Pediatric Infectious Disease Concerns in Primary Care

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Objectives

• Review challenging pediatric infectious diseases which may be seen in a primary care setting.
• Identify initial steps helpful in initiating an infectious diseases work-up.
• Recognize warning signs that should alert a primary care provider to a possibly fatal, pediatric infectious disease.
Conflict of Interest Disclosure

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I do not intend to discuss an unapproved or investigative use of a commercial product or device in my presentation.
Cervical Adenopathy

- Posterior auricular
- Occipital
- Superficial cervical
  - Lower ear and parotid
- Deep cervical
  - Other nodes of head and neck, occipital scalp, ear, back of neck, tongue, trachea, nasopharynx, nasal cavities, palate, esophagus
- Posterior cervical
- Preauricular
- Parotid
- Tonsillar
  - (jugulodigastric)
- Submental
  - Lower lip, floor of mouth, apex of tongue
- Submandibular
  - Cheek, side of nose, lower lip, gums, anterior tongue
- Supraclavicular
  - Thorax and abdomen

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Cervical Adenopathy

• Acute (55%):  
  – Reactive  
  – Bacterial  
  – Viral  

• Chronic (45%):  
  – Neoplastic disease  
  – Non-tuberculous Mycobacteria  
  – Cat-scratch lymphadenitis  
  – EBV  
  – HIV
Cervical Adenopathy - Bacterial

- **Presentation:**
  - Fever
  - Acute swelling with pain
  - Erythema & induration

- **Diagnosis:**
  - CBC w/ diff
  - Blood Culture

- **Management:**
  - Cephalexin vs Clindamycin
Cat Scratch Adenitis

• Bartonella hensellae
• Presentation:
  – Sub-acute onset
  – Rare fever
  – Minimal erythema initially
  – Papule at inoculation site
• Diagnosis: serology
• Management:
  – Tincture of time VS Azithromycin
  – Surgical I&D
Cervical Adenopathy - Mycobacterial

• Non-tuberculous Mycobacteria (MAI) VS M. tuberculosis
• Presentation:
  – Cervical vs supra-clavicular nodes
  – Afebrile
  – Minimally tender
  – Minimal erythema
  – PICA
• Diagnosis: History + PPD
Cervical Adenopathy - Mycobacterial

• Treatment – NTM:
  – Azithromycin vs Clarithromycin
  – Ciprofloxacin OR
  – Rifampin/Rifabutin

• Surgery:
  – Excisional Biopsy
  – Fistula formation
  – Location and surgical risk
  – Spontaneous resolution?
Epstein-Barr Virus

Prolonged fever
Rash with abx
Prominent LAD
Pharyngitis w/ exudate
FATIGUE! (> 10 y.o.)
Atypical < 10 y.o.
Epstein-Barr diagnosis
### TABLE 4: Sample Clinical Scenario for Evaluation and Treatment of the Infant Exposed to HIV-1 in the United States

<table>
<thead>
<tr>
<th>Timing (Infant Age)</th>
<th>Action</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>History and physical examination; assess risk of other infections; start ARV prophylaxis; check hemoglobin level</td>
<td>HIV-1 NAAT is not needed at birth in this setting, because risk of in utero transmission is low; for infant whose mother had high virus load during pregnancy, consider HIV-1 NAAT at this time</td>
</tr>
<tr>
<td>14 d</td>
<td>HIV-1 NAAT</td>
<td>If result is negative, repeat at 4 wk&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
<tr>
<td>4 wk</td>
<td>HIV-1 NAAT</td>
<td>If result is negative, HIV-1 infection is presumptively excluded (given previous negative result at ≥ 2 wk of age)</td>
</tr>
<tr>
<td>6 wk</td>
<td>Stop ARV prophylaxis</td>
<td>PCP prophylaxis is not needed if HIV-1 NAAT result is negative at 14 d and 4 wk of age&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>8 wk</td>
<td>No HIV-1 NAAT needed if previous test results were negative at 14 d and 4 wk of age</td>
<td>A single negative result of HIV-1 NAAT performed at 8 wk of age allows presumptive exclusion of HIV-1 infection&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>4 mo</td>
<td>HIV-1 NAAT</td>
<td>If negative, HIV-1 infection is definitively excluded in the infant with previous presumptive exclusion</td>
</tr>
<tr>
<td>12–18 mo</td>
<td>Enzyme immunoassay for antibody to HIV</td>
<td>To confirm the absence of HIV infection&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- HIV DNA PCR at 2 & 4 weeks
- AZT 2 mg/kg/dose Q6 until 5-6 weeks old
- F/U Peds ID at 4 weeks
- Presumptive negative at 4 weeks
- Definite negative at 4 months

Pediatrics 2009; 123 (1), 175
Perinatal HIV – today…

• 66% reduction in risk of perinatal transmission
• 5-10% transmission
• On-going issues:
  – Breastfeeding
  – C-section benefit?
  – Identifying HIV-infected mothers
New trends in HIV/AIDS

• Few perinatal HIV cases
• International refugees/adoptees
• Emerging teen-young adult HIV:
  – Immortality beliefs
  – HIV/AIDS ≠ Death Sentence
  – High risk exposures:
    • Intercourse
    • IVDU
    • Substance abuse and High risk associates
Adolescent presentation

• Generalized lymphadenopathy
• FUO
• Weight loss (unintentional)
• Organomegaly
• Acute antiretroviral syndrome
• “heterosexual”
• “no risks”
Pediatric HIV/AIDS

• Clinical therapy:
  – HAART
  – Opportunistic infections
  – Nutrition, lipodystrophy

• Socioeconomic:
  – Orphan
  – Medication adherence
  – Depression and psychosis
  – Social isolation
Periodic Fevers

Typical temperature chart of *P. vivax* infection showing tertian periodicity related to the maturation and rupture of erythrocytic schizonts.

Typical temperature chart of *P. malariae* infection showing quartan periodicity.

Typical temperature chart of *P. falciparum* infection showing irregular tertian periodicity and the influence of successful treatment.
Periodic Fevers

- Common
- Truly periodic?
- 12 febrile illnesses/year
- Viruses
- AOM
- Pharyngitis
- UTI
- Periodic Fever Syndromes
Periodic Fever Syndromes

- FMF
- TRAPS
- Cyclic Neutropenia
- Hyperimmunoglobulin D Syndrome
- PFAPA
FMF

• Familial Mediterranean Fever

• Presentation:
  – Fever X 3 days
  – Serositis: peritonitis, pleuritis, arthritis
  – Exploratory laparotomy

• Diagnosis:
  – Clinical criteria published
  – Mutation analysis MEFV gene

• Treatment: Colchicine
TRAPS

• TNF Receptor Associated Periodic Syndrome

• Presentation (Q 5 – 6 weeks):
  – Fever X 5 – 14 days
  – 80%: myalgias, rash, conjunctivitis, periorbital edema

• Diagnosis:
  – Exclude alternate Dx
  – ↑ ESR and CRP
  – Mutation analysis TNFR1 gene

• Treatment: steroids > NSAIDs
Cyclic Neutropenia

- Cyclical retention of Neutrophils
- Periodic peripheral neutropenia
- ANC = % pmn X total WBC
- Presentation: Fevers and mucositis

Diagnosis:
- CBC w/ diff
- Timing!!!

Management:
- Heme/Onc referral
- GCSF
Hyperimmunoglobulin D Syndrome

- IgD and Mevalonate Kinase Deficiency
- Partially predictable events
- Presentation (3 – 7 days):
  - Fever + rigors
  - GI symptoms (N/V/D)
  - Lymphadenopathy
  - (rash, arthritis, splenomegaly)
- Diagnosis: ↑ IgD and IgA
- Treatment: NSAIDs > steroids
PFAPA

• Periodic Fever, Aphthous stomatitis, Pharyngitis, and Adenitis

• Presentation (3 -4 days):
  – Strikingly predictable fever episodes
  – Associated cervical LAD, aphthous ulcers
  – Sore throat vs abdominal pain

• Diagnosis:
  – Exclude alternate Dx
  – ESR and CRP, +leukocytosis

• Treatment: Prednisone > T&A
Routine illnesses gone bad…
Neonatal Herpes simplex disease

- SEM (Skin, Eye, Mucous Membrane)
- Disseminated
- Encephalitis
- Significant minority without skin lesions:
  - 39% of pts with disseminated, 32% of CNS and 17% of SEM (skin, eye, mucous membranes)
Herpes
Neonatal Herpes simplex disease

• Risk of transmission:
  – Primary disease = 50%
  – Reactivated disease = 5%

• Transmission: >70% cervical lesions

• Maternal (paternal) history unreliable!
  – Kaiser & Washington studies

• Maternal suppressive Acyclovir?
Herpes simplex

- Tests: Viral culture and FA staining of lesions. Throat, CSF, brain, urine cultures, CSF PCR
- Treatment: Acyclovir
- Prevention: Deliver by C-section if active lesions
Neonatal HSV recurrence

• Unclear risk of recurrence
• >2 episodes recurrence = cognitive risk
• Role of suppressive Acylovir?
  – Kimberlin et al.
  – 74 neonates (45 CNS + 29 SEM)
  – Acyclovir 300 mg/m²/dose TID X 6 mo.
  – Improved neurodevelopmental outcomes

NEJM 2011;365:1284
Croup...
Croup

• Acute laryngotracheobronchitis
• Spasmodic croup
• Varying degrees of laryngeal obstruction (subglottic edema)
• Age:
  – 6 months - 6 years
  – Incidence = 3/100 children < 6 y.o.
• Significance:
  – 1.3% hospitalized
  – Annual cost for hospitalization = $56 million
Croup

- Parainfluenza 1
- Peak incidence in fall
- Others:
  - Parainfluenza 3
  - RSV
  - Influenza A & B
  - Adenoviruses
Croup

• Symptoms:
  – Nasal stuffiness, sore throat
  – Fever within 24 hours
  – Harsh, seal-like barking cough
  – Inspiratory stridor, retractions, dyspnea
• Degree of obstruction wax and wane
• Acute symptoms last 3-4 days
• Hypoxemia and CO2 retention may occur from progressive obstruction
Croup-Differential Diagnosis

- Infectious
  - Epiglottitis
  - Bacterial tracheitis
  - Diphtheria
  - Retropharyngeal abscess
  - Peritonsillar abscess
- Noninfectious
  - Foreign body
  - Trauma
  - Allergic/angio-neurotic edema
  - Upper airway burns
  - Vascular ring

Complications: Pneumonia
Croup-Diagnosis

- Clinical diagnosis
- Presence of
  - Sudden onset
  - High fever
  - Increased WBC (left shift - differential)
  - Muffled/hot-potato voice
  - Drooling
  - =BAD
Rocky Mountain Spotted Fever

Doc -- PLEASE don't miss this one!
The rash is usually absent at the onset, and may not appear.

"The usual" antibiotics that kill most bugs don't affect RMSF.

Easy to treat; often fatal if missed!

Uh, there weren't any ticks on me when I got home.

rash moves centripetally and becomes hemorrhagic

check palms and soles

spring and summer
Rocky Mountain Spotted Fever

- *Rickettsia rickettsii*
- 16 patients:
  - 13 (81%) children (<12 years)
  - 15 (94%) hospitalized
  - 2 deaths
- Tick-infested dogs
- 4 patients + tick bites; all + contact with dogs
- *Rhipicephalus sanguineus*

NEJM 2005, 353:587-594
Reported RMSF, 2008-2013

*2013 data reporting not complete

Number of Cases
- 0 - 0
- 1 - 1
- 2 - 2
- 3 - 5
- 6 - 14
- 15 - 117

Data and slide courtesy of Dr. J. McQuiston, Rickettsial Branch-CDC
Community Risk Factors

Slide courtesy of Dr. J. McQuiston, Rickettsial Branch-CDC
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Rocky Mountain Spotted Fever

• Rash:
  – Characteristic
  – “drives” the diagnosis
  – Absent 60%!

• New RMSF criteria:
  – Fever > 48 hours
  – No alternative explanation
  – Exposure to endemic area
Rocky Mountain Spotted Fever

• Diagnosis:
  – Immunohistochemical stains (skin/tissue biopsy)
  – Seroconversion with >4-fold rise
  – PCR amplification of *R. rickettsii* DNA

• Treatment:
  – Doxycycline
  – Adults: 100 mg po BID
  – Children < 45 kg: 2.2 mg/kg/dose BID
  – 10 days
Fever in Infants (1 – 90 days)
Fever in Infants (1 – 90 days)

- 20% ED visits
- 8% - 10% SBI
- Risk stratification:
  - Low-risk: 1.4% SBI
  - High-risk: 21% SBI
- UTI = most common SBI (80%)
- E. coli most common pathogen
- Incidence SBI in viral infection = low
Fever in Infants (1 – 90 days)

- Low-risk vs. High-risk:
  - Clinically ill?
  - Yale Toxicity Score
  - Modified Rochester criteria
  - CBC/diff & UA are key

- Presence of virus:
  - Upper respiratory viruses year-round
  - HSV I/II?
Toxic appearance (Yale Scale)

- Lethargy
- Poor/absent eye contact
- Failure to recognize parents/interact with toys
- Poor perfusion of extremities
- Acrocyanosis
- Mottling
- Capillary refill > 2 seconds
- Hyper/hypoventilation
Decision making tools - WBC

- SBI risk:
  - < 15K: 21%
  - 15K: 29%
  - >20K: 49%

- WBC and/or Band count: sensitivity 11-55%

- PPV WBC > 15K = 6%

- Unnecessary Rx: 85-95% cases
Infant sepsis Evaluation

• Procalcitonin assay:
  – Highly reliable
  – NPV 96%
  – Ideal marker of SBI, use in ED setting
  – Not readily available – Urgent Care clinics

• C-reactive protein:
  – CRP < 5 mg/dL: 1.9 - 9.7% risk SBI
  – CRP > 10 mg/dL: 86.5% risk SBI
  – NPV = 90%
  – Limitations: Time-specific (< 12 hrs.)
Fever in Infants (1 – 90 days)

- University of Utah
- Evidence-based clinical practice
- D/C febrile infants at 24 hours if:
  - Positive viral testing (except rhinovirus)
  - Negative bacterial cultures
- Protocol incl. modified Rochester criteria
- 85% Bld Cx + in 24 hours; 95% in 36 hours
Fever in Infants (1 – 90 days)

• High-risk:
  – Age ≤ 28 days
  – WBC <5,000 or >15,000
  – Absolute band count ≥ 1,500
  – UA > 10 WBC/hpf
  – Prematurity (<37 wks) AND underlying medical condition

• Labs: CBC/diff, Bld Cx, U/A, U Cx, AST/ALT (infants ≤ 42 days), viral studies
Fever in Infants (1 – 90 days)

• Impact:
  – Reduced hospital stay
  – Improved cost savings ($3000/admit)
  – Improved parent satisfaction (98%)
  – Reduced antibiotic use
  – Improved use of risk-screening labs
  – ↑ capture meningitis/bacteremia (91% to 99%)
  – No missed SBI (2-year follow-up)
Fever in Infants (1 – 90 days)

• Application to your facility?
  – ARUP multiplex PCR for respiratory viruses
  – Microbiology lab practices
  – Epidemiologic mix

• Study/apply locally

• Stay tuned…
Questions?