

## Fever and Infections in Pediatrics

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## Pediatric Fever and illness

- The most common reason for children to be taken to the doctor for acute illness
- Major concern for parents
- Fever occurs in response to infection or inflammation
- Can be a result of a simple self limiting infection or a life threatening condition
- Has to be approached carefully

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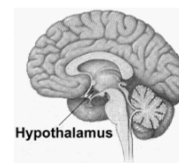
## Definition of Fever



- Core body temp is normally maintained within 1-1.5 degree C in the range of 37-38 degrees C
- Rectal temp > 38 degrees C (>100.4 degree F) is considered fever
- Body temp is maintained by a complex regulatory system in the anterior hypothalamus (like a thermostat)
- Development of fever begins with the release of endogenous pyrogens

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## Defining Fever



- Endogenous pyrogens stimulated by exogenous microbes and microbial toxins
- They include cytokines such as Interleukin 1 and 6, TNF, and interferon
- They reach the hypothalamus liberating arachidonic acid which metabolizes into prostaglandin E2
- Causes an elevation in the hypothalamic thermostat

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## Effects of Fever on the Body

- For each 1 degree C elevation in body temp with fever
- Metabolic rate increases 10-15%
- O<sub>2</sub> consumption increases 13%
- HR increases 10-15 BPM
- Acute phase response: increased leukocytes, CRP, Thrombocytosis

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## Benefits of Fever

- Protective role in the immune system
- Inhibition of growth and replication of microorganisms
- Enhances lymphocytes response to mitogens
- Increases bactericidal activity of neutrophils
- Increases antibody production (IgM)
- Decreases availability of free iron for bacterial replication



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## Patterns of Fever

- Varies depending on age
- Neonates may not have the ability to mount a febrile response despite significant infection
- Older infants and children <5yo may have an exaggerated response (temps up to 105 degrees F) even with benign viral infections
- Fever to this degree in children > 5yo of adolescents suggests a serious process
- Degree of Fever does not predict the source

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## Attenuated Fever Response

- Neonates
- Corticosteroids
- Malnourished individuals
- Uremia
- Immune deficiency

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## Approach to Fever: personal history

- Age
- Travel
- Exposures
- Recent antibiotics



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## Approach to Fever: Underlying disease

- Splenectomy
- Surgical implants / Central venous lines
- Immunodeficiency
- Chronic disease

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## Approach to Fever: Symptoms and Exam

- Ear pain
- Sore throat
- Respiratory symptoms
- GI / Abdominal symptoms
- Joint pain
- Need a full exam
- Overall appearance is most important (toxic or non toxic)
- Look for focal findings
- Neurologic exam

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Let's move on and treat the patient



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## Management Based on Age

- Neonates
- 28-90 days
- 3 – 6 months
- 6 – 24 months
- >24 months

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## Management < 28 days

- Neonates frequently do not show early signs of serious bacterial infections (SBI)
  - Rates of serious bacterial infection in febrile infants < 2 months is 8-14%
- Poor immunity
- Maternal pathogens (GBBS, E. coli) and Listeria
- Infants less than 28 days of age should have full evaluation including an LP and hospitalization with IV antibiotics
  - Ampicillin and Cefotaxime or Gentamicin

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## Management 29-60 Days

- Work-up CBC/D, BCX, UA/UCX (consider CRP and LP)
- Stool and CXR based on history / exam
- With normal labs and well appearing consider hospitalization for observation (await cultures 24-48 hours) antibiotics +/-
- Antibiotics and admission for patients with abnormal labs
  - Positive UA, WBC >15,000, Band >1500
  - LP if not already done
- Ceftriaxone or Cefotaxime

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## Management 60-90 Days

- At risk for occult bacteremia
  - Pneumococcus and HIB
- Exam may still be unreliable
- Beginning to develop immunity
- Limited investigations (blood and urine)
- Abnormal – management as previously described
- Low risk – follow-up within 24 hours with or without antibiotics
  - Strongly consider LP if giving antibiotics

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## Management 3-6 months

- Occult Bacteremia remains a concern
- Exam more reliable in identifying children at risk particularly those with meningitis
- Pneumococcal vaccine begins to have protective effect to what extent ?
- Fever cut-off raises to  $\geq 39$



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## Management 3-6 month cont....

- In patients without well defined source
  - ASOM, Bronchiolitis, Stomatitis, Croup, etc. treat the source
- Screen blood and urine without a defined source
- WBC >15,000 (send cultures) consider antibiotics (consensus recommendations)
- WBC >20,000 or ANC  $\geq 10,000$  give antibiotics
- Follow-up within 24 hours

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## Management 6-24 months

- In a fully immunized infant with fever  $\geq 39$
- Urine based on age and sex
  - Circumcised males >6 months unnecessary unless clinical condition dictates
  - Uncircumcised males until 1 year of age
  - Females until 2 years
- Consensus recommends blood <36 months
  - Prior to pneumococcal vaccine

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## Fever

- Fever in children with underlying illness
  - Oncology patients
    - At risk of overwhelming sepsis
    - When febrile: CBC, CXR, blood culture, urine culture, and LP when clinically indicated
    - Neutropenic patients at risk for Pseudomonas and other gram negative; combination of tobramycin and ceftazidime
    - Indwelling IV devices add vancomycin to tobramycin and ceftazidime

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## Fever in children with underlying illness

- Acquired Immunodeficiency Syndrome
  - Repeated risk of infection with common bacterial pathogens, risk of Pneumocystis carinii, mycobacterial infections (TB, AI), cryptococcosis, cytomegalovirus, Epstein-Barr virus, lymphoma and other malignancies
  - Low CD4 similar approach to neutropenic cancer patient; septic work up and broad spectrum antibiotic

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## Fever in child with underlying illness

- Sickle cell anemia
  - Repeated splenic infarction leads to functional asplenia susceptible to overwhelming infection esp. encapsulated organisms such as pneumococci and H. flu
  - Sickle cell patients with fever should have CBC and retic count infection esp. Parvovirus can cause aplastic crisis
  - Osteomyelitis should be suspected in fever and bone pain
  - CBC, blood culture, stool culture, and urine culture recommended
  - At risk for Salmonella bacteremia; antibiotic choice should include third gen ceph; hospitalization recommended

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## Fever in child with underlying illness

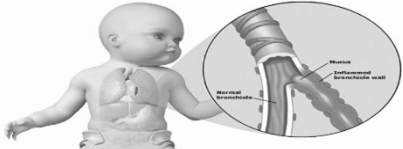
- Congenital heart disease
  - Children with valvular heart disease are at risk for endocarditis
  - Fever without obvious source with a new or changing murmur; hospitalization, serial blood cultures, echo, antibiotics against: S. viridans, S. aureus, S. fecalis, S. pneumo, enterococci, H. flu, and other gram neg rods
  - Suggested antibiotics include Vancomycin and Gentamycin until cultures are positive

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## Fever in child with underlying illness

- Ventriculoperitoneal shunts
  - Fever in this group must be evaluated for shunt infection esp if patient displays headache, stiff neck, vomiting, or irritability
  - Shunt reservoir should be aspirated and examined for pleocytosis and bacteria
  - Most common pathogen is S. epidermidis
  - CT head also warranted

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### Bronchiolitis and Fever

For those <29 days old  
RSV infection doesn't significantly alter the rate of SBI

For those 29-60 days old  
Those with clinical bronchiolitis (with or without documented RSV infection) are at significantly lower risk for SBI compared to others

For older children: far less risk of SBI, essentially you have a source for fever

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### Case example: putting it to work

- 8 year old girl is admitted to the surgical ward with severe abdominal pain
- Previously fit and well
- The resident is concerned about appendicitis

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### Lab evaluation

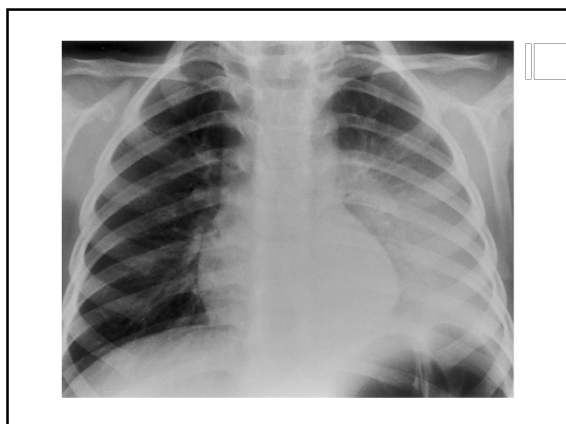
- Hb 12.4
- WCC 22 with increased neutrophils
- Plts 553
- CRP elevated

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### Critical thinking in decision making

- The surgical team ask you to see her the next day as they don't think she has an appendix
- What are your differentials?
- What are you looking for on examination?

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### Pneumonia "wow" great diagnosis

- What treatment are you going to recommend for a community acquired pneumonia?

