surroundings
  - Decreased general tone

- Skin
  - Rash
  - Petechiae
  - Cellulitis

3. Diagnostic testing
   - CBC and blood culture
     - WBC >15,000: increased 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
4.1.08

4. CRP
   - Not specific: thus generally not helpful
   - Elevates w/bacterial and viral infections
   - May help in evaluating progress of known dz

4. 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

4. 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 concer
     - 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
        o Parenteral ceftriaxone, or
        o 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:
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:


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?

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