Pediatric Board Review 2012:
Infectious Diseases, Part I

Camille Sabella, MD

Goals and Objectives

- Review presentations of common pediatric infectious diseases
- Discuss evaluation and treatment of infections seen by pediatricians
- Present cases in test format, similar to that used in the examination

Case 1:

- A 9 month old child, who attends a day care center develops high fever and lethargy; he experiences a 5 minute tonic-clonic seizure.
- CSF examination:
  - 10,000 WBC (90% PMNs and 10% lymphs)
  - Protein: 130 mg/dL
  - Glucose: 5 mg/dL
**Question 1**

- Of the following, the most likely etiologic agent is:
  - A. *Herpes simplex type 1* (HSV-1)
  - B. *Streptococcus pneumoniae*
  - C. *Escherichia coli*
  - D. *Cryptococcus neoformans*
  - E. *Mycobacterium tuberculosis*

---

**Meningitis: Cerebrospinal Fluid Findings**

<table>
<thead>
<tr>
<th></th>
<th>Bacterial Partially-treated</th>
<th>TB</th>
<th>Viral</th>
<th>Para-mening focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells/mm³</td>
<td>20-5000 PMN</td>
<td>20-5000</td>
<td>&gt;1000</td>
<td>Mostly L</td>
</tr>
<tr>
<td></td>
<td>20-5000 PMN</td>
<td></td>
<td></td>
<td>&lt;1000 PMN, L</td>
</tr>
<tr>
<td>Glu</td>
<td>low</td>
<td>low/N</td>
<td>low</td>
<td>normal</td>
</tr>
<tr>
<td></td>
<td>low</td>
<td>low/N</td>
<td>normal</td>
<td></td>
</tr>
<tr>
<td>Pro</td>
<td>high</td>
<td>high</td>
<td>high</td>
<td>high/N</td>
</tr>
<tr>
<td>Gram Stain</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Culture</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Bacterial Meningitis: Signs and Symptoms**

- Fever
- Stiff neck (> 2 years)
- Mental status change
- Full fontanel
- Infant < 2 years:
  - Acutely ill without other source
Bacterial Meningitis: Pathogens

- Newborns:
  - Group B streptococcus
  - *E. coli*, other enterics
  - *Salmonella*
  - *Listeria monocytogenes*

- After 6 weeks of life:
  - *Neisseria meningitidis*
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae* (type b)

- After Head Trauma:
  - *Streptococcus pneumoniae*

- Post-neurosurgery:
  - *Klebsiella sp*
  - *Pseudomonas aeruginosa*
  - *Staphylococci*
Bacterial Meningitis: Empiric Treatment

- Newborns:
  - Ampicillin + gentamicin or cefotaxime
- After 6 weeks of age:
  - Cefotaxime or ceftriaxone or chloramphenicol
  - Vancomycin
    »To cover penicillin or cephalosporin-resistant pneumococci

Bacterial Meningitis: Organism Specific Therapy

- Meningococcus: Penicillin for 7 days
- H. influenzae: 7 days-10 days, longer in complicated cases
  - Beta-lactamase negative: Ampicillin
  - Beta-lactamase positive: Ceftriaxone
- Pneumococcus: 10 days minimum
  - Penicillin-sensitive: Penicillin
  - Relatively penicillin-resistant: Ceftriaxone
  - Penicillin-resistant: Vancomycin + Ceftriaxone + ?

Meningitis: Steroid Therapy (AAP)

- Consider only for children > 6 weeks old
- Dexamethasone may be beneficial in cases of H. influenzae meningitis
  »Decreases risk of hearing loss
- Dose: 0.6mg/kg/d in 4 doses for 2-4 d
- Must be given prior or just after antimicrobial therapy, likely not effective if >1 h after antibiotic
Meningitis: Steroid Therapy (AAP)

- Not for suspected or proven non-bacterial meningitis
- Not for partially treated meningitis with negative cultures
- Stop therapy if bloody stools develop and monitor closely

Meningitis: Hospital Precautions

- Droplet Isolation for 24 hours
  - *N. meningitidis*
  - *H. influenzae*

Question 2

- Culture of the cerebrospinal fluid reveals *Neisseria meningitidis*. Which of the following statements is true?
  - A. Meningococcal vaccine should be given to all contacts at the child’s day care center.
  - B. The occurrence of a seizure at the onset predicts a poor prognosis
  - C. The overall prognosis is better than if the child had meningococcemia without meningitis
  - D. Rifampin prophylaxis should be given for family contacts of this child but not for the child care contacts
MENINGOCOCCEMIA: POOR PROGNOSTIC FACTORS

- Hypotension
- WBC ≤ 10,000/mm³
- Petechiae within 12 h of presentation
- Absence of meningitis

Prophylaxis: Meningococcal Disease (high risk contacts, index case)

- Rifampin:
  - 20 mg/kg/d q 12 h X 2 days
  - (600mg/dose, max)
  - If age < 1 m: 5 mg/kg q12h X 2 days

- Ceftriaxone:
  - ≤12y: 125 mg IM
  - >12y: 250 mg IM

- Ciprofloxacin (if ≥ 18 y, not pregnant)
  - 500mg po
Case 2

- A previously healthy 2 year old boy develops a productive cough, high fever and respiratory distress 2 days following mild cold symptoms. Physical findings reveal an moderately ill-appearing child with a temperature of 39.5 degrees C and respiratory rate of 60/minute. He has decreased breath sounds in the right lung and nasal flaring. A chest radiograph reveals a right middle lobe infiltrate.

Question 3

- Of the following, the most appropriate initial therapy is to intravenously administer:
  - A. ampicillin
  - B. clindamycin
  - C. cefazolin
  - D. nafcillin
  - E. vancomycin
CAP-Inpatient Antibiotic Therapy

- Ampicillin or penicillin
- 3rd generation cephalosporin
  - If not fully immunized, if there is high-level pneumococcal resistance, or those with life-threatening infections, including empyema
- Add macrolide when atypical pathogens are significant considerations
- Add vancomycin or clindamycin if S aureus is suspected clinically
  - Infants with severe illness
  - Septic patients

Pen-susceptible Pneumococcus

- Preferred: Ampicillin (150-200 mg/kg/day) or Penicillin
- Alternatives: Ceftriaxone (50-100 mg/kg/day) or Cefotaxime, Clindamycin, Vancomycin

S pneumoniae with MIC $\geq$4 ug/mL to Penicillin

- Ceftriaxone preferred (100 mg/kg/day)
- Alternatives: Ampicillin (300-400 mg/kg/day), Levofloxacin, clindamycin, vancomycin
### Other Organisms

- **GAS**
  - Penicillin or Ampicillin

- **MSSA**
  - Cefazolin or Oxacillin

- **MRSA**
  - Vancomycin or Clindamycin (if susceptible)
  - Linezolid alternative

### Case 3

A 12-year old boy presents with a 10 day history of sore throat, dry cough, fever. On physical examination, the child is well appearing, has a temperature of 39.2 degrees C., a respiratory rate of 28 breaths/minute and scattered rales bilaterally. A CXR is shown.
Question 4

• The most likely pathogen is:
  A. *Mycobacterium tuberculosis*
  B. *Mycoplasma pneumoniae*
  C. *Streptococcus pneumoniae*
  D. *Streptococcus pyogenes* (Group A)
  E. *Staphylococcus aureus*

Question 5

• The best test to make this diagnosis is:
  A. Bacterial throat culture
  B. Blood culture
  C. Throat swab PCR
  D. IgG and IgM specific titers
  E. Cold agglutinin titers

**Diagnosis of Mycoplasma infection**

• PCR
  - More widely available now
  - 80-100% sensitivity
  - Positive result in setting of classic clinical history suggests causation

• Titers
  - Poor specificity of IgM antibodies
  - 4-fold increase or seroconversion reliable

• Cold agglutinins
  - 50% sensitivity
  - Poor specificity
Case 4

- A 10 month old infant is seen in your office with a history of fever to 103 degrees F. for the past 3 days. She is not in day care. The child is playful and the physical examination is unremarkable except for fever. There are no ill contacts at home.

Question 5

- The most likely virus causing this child’s fever is:
  - A. Parvovirus B19
  - B. Human herpes virus 6
  - C. Epstein-Barr virus
  - D. Cytomegalovirus

Human Herpesvirus 6 /Exanthem Subitum/ Roseola Infantum

- Fever: 3-5 days
- URI, mild
- Cervical adenopathy
- Rash: maculopapular < 48 hours
Roseola Infantum

- Complications
  - seizures
  - meningitis
  - encephalitis

Fever in Young Children

- N=243 (<2 years)
  - 34 (14%) HHV-6 isolated
  - Rash: 3/34

Pruksananhonda P, Hall CB et al.
Primary HHV-6 infection*

- Age: 9-21 months (40% by 12 m)
- Transmission: no seasonality
- Symptomatic: 90%
  - Fever 58% (mostly older infants)
  - Fussiness 70%
  - URI: 26%
  - Rash 31%
  - Roseola: 24%
  - Visit to physician

Case 5

A 30 year old teacher calls your office seeking advice. She is 10 weeks pregnant and there has been an outbreak of “slapped cheek” disease in her school with some cases in her classroom.
Question 6

- Of the following, the best advice for this teacher would be:
  - A. Advise her that the risk to the fetus is low
  - B. Recommend an ultrasound to look for hydrops fetalis in the beginning of her third trimester
  - C. Recommend referral to a high risk obstetrical service to follow serial U/S and to prepare for in utero transfusion
  - D. Recommend that she takes a leave of absence from work until the outbreak is over

Parvovirus B19 Infection:
Epidemiology

- 50% of children have specific IgG antibody by age 15y
- 50-80% of adults are sero-positive
- Late winter/spring most common
- Respiratory spread
  - 50% transmission rate with household exposure
  - 10-60% transmission following school or daycare exposure
  - Nosocomial transmission has been documented

Parvovirus: Manifestations

- Asymptomatic
- Slapped Cheek Disease
- Transient Aplastic Anemia
- Stillbirth/ Hydrops/ Congenital Anemia
- Anemia: Immune suppressed host
- Arthritis
HPV-B19: Clinical Course

- Most persons are completely asymptomatic
- Stage 1
  - Occurs after 4-14 days incubation
  - Period of transmission
  - Mild prodromal illness (fever, HA, GI symptoms)
    - May be unrecognized
  - Viremia
  - Erythroid progenitor depletion
  - Development of IgM-specific antibodies

THE MAIN EVENTS IN HPV INFECTION

HPV-B19: Clinical Course

- Stage 2
  - Occurs 3-7 days after prodrome
  - Facial exanthem- "slapped cheek"
    - Bright red
    - Spares nasal bridge and perioral areas
  - Clearance of viremia
  - Development of IgG-specific antibody
HPV-B19: Clinical Course

- Stage 3
  » Occurs 1-4 days after appearance of facial rash
  » Lacy, erythematous, reticular, maculopapular rash
    - Trunk and extremities most common
    - May be pruritic
    - Often evanescent-recurring over 1-3 weeks
  » Arthropathy
EPIDEMIOLOGY OF PARVOVIRUS B19 INFECTIONS

- At least 50% of women are seropositive for the virus prior to pregnancy
- Likelihood of infection after a close exposure estimated to be 30-50%
- Estimates of fetal loss following infection during pregnancy range from 2-6%
- Thus, overall risk of fetal loss due to this virus is 1-2%

HPV-B19: Infection control issues

- Children with EI
  » May attend school or daycare—not contagious
- Children hospitalized with TAC
  » Droplet precautions
- Pregnant women exposed at home or school
  » Given high prevalence of infection in the community, high rate of silent infection, low risk of adverse effect on fetus, routine exclusion from workplace NOT advised
  » Serologic testing may be offered for reassurance as most are positive
  » Fetal US may prove useful

Case 6

- A 6 month old infant born to a woman with HIV infection is seen in your office with a 3 day history of URI symptoms with cough. She has developed a high fever today and on exam is mildly tachypneic but otherwise has no focal findings. CXR shows an interstitial, diffuse infiltrate.
Question 7

Appropriate interventions at this point would include all of the following except:

A. Obtaining an NP swab for DFA for RSV, adenovirus, parainfluenza and influenza viruses
B. Obtaining a blood culture and treating with ceftriaxone
C. Administering high dose intravenous trimethoprim-sulfamethoxazole to the infant
D. Sending a serum HIV antibody test on the infant
HIV Infection: Diagnosis, Infants < 18 months

- Maternal antibody transmitted
  - May persist for 18 months
  - Thus, can only use to diagnose HIV in those >18 months of age

CONFIRM TESTS!

HIV Infection: Infants <15 months: Diagnosis is virologic

- PCR (DNA or RNA)
  - 14-21 days
  - 1-2 months
  - 4-6 months

- Elective:
  - Birth: PCR DNA*
  - ELISA at 12-18 months

*30-40% of infected infants are PCR + by 48 hours

In nonbreastfed children younger than 18 months of age with negative HIV virologic test results, presumptive exclusion of HIV infection is based on:

- Two negative HIV DNA or RNA virologic test results, from separate specimens, both of which were obtained at 2 weeks of age or older and one of which was obtained at 4 weeks of age or older; OR
- One negative HIV DNA or RNA virologic test result from a specimen obtained at 8 weeks of age or older; OR
- One negative HIV antibody test result obtained at 6 months of age or older; AND
- No other laboratory or clinical evidence of HIV infection (ie, no subsequent positive results from virologic tests if tests were performed and no AIDS-defining condition for which there is no other underlying condition of immunosuppression).
In nonbreastfed children younger than 18 months of age with negative HIV virologic test results, definitive exclusion of HIV is based on:

- At least 2 negative HIV DNA or RNA virologic test results, from separate specimens, both of which were obtained at 1 month of age or older and one of which was obtained at 4 months of age or older;
- At least 2 negative HIV antibody test results from separate specimens obtained at 6 months of age or older; and
- No other laboratory or clinical evidence of HIV infection (ie, no subsequent positive results from virologic tests if tests were performed and no AIDS-defining condition for which there is no other underlying condition of immunosuppression).

HIV Infection: Transmission

- In Utero/Perinatal (20-30%)
  - Can be almost completely prevented if mother and infant are treated
- Breastfeeding
- Blood/blood products
- IV drug use
- Sexually transmitted

HIV Infection: Manifestations

- Pneumocystis jiroveci pneumonia (PCP)
- Lymphoid interstitial pneumonitis (LIP)
- Failure to thrive
  - Lymphadenopathy
  - Hepatosplenomegaly
  - Abnormal CBC
- Recurrent bacterial infections
  - *Streptococcus pneumoniae*
Pediatric AIDS: Immune Defects

T cell defect: Lymphopenia, CD4 +

Qualitative T cell defects
- Cytotoxic responses: abnormal
- Proliferative responses: abnormal
  - antigens
  - mitogens

B cell hyperactivity
- Elevated IgG, IgA, IgM
- Poor antibody response to vaccines

Pediatric AIDS: PCP
Prophylaxis

- Begin TMP/SMX prophylaxis:
  - Infants born to HIV infected mother
  - At 4-6 weeks of age
  - Can stop if meets criteria for presumptive or definitive exclusion of HIV
  - After an episode of PCP
  - Low CD4 count: (<20%)
    - <1500 cells/ml (<30%)  0-12 months

Antiretroviral Therapy

Low CD4 count:

- <1750 cells/mm³ (<30%)  0-12 months
- <1000 cells/mm³ (<25%)  13-24 months
- <750 cells/mm³ (<20%)  2-6 years
- <500 cells/mm³  >6 years
Case 7

- A 2 year old boy has had swollen lymph nodes in the left anterior cervical chain for several weeks. He has had low grade fever but no other illness. He lives in a suburban area, is not in child care, and has no known exposure to anyone with tuberculosis. His PPD shows 9 mm induration. His chest radiograph is normal.

Question 8

- The best therapy for this child is:
  - A. Course of INH, rifampin and pyrazinamide
  - B. A biopsy of the node mass for culture
  - C. A course of clarithromycin and rifampin
  - D. Complete excision of the lymph node
  - E. Course of INH for 9 months

NTM Adenitis in Healthy Children

- Complete excision is curative
- Antimicrobial therapy
  - No additional benefit (RCT’s)
  - May be used for incomplete excisions or for recurrent disease
- Biopsy may result in fistulous tracks
Definition of Positive PPD (5 TU)

- Reaction ≥ 5 mm
  - contact with person with known or suspected TB
  - immunocompromised child
  - child suspected of having tuberculous disease

Definition of Positive PPD (5 TU)

- Induration ≥ 10 mm
  - children less than 4 years of age
  - children with any chronic condition
  - children whose exposure to TB is deemed to be increased

- Induration ≥ 15 mm
  - children who are 4 years and older and have no risk factors for tuberculosis
Interferon-gamma release assay (IGRA):
- Similar sensitivity to TST
- Increased specificity over TST
- Antigens used not found in BCG or other mycobacterial species
- Cannot distinguish latent from active infection
- Not reliable in children less than 5 years of age
- Can be used in place of TST for children 5y of age and older
- Preferred in asymptomatic children over age 4y who have received BCG vaccine

Treatment of Latent TB Infection
Indications:
- PPD or positive IGRA without active disease (even if BCG) and/or child exposed to adult with active disease (for 3m)
- INH for 9 months daily (12 months if HIV+)
  - DOT can be 2X/week for 9 m-if not adherent
- Rifampin: 6 months daily

TB in a Child is a Sentinel Event
- Identify the adult contact!
- Diagnosis: often clinical initially and therapy empiric
  - first morning sputum: send
  - clinical setting (e.g. Aseptic meningitis in a young child with exposure)
Answers to Questions
- 1. B
- 2. C
- 3. A
- 4. B
- 5. C
- 6. B
- 7. A
- 8. D
- 9. D