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### Facts about Pneumonia

- Pneumonia diagnosed in nearly 2% of infants < 1 year and in 4% of children aged 1 to 5 years.
- Responsible agent determined in < 10%
- Estimated that 85% of pediatric pneumonias are caused by viral agents.
- Approximately 50% of the documented viral pneumonias in children are caused by respiratory syncytial virus; 25% by parainfluenza virus types 1 and 3
- A smaller number from influenza and adenovirus
- Bacterial and atypical agents also seen

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### Treatment

- Ceftriaxone or Cefuroxime
- Cefotaxime
- Add in Vanco if the patient is really sick or MRSA
- Macrolide added in for atypicals (Mycoplasma)
- After inpatient treatment, oral antibiotics as an outpatient
- Amoxicillin first choice (80 mg/Kg/day divided BID)
- Augmentin if previous use of antibiotics
- Finish Macrolide

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### Bacterial And Fungal Causes of Pneumonia Related to Age of the Pediatric Patient

Age Group	Common Pathogens
0-48 hrs.	Group B. Streptococci
1-14 days	Escherichia coli, Klebsiella pneumoniae, other Enterobacteriaceae, Listeria monocytogenes, Staphylococcus aureus, anaerobic bacteria, group B streptococci
2 wks to 2 mos (premature neonates)	Enterobacteriaceae, Group B streptococci, Staphylococcus aureus, Staphylococcus epidermidis, Candida Albicans, Haemophilus influenzae, Streptococcus pneumoniae
2 mos to 5 yrs	Haemophilus influenzae, Streptococcus pneumoniae
5-10 yrs	Streptococcus pneumoniae
10-21 years	Mycoplasma pneumoniae, Chlamydia pneumoniae (TWAR agent), Streptococcus pneumoniae

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Bacterial Pneumonia	Agent	Dosage
Outpatient Pneumonia	Oral amoxicillin	80-90 mg/kg/day ÷ BID
	Oral amoxicillin-clavulanate	80-90 mg/kg/day of amoxicillin ÷ BID
	Oral cefuroxime axetil	30 mg/kg/day ÷ BID
	Oral cefdinir	14mg/kg BID
Inpatient Pneumonia (Initial empiric therapy)	Intravenous ceftriaxone	100 mg/kg/day ÷ q12h
Pneumococcal susceptible Penicillin MIC ≤ 2 mcg/ml	Intravenous penicillin	250,000-400,000 U/kg/day ÷ q4-6h
Pneumococcal nonsusceptible to penicillin, susceptible to cephalosporin	Intravenous ceftriaxone or Intravenous cefotaxime	100 mg/kg/day ÷ q12h 225-300 mg/kg/day
Pneumococcal nonsusceptible to penicillin, nonsusceptible to cephalosporin	Intravenous vancomycin	40-60 mg/kg/day ÷ q6h

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### Considerations for Inpatient Management of Pneumonia

- Toxic appearance
- Respiratory distress
- Pleural effusion
- Age considerations:
  - <3 months
  - <3 years with lobar pneumonia
  - <5 years with lobar pneumonia (more than 1 lobe)
- Existing chronic disease
  - Pulmonary (including asthma)
  - Metabolic disorders
  - Cardiac
  - Anemia (including sickle cell disease)
  - Renal
  - Malignancies
  - Diabetes Mellitus
  - Immunocompromised host
  - Progression during outpatient therapy

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### Urinary Tract Infections

- Multicenter, prospective ED study of 1025 infants < 60 days old with T > 38.0°
- 9% had pyelonephritis
  - Uncircumcised males - 21%
  - Circumcised males - 2%
  - Females - 5%
  - Highest fever > 39.0 - 16%



Zorc JJ, Pediatrics 2005

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## UTI: Diagnostic Studies

### ▪ Routine Urinalysis

- White blood cell count  $\geq 10$ /high-power field
- Leukocyte esterase (Correlates with pyuria)
- Nitrites (bacteria slowly reduce nitrate to nitrite)
- Bacteria (Presence in unspun urine correlates with  $10^5$  bacteria/ml)
- White blood cell casts (Indicative of pyelonephritis)

### ▪ Serum C-Reactive Protein

- Elevated with pyelonephritis

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## UTI- Do You Need to Look Further?

- Cohort of 1895 infants 29-60 days old with fever and pyelonephritis
  - 63% males
  - 44% WBC  $> 15,000$
  - 6.5% bacteremia
    - 88% E. coli
  - 5 bacterial meningitis

Schnadower D, Pediatrics 2010

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## Criteria for Culture Diagnosis

<i>Specimen</i>	<i>Positive Result</i>
Suprapubic aspiration	$>100$
Catheterized urine	$>50,000$
Clean-voided (male)	$>100,000$
Clean-voided (female)	$>100,000$
Bagged urine	Not Acceptable

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## Treatment of UTI

- Choice based on most likely organism
- Clinical trial by Hoberman compared IV cefotaxime (200 mg/kg/day X 3 days, followed by oral cefoxime) with oral cefoxime (16 mg/kg once, followed by 8 mg/kg/day for 14 days) in children with febrile UTI
- Comparable outcomes seen
- Await sensitivities and choose outpatient antibiotics (Bactrim, Cefdinir etc)
- AAP recommends parenteral antibiotics in toxic children or those who cannot tolerate oral intake

Hoberman et al. NEJM 2003;348:195-202

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## Recommendations for Radiographic Evaluation

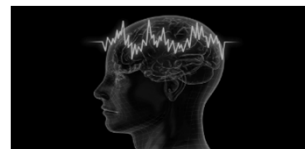
- AAP subcommittee recommends VCUG and ultrasound for all children  $< 2$  years
- However, Hoberman et al reported that ultrasound at the time of acute UTI is of little value and that VCUG only useful if prophylactic antibiotics will be given
- Area of continued controversy

Hoberman et al. NEJM 2003;348:195-202

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## Febrile seizure

- Ages 6 mo to 6 years old (considered simple)
  - Rapid rate in rise of Temp
  - 10% of all children
  - Twice as likely to have more of them if it occurs
  - No need for a work up
- If outside those ages, needs work up



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## Febrile seizure

- Synopsis of the American Academy of Pediatric practices parameters on the evaluation and treatment of children with febrile seizures (Paediatrics 1999)
  - LP strongly suggested in the first seizure in infants less than 12 month because signs and symptoms of meningitis may be absent in this age group
  - 12-18 months LP strongly suggested because sign of meningitis may be subtle in this age group
  - 18+ months LP only if signs and symptoms of meningitis

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## Febrile seizure

- EEG is not perform in a neurologically healthy child with simple febrile seizure
- The following routine lab should not be performed in simple febrile seizure: CBC, lytes, Ca, phos, Mg, or glucose
- Neuro-imaging should not be performed routinely on simple febrile seizure
- Anticonvulsant therapy is not recommended in simple febrile seizure

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## Kawasaki disease (Multisystem vasculitis)



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## Kawasaki's disease

- Persistent fever for >5days
- Conjunctivitis
- Oropharyngeal changes
- Changes in the peripheral extremities
- Skin rash
- Cervical lymphadenopathy

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## Kawasaki's and atypical cases

- Atypical or incomplete cases recognised
- Pathogenesis unknown
- Infectious agent suspected
- Under diagnosed

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## Kawasaki's Investigations

- Mild anaemia
- Raised WCC
- Raised inflammatory markers
- Raised platelets
- Elevated AST
- Albumin < 3.0
- Cardiac abnormalities of coronary arteries (need an ECHO)

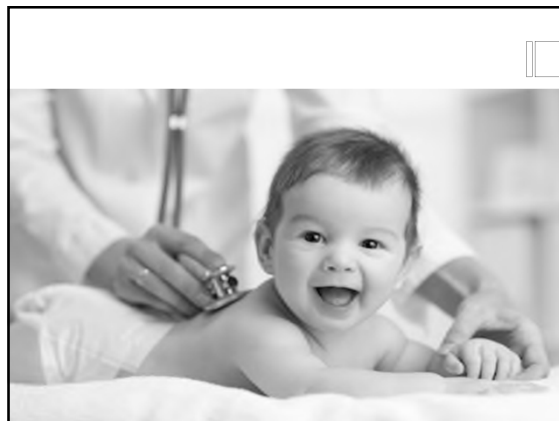
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## Kawasaki's Treatment

- IV Immunoglobulin 2g/kg within 10 days
- High dose aspirin 30-50mg/kg/24hrs until fever settles.
- Then reduced 3-5mg/kg o.d. for 4-6 weeks and until know echo normal
- Pediatric cardiology follow up, communicate with them

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## Fever is not always such a mystery

- You have a source (positive viral testing like influenza, RSV)
- Older children
- Obvious symptoms and exam findings (lymphadenopathy) with positive lab test (+ monostest / EBV)
- Always use clinical judgment, except always beware of the neonates (they will fool you)
- Call your favorite pediatrician or pediatric ID specialist

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## Thanks



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