Pediatric I.D. Cases Walking Through Your Office Door

Stephen C. Eppes, M.D.
Christiana Care Health System
Sidney Kimmel Medical College at Thomas Jefferson University
Disclosures
The Case of the Non-Lactose Fermenter

- 70 day old previously well infant
- Two day history of diarrhea with a small amount of blood, feeding less well, and maximum recorded temp of 101°
- Physical exam in office is normal
- Stool studies are performed
The Case of the Non-Lactose Fermenter: Questions

a) Full sepsis work-up?
b) Hospitalization?
c) IV antibiotics?
d) PO antibiotics?
The Case of the Non-Lactose Fermenter

- Sent home on no antibiotics with instructions for follow up
- Next day lab reports stool is growing 4+ non-lactose fermenter
- *Clostridium difficile* toxin assay is (+)
- Phone call with family – condition unchanged, temps about 100° with 5 loose to watery stools in last 24 hours
Salmonella in Young Infants

- The following day, *Salmonella* sp. identified by lab
- Phone call indicates no change in status of child
- What do you do now?
Well, if you didn’t do it before, take a good history as far as potential exposures (family members, food preparation, reptiles)

- Recognize that young infants are at risk for extraintestinal spread
- Begin PO antibiotic (e.g. TMP-SMX)
- Check species identification and susceptibility
- Monitor patient carefully
Salmonella in Young Infants

Should the baby have been empirically treated earlier?

Yes – especially if there was epidemiologic reason to suspect a bacterial pathogen (e.g. *Salmonella*, *Shigella*)

Possible downside to use of antibiotics –

- (1) unnecessary antibiotic exposure
- (2) prolonged carriage
- (3) *E. coli* 0157:H7
5 y.o. Korean girl, recently moved to U.S.
Had BCG at one month of age
No known TB exposures
Asymptomatic, exam normal
PPD 8 mm
Chest radiograph showed: “suggestion of a small infiltrate of bilateral suprahilar region"
In addition to reviewing the CXR yourself you would:

a) Disregard 8 mm TST
b) Order IGRA
c) Repeat PPD in 1 year
d) Treat with INH for 9 months
e) Test family members
Only the area of *induration* should be measured.
Definitions of Positive TST in Pediatrics

- Induration ≥ 5 mm
  - Close contact with active TB
  - Suspected tuberculous disease
    - Clinical, e.g. meningitis
    - Radiographic findings
  - Immunosuppressive conditions or therