Evaluation of the Febrile Infant

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IWK Pediatric ED

Disclosure

• No financial or other conflict of interest
Outline

• Definitions and background
• Illustrative Cases
• Construct a workable / working framework for evaluation of the young febrile infant
• Review the various components of risk assessment
• A few odds and ends

Objective

• An approach to “What am I supposed to do with this here...?”
Evaluation of Fever

The evaluation and management of the febrile infant < 91 days of age is one of the most common yet complex issues in pediatrics.


What is a fever?
Fever in Infants

- Fever is the most common reason for parents to seek medical care
- Fever accounts up to 20% pediatric ER visits
- Parents continue to worry that fever can cause brain damage, or even death (Crochetti *Pediatrics* 2001; 107: 1241-1246.)
- While most febrile infants have a benign viral illness the challenge is to find those with SBI

How to Measure Fever

- Temperature measured at the axilla shows insufficient agreement to rectal temperatures. More research is needed in neonates.
- Infrared ear thermometry would miss 3 or 4 of ten febrile children.
  — Dodd, J Clin Epi, 2006; 59: 354-357.
- Rectal temp if you really need to know.
  — And when very young, you really need to know.
Definitions

- Fever in young infants is considered a rectal temperature of greater to/equal 38 degrees
- Serious bacterial infection (SBI)
  - Bacteremia
  - Urinary tract infection (UTI)
  - Meningitis
  - Bacterial pneumonia
  - Bacterial enteritis

Cases
Case 1: Sick 3 month old

- Previously well three month old with a 12 hour history of fever
  - Progressive lethargy
  - Decreased intake
  - Respiratory distress
- Initial assessment
  - Temperate 38.3 degrees
  - Looks unwell, mottled, decreased responsiveness

Case 2: Febrile 15 day old

- Term infant - uncomplicated pregnancy
- Normal Labour and Delivery
- Home on second day of life
- Breast feeding well
- Temperature 38.3 rectally at home and in ER
- Nothing specific on examination
Case 3: Febrile 7 week old

- Term infant, previously well, normal L&D
- Sibling in day care
- Fever (38.3) without obvious source for 12 hours
- Perhaps slightly less intake
- No specific findings on exam - alert and appropriately responsive

Clinical Approach
Literature Review

- PubMed Search Terms: fever and infants
  - 21,524 citations
- PubMed Search Terms: management of febrile infants
  - 3,356 citations

Decision Making Framework

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<th>Age</th>
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### Sick Infants

- Regardless of age, sick patients require:
  - Appropriate resuscitation
  - Investigation (LP usually required – when stable)
  - Treatment
- Hospitalization is generally required for a young febrile infant who is unwell or septic
More on this later...

Sick Infants / Culture / IO

- In the middle of the night, in the middle of nowhere...
  - Remember IO access
  - Cultures are important – but mostly useful to guide ongoing treatment. Get what you can.
IO and Labs

• What can you send from an IO?
  – Particulate matter from an IO sample can cause problems with lab analyzers
  – YES: Point of Care glucose, I-Stat: glucose, pH and lactate are reliable
  – YES: Blood culture can be sent from IO aspirate.

• From the Royal Children's Hospital in Melbourne's IO Practice Guideline:
  – https://www.rch.org.au/clinicalguide/guideline_index/intraosseous_access/#laboratory-tests

Sick Infants

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## Well Infants – Fever Without Source

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Yale Observation Scale

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<tr>
<th>Observation item</th>
<th>Normal (Score=1)</th>
<th>Moderate Impairment (Score=2)</th>
<th>Severe Impairment (Score=3)</th>
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<tr>
<td>1. Quality of cry</td>
<td>Strong with normal tone OR Content and not crying</td>
<td>Whimpering OR Sobbing</td>
<td>Weak OR Moaning OR High pitched</td>
</tr>
<tr>
<td>2. Reaction to parent stimulation</td>
<td>Cries briefly then stops OR Content and not crying</td>
<td>Cries off and on</td>
<td>Continual cry OR Hardly responds</td>
</tr>
<tr>
<td>3. State variation</td>
<td>If awake → Stays awake OR If asleep and stimulated → wakes up quickly</td>
<td>Eyes close briefly OR Awakes up with prolonged stimulation</td>
<td>Awake OR Falls to sleep OR Does not wake up</td>
</tr>
<tr>
<td>4. Color</td>
<td>Pink</td>
<td>Pale extremities OR Cyanotic OR Mottled</td>
<td>Pale OR Cyanotic OR Mottled OR Ashen</td>
</tr>
<tr>
<td>5. Hydration</td>
<td>Skin normal, eyes normal AND Mucous membranes moist</td>
<td>Skin, eyes normal AND Mouth slightly dry</td>
<td>Skin dry/dry OR Dry or mucus membranes OR OR Sunken eyes</td>
</tr>
<tr>
<td>6. Response (talk, smile) to social overtures</td>
<td>Smiles OR Alerts (≤2 mo)</td>
<td>Brief smile OR Alerts briefly (≤2 mo)</td>
<td>No smile, Face anxious/dull/ expressionless OR No alerting (≥3 mo)</td>
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Clinical Appearance

- YOS of 10 or less has a 2.7% risk of SBI
- YOS interesting... but not much utility – but we probably do this clinically – if informally.
- **Clinical appearance: sensitivity for predicting SBI: 58%**
  - Woll, C. Peds Emerg Care 2017; 33: 748
**Well looking Neonate (<29d)**

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**Fever, SBI and Neonates**

- Various retrospective studies / few prospective
  - In neonates: SBI rates of 7-25% in range of studies
- Dorney, K.; Cur Opin Ped 2017; 29: 280
  - Age 0-28 days: 13% - (Age 29-60: 8.5%)
  - Meningitis 0.3% - UTI alone 84%
Febrile Neonates

• Bilavsky, E., et.al, A search for the ‘Holy Grail’ in the evaluation of febrile neonates aged 28 days or less: A prospective study, Scandanavian J ID 2011; 43: 264-268.
• Authors used the Rochester Criteria (more later)
• Total SBI rate 14%
  – 38% high risk
  – 62% low risk of whom 3.5% had SBI
  – NPV 96.5% (Close but not good enough).
  – Sensitivity: 84%

Febrile Neonates

• Aronson, P., Pediatr Emer Care 2019; 35: 22-7
• Retrospective cohort <60d with SBI
  – From 5011 febrile infants <60d
    • 1.7% bacteremia – 0.3% meningitis
• Sensitivity of low risk criteria: 92.7%
• Low risk criteria would have missed 1 infant younger than 28d with meningitis
• Confirms utility of Blood Culture in < 60 days
Week by Week <28 days

  - Retrospective review of 449 febrile neonates
  - Total SBI rate was 19.4% (90% UTI)
  - Low risk: 6.2% SBI (one meningitis)
    - WBC>15,000 PPV 33% for bacteremia
  - Week by week analysis: no difference for neonates aged 1-4 weeks

Bottom Line So Far

- The management of fever in this group is challenging because of its relatively high rate of SBI, concomitant with the lack of specific signs and symptoms to discriminate SBI from a simple viral infection.
Febrile Neonates

- No good predictors of SBI in neonates using history, exam and available lab tests
- A full septic workup is required followed by hospitalization for antibiotics pending cultures
- Well looking febrile <29d with normal labs can still have SBI – UTI / bacteremia / meningitis

Well looking Neonate (<29d)

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Two thirds done...

Over 2 months

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Fever in Young Infants

FWS over 2 months of age

- Hsiao, Pediatrics 2006;117;1695-1701:
  - Prospective study, N=449
  - SBI 10.3% age 2-6 months, bacteremia 0.9%
  - Consider UTI in this group – some risk factors:
  - Females: < 12 mos, T > 39, T > 2 days, Caucasian
  - Males: < 6 months, uncircumcised

Fever over 2 months of age

- Occult pneumonia - Consider CXR?
  - Retrospective study: N=1084
  - 57 or 1084 patients with fever and no clinical signs of pneumonia (5.7%).
  - Temp > 3 days; WBC > 20,000 had LR>2
    - Likelihood Ratio of 2 is not that helpful
    - We don’t often do CBC’s on febrile infants / children
Bacteremia over 2 months

  - 0.7% pathogen (7:1 contaminant)
  - 0.25% pathogen (7.6:1 contaminant)
- Waddle, Arch Dis Child 2009; 94: 144-147.
  - 0.4%
  - 0.34% pathogen (5:1 contaminant)

- Rate of bacteremia post PCV and HiB immunization makes good case for not doing blood cultures routinely.
  - Really sick, really young, really complicated...

UTI in Fever over 2 Months

- Waddle, Arch Dis Child 2009; 94: 144-147
  - Retrospective, linked patients to blood cultures
  - Bacteremia 0.4% (UTI : Bacteremia - 20:1)
  - UTI: 3-4% in boys < 1; 8-9% in girls < 2.
Fever over 2 months of age

- Clinical assessment more reliable
- Bacteremia less common (<1%)
- Consider UTI – low threshold for urine
- Occult pneumonia ??
  - prolonged T, WBC > 20,000
- Viral illness most common

Collecting Urine

- Catheter vs. bag specimen (PUC)?
  - Al-Orifi, J Pediatr 2000; 137: 221-6
    - Large cohort study Montreal Children’s
    - Contamination rate PUC = 62.8%
    - Suggests screening with PUC if concern for UTI
    - Catheter specimen if UA from bag positive
      - Positive UA: leukocytes, nitrates, >10 WBC
Alternative Collection

**ORIGINAL ARTICLE**

*Accuracy of a new clean-catch technique for diagnosis of urinary tract infection in infants younger than 90 days of age*

María Luisa Hermoso MD PhD1,2, Alfredo Tagarro MD PhD1,2, Aureli García-Peñalver MD3, Aída Sánchez MD2,3, Alfredo Colette MD PhD1,2, Pablo Gil MD PhD


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**Over 2 months**

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# Fever 29 – 56 days

Almost, nearly done...

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Fever 29 to 56 days

• Reported rates of SBI vary by study – 10-25%
  – UTI by far the most common
  – Bacteremia with negative UA: 1% (Gomez 2010)

• Various Risk Assessment Tools
  – Rochester
  – Philadelphia
  – Boston and others

Rochester / Philadelphia Criteria

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<td><strong>Rochester Criteria</strong></td>
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<tr>
<td>Infant appears generally well</td>
</tr>
<tr>
<td>Infant has been previously well</td>
</tr>
<tr>
<td>Born at term (&lt;37 weeks’ gestation)</td>
</tr>
<tr>
<td>Did not receive perinatal antimicrobial therapy</td>
</tr>
<tr>
<td>Was not treated for unexplained hyperbilirubinemia</td>
</tr>
<tr>
<td>Has not received and was not receiving antimicrobial agents</td>
</tr>
<tr>
<td>Had not been previously hospitalized</td>
</tr>
<tr>
<td>Had no chronic or underlying illness</td>
</tr>
<tr>
<td>Was not hospitalized longer than mother</td>
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<tr>
<td>No evidence of skin, soft tissue, bone, joint, or ear infection</td>
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<tr>
<td>Laboratory values</td>
</tr>
<tr>
<td>WBCs 5,000 to 15,000/mm³</td>
</tr>
<tr>
<td>Absolute band count ≤1,500/mm³</td>
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<tr>
<td>≤10 WBCs per high-power field on microscopic exam of spun urine</td>
</tr>
<tr>
<td>≤5 WBCs per high-power field on microscopic exam of a stool smear (for infants with diarrhea)</td>
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<tr>
<td>WBC = white blood cell; CSF = cerebrospinal fluid</td>
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Rochester Criteria (1985)

- Pre-conjugate vaccine era epidemiology notable for higher incidence of bacteremia: HIB, pneumococcus; GBS and listeria in neonates
- Current epidemiology: most common SBI is UTI, bacteremia species have changed
  - E.coli, GBS, Staph aureas, Klebsiella, enterococcus
  - GBS incidence has also declined - IAP
    - Woll, C., Peds Emerg Care 2017; 33: 748

Rochester Criteria

- Has been well (No previous antibiotics)
- Is well (Appears well / no clinical focus)
- WBC 5-15,000
- Bands < 1500
- Normal UA
- Appealing as no LP initially
Risk Assessment Tools

  – prospectively enrolled >400 infants less than 56 days of age to either the Rochester or Philadelphia criteria
  – SBI 25% of the total group
  – Three infants classified as low risk had SBI but no adverse outcome (all three bacteremia)

• Rochester Criteria: NPV 97.3%
• Philadelphia Criteria: NPV 97.1%

Lab Components

• Blood Culture
• UA
• CBC
• Blood Culture
• Others: CRP, PCT – not part of Rochester
CBC: sensitivity 70-80%

  - Prospective study, N=1257
  - Sensitivity in range of 0.7 for WBC, ANC, %ANC
  - Still a useful part of routine work-up but perhaps better diagnostic markers such as CRP, PCT?
  - WBC Sensitivity 0.81 / ANC 0.80

Low WBC?

- What about leukopenia (WBC < 5000)?
- Gomez, PIDJ 2012; 31: 92-95.
  - Retrospective, N=1365 (81 with WBC 2500-4900)
  - Total SBI 14.8% leukopenia, 15.5% normal WBC
  - No difference with ANC < 1000 or ANC < 500
- Comment in Discussion: “the risk of bacteremia is related to the general appearance and urine dipstick result.”
### UA in Febrile Infants

  - Sensitivity of UA for UTI – 64%
  - Negative Predictive Value – 96%
  - Retrospective study

- **Tzimenatos, Pediatrics 2018; 141: e20173068**
  - Secondary analysis of prospective study
  - Of 4147 patients < 60d, 7% had UTI’s (> 50,000)
  - Sensitivity of UA: 0.94 – Specificity 0.91

### Blood Cultures

- **Gomez, PIDJ 2010; 29: 43-47.**
  - 1% with negative UA

- **Rudinsky, Acad Emeg Med 2009; 16:585-590.**
  - 0.7% (7:1 contaminant : pathogen)

- **Colvin, Clinical Pediatrics 2012, 51: 51-57.**
  - 0.7%

- **Manzano, Arch Dis Child 2011; 96: 440-446.**
  - 0.3% (age 1-36 months)
CRP in Fever Evaluation

• CRP: acute phase reactant released from the liver in response to an inflammatory stimulus
  – released 4-6 hours after stimulus
  – doubles every 8 hours
  – peaking between 36 and 50 hours.
  – The half-life of CRP is short, in the range of 4 to 8 hours.

CRP in Fever Evaluation

  – 10 Studies and 2046 patients
    • Sensitivity .77
    • Positive LR 3.64; Negative LR 0.29
  – moderate and independent but limited value in ruling out SBI in an infant with fever due to the overlap between CRP values in bacterial and viral infections
Procalcitonin (PCT)

- PCT released liver / monocytes in response to bacterial infection
  - Detected within 4 hours of onset of infection
  - Peak after 6 hours – sustained 8-24 hours
  - Different cut off points in different studies
  - Challenge of sensitivity vs. specificity

Procalcitonin in Fever

  - Systematic Review of 7 studies on PCT
  - Overall RR = 3.97 for SBI with PCT > 0.3 ng/ml
  - PCT alone is inferior to clinical prediction rules
  - May be an adjunct to prediction rule
Procalcitonin in Fever


<table>
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<tr>
<th>Study Name</th>
<th>Relative Risk</th>
<th>95% CI</th>
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<td>Andreola, et. al. 2007 (35)</td>
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<td>Olaciregui, et. al. 2009 (41)</td>
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<td>Woelker, et. al., 2012 (40)</td>
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ROC for PCT and CRP

Combined Lab Scores

- Galetto-Lacour 2010: lab score combining CRP, PCT, UA
  - Sensitivity 78% - Specificity 90%
- Olaciregui 2009: well infant, FWS, negative UA, WBC 5000-15000, CRP < 30mg/L, PCT < 0.5 ng/L
  - NPV 96% (100% for bacteremia / sepsis)
- Garra 2005: Rochester criteria
  - NPV 97.3%

Clinical Predication Rule

- Prospective observational study of febrile infants less than 60 days of age.
  - 908 infants to derive the rule, 913 to validate.
- Low risk: neg. UA, ANC < 4090, ProCal < 1.71
- Negative predictive value: 99.6%
  - No missed bacterial meningitis (3 HSV < 29 days)
Clinical Predication Rule

Figure 2. Recursive Partitioning Analysis

Risk Assessment Tools

  - Systematic review 21 studies over 23 years
  - Prospective and retrospective – N=8540
  - Various risk criteria used: Rochester, Philadelphia, Boston or comparisons
  - The proportion of low risk patients declined over the 23 years
  - Prospective studies with no treatment option had the lowest rate of missed SBI
Risk Assessment Tools

• “The careful application of these low risk criteria was very effective in identifying children from whom empiric antibiotic therapy could be withheld.” Huppler 2010

• “Fever is not caused by a deficit in ceftriaxone.”
  • Girodias and Bailey, Paed Child Health 2003; 8: 78-82.

Fever 29-56 days

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### Febrile Infant (Girodias 2003)

#### Neonate
- 0-28 days
- CBC
- Catheter Urine
- Blood Culture
- LP
- +/- CXR, +/- Stool

**Disposition:**
- Hospitalize, Empiric antibiotics
- Ampicillin / Gentamicin
- Ampicillin / Cefotaxime

#### 1-2 (or 3) Months
- 29-56 (or 90) days
- CBC
- Catheter Urine
- Blood Culture
- +/-LP
- +/-CXR

**Disposition:**
- Home with follow up +/- Antibiotics
- Hospitalize +/- Antibiotics
- Ampicillin / Cefotaxime

#### Over 2 (or 3) Months
- Over 2 or 3 months
- +/- CBC
- +/- Blood culture
- +/- Urine
- +/- LP
- +/- CXR

**Disposition:**
- Likely Home
- Treat and follow up as appropriate
## Febrile Infant (Girodias 2003)

### Neonate
- 0-28 days
- CBC
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- Blood Culture
- LP
- +/- CXR, +/- Stool

**Disposition:**
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### 1-2 (or 3) Months
- 29-56 (or 90) days
- CBC
- Catheter Urine
- Blood Culture
- +/- LP – IF ABx
- +/- CXR

**Disposition:**
- Home with follow up
- +/- Antibiotics
- Hospitalize
- +/- Antibiotics
- Ampicillin / Cefotaxime

### Over 2 (or 3) Months
- Over 2 or 3 months
- +/- CBC
- +/- Blood culture
- +/- Urine
- +/- LP
- +/- CXR

**Disposition:**
- Likely Home
- Treat and follow up as appropriate

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### Fever Pathway CHOP 2019

ED Pathway for Evaluation/Treatment of Febrile Young Infants (0-56 Days Old)

- Study and Note
- Fever Initial Notes
- Fever Episodes

**Low Risk for Bacterial Meningitis:**
- CSF normal
- White blood cell count ≤ 1500
- No symptoms or toxic findings
- Blood count normal
- No seizures

**High Risk:**
- CSF abnormal
- White blood cell count > 1500
- Toxic appearance
- Seizures

Recall Low Risk Criteria, including CBC and enhanced ED (without ESR)

- High Risk
- Low Risk
- No additional studies

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73

74
Case 1: Sick 3 month old

- Previously well three month old with a 12 hour history of fever
  - Progressive lethargy
  - Decreased intake
  - Respiratory distress
- Initial assessment
  - Temperate 38.3 degrees
  - Looks unwell, mottled, decreased responsiveness
Case 1: Unwell Infant

• Regardless of age, sick patients require:
  – Appropriate resuscitation
  – Investigation (Blood/Urine/CSF cultures)
    • Defer LP if unstable
  – Treatment: Ampicillin/Cefotaxime +/- Vanco
• Hospitalization required for a young febrile infant who is unwell or septic

More on this later...
Case 2: Febrile 15 day old

- Term infant - uncomplicated pregnancy
- Normal Labour and Delivery
- Home on second day of life
- Breast feeding well
- Temperature 38.3 rectally at home and in ER
- Nothing specific on examination

Evaluation of FWS – Case 2

<table>
<thead>
<tr>
<th>Neonate</th>
<th>29-56 days</th>
<th>Over 2 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-28 days</td>
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</tr>
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<td>+/- CBC</td>
</tr>
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<td>+/- Blood culture</td>
</tr>
<tr>
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<td>+/- Urine</td>
</tr>
<tr>
<td>LP</td>
<td>+/- LP</td>
<td>+/- LP</td>
</tr>
<tr>
<td>Disposition:</td>
<td>Disposition:</td>
<td>Disposition:</td>
</tr>
<tr>
<td>Hospitalize</td>
<td>Home with follow up</td>
<td>Likely Home</td>
</tr>
<tr>
<td>Amp / Cefotaxime</td>
<td>+/- Antibiotics</td>
<td>Treat and follow up as appropriate</td>
</tr>
<tr>
<td>Disposition:</td>
<td>+/- Antibiotics</td>
<td>Disposition:</td>
</tr>
</tbody>
</table>
Case 3: Febrile 7 week old

- Term infant, previously well, normal L&D
- Sibling in day care
- Fever (38.3) without obvious source for 12 hours
- Perhaps slightly less intake
- No specific findings on exam - alert and appropriately responsive

### Evaluation of FWS – Case 3

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<tr>
<td>LP</td>
<td>LP</td>
<td>+/- LP</td>
</tr>
<tr>
<td>+/- CKR, +/- Stool</td>
<td>+/- CKR</td>
<td>+/- CXR</td>
</tr>
</tbody>
</table>

**Disposition:**
- Hospitalize, Empiric antibiotics
- Home with follow up without antibiotics
- Hospitalize if social or geographic risk factors
- No Abx if low risk
- LP if empiric ABx
- Likely Home
- Treat and follow up as appropriate
Odds and Ends

Other Scenarios

• What if the UA is positive?
• SBI in bronchiolitis / viral co-infection
• Fever at home versus documented ED fever
• Fever after recent vaccination
• Hyperpyrexia
• Neonatal HSV
Rochester and Positive UA

- Paquette, K. Pediatr Emer Care 2011; 27: 1057-1061. – LP necessary with +UA?
  - Retrospective N=392
  - Four patients had meningitis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, d</td>
<td>71</td>
<td>49</td>
<td>41</td>
<td>33</td>
</tr>
<tr>
<td>Clinical</td>
<td>38.5°C (rectal), rash, irritability, lethargy, and decreased feeding</td>
<td>39.7°C (oral), hypotension responsive to bolus, lethargy, potential rash</td>
<td>38.6°C (oral), shortness of breath, grunting, tachycardia, and decreased feeling</td>
<td>38.0°C (oral), tachypnea, tachycardia, tachycardia, and decreased breathing</td>
</tr>
<tr>
<td>Peripheral WBC</td>
<td>9.3 x 10^9/L</td>
<td>4.9 x 10^9/L</td>
<td>6.1 x 10^9/L</td>
<td>2.3 x 10^9/L</td>
</tr>
<tr>
<td>Blood culture</td>
<td>E. coli</td>
<td>K. pneumonia (G)</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Urine culture</td>
<td>E. coli &gt;10^5/mL</td>
<td>K. meningitidis (G)</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>CSF culture</td>
<td>E. coli</td>
<td>E. coli</td>
<td>Negative</td>
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RBC indicates red blood cells.
Rochester and Positive UA

• Paquette, K. Pediatr Emer Care 2011; 27: 1057-1061. – LP necessary with +UA?
  – Retrospective N=392
  – NPV for +UA in meningitis: 98.2%
  – Routine LP may not be necessary if +UA

• IWK practice: variable (younger than 6 weeks often get LP / admitted for IV Abx if UTI).

SBI and Bronchiolitis

  – Systematic Review 11 studies
  – No meningitis
  – UTI prevalence 3.3%

• Routine UTI screening reasonable in the context of fever and clinical bronchiolitis in young infants.
SBI – Viral Co-Infection

• Mahajan, P. J Pediatr 2018; 203: 86-91
• Secondary analysis for prospective PECARN study involving 6014 infants – this study 4778
• Viral positive vs negative: SBI 3.7% vs. 12.7%
• Virus positive – most SBI’s UTI though of the entire group: SBI 3.7% / UTI 2.8% / Bacteremia 0.8% / Meningitis 0.4%
• Febrile infants <60d with viral infections are at significantly lower, but not negligible risk of SBI’s including bacteremia and meningitis.

Reported versus ED Verified

• A fever measured at home is equally important to a fever measured in the ED
  – Prospective study – N=399, 35.8% by history only
  – SBI 8.4% versus 18% with ED documented fever
  – All were UTI’s in the fever by history only
Reported versus ED Verified

– Secondary analysis for prospective PECARN study involving 6014 infants
  • This study 3825:
– SBI in Hx versus documented: 8.8% versus 12.8%
  • <28 days: SBI 12% / UTI 9.5% / Bacteremia 3.5% / Meningitis 1.6%
  • 29-60 days: SBI 7% / UTI 6.6% / Bacteremia 0.5% / Meningitis 0.6%
– The small risk reduction in this group is unlikely to alter decision making

Fever / Recent Immunization

• Wolff; Acad Emerg Med 2009; 16: 1284
• Retrospective Review: 1978 total, 213 recently immunized
• Of the total group of recently immunized infants:
  – Prevalence SBI: 2.8%
  – RR: 0.41
• RI presenting within 24 hours of immunization:
  – Prevalence of SBI: 0.6%
  – RR: 0.09
• Presenting after 24 hours of immunization
  – Prevalence of SBI: 8.9% (= baseline for the larger group)

Among febrile infants, the prevalence of SBI is less in the initial 24 hours following immunizations. However, there is still a substantial risk of UTI. Therefore, urine testing should be considered in febrile infants who present within 24 hours of immunization.
Hyperpyrexia

- Rosenfeld-Yehoshua, Eur J Ped 2018; 177: 337
- In the era of conjugate vaccines, is a fever above 40°C associated with higher risk for SBI?
- Systematic Review – 11 studies (most pre 2000)
  - Under 3 months of age: OR 3.21
  - Older children: OR 1.36
- *In this meta-analysis...fever above 40°C was associated with increased risk for SBI in young infants, but the risk in older children was minimal.*

Neonatal HSV

- HSV may present as fever in neonates
  - Long, PIDJ 2011; 30: 556-561
    - 50% presented with non-specific symptoms (<21d)
    - 11% had maternal Hx/ one third visible lesions
    - One third had CSF WBC < 20, half RBC < 100
    - Overall rate of HSV - 0.2% febrile neonates
Neonatal HSV

- 20-40% of neonatal HSV cases never manifest skin lesions
- Typically HSV type 2 acquired during delivery
- Primary maternal infection at time of delivery: 40-50% risk of transmission
- Secondary maternal infection: 1-2% risk of transmission at time of delivery
Neonatal HSV

- Weeks 2-3 most common
- In septic-appearing neonate, especially if **lethargy, seizures**, unexplained acute hepatitis, HSV risk factors → consider acyclovir
- Treatment: Acyclovir 60 mg/kg/day IV divided Q8H
Conclusions

- Young febrile infants have a significant risk of SBI with UTI being the most common source
- All sick infants require an appropriate investigation and treatment (don’t forget LP)
- There are no good predictors of SBI in neonates using history, exam and available lab tests
- The careful application of risk assessment tools is effective in febrile infants 1-2 months of age
- Rochester still works – CRP, PCT still not proven
- PCT may have a role as part of a decision rule

References

- Murphy, et.al. Occult pneumonia... Acad Emerg Med 2007; 14: 243-249.
- Bilavsky, et.al. CBC for febrile infants... Acta Ped 2010; 99: 1380
References

- Galetto-Lacour, et.al. Validation lab score... Arch Dis Child 2010; 95: 968-973.
- Long, PIDI 2011; 30: 556-561
- Rosenfeld-Yehoshua, Eur J Ped 2018; 177: 337

- Girodias and Bailey Approach to the febrile child: A challenge bridging the gap between the literature and clinical practice. Pediatr Child Health 2003; 8: 76-82. *** Useful, practical review though a bit dated. ***

Questions/Comments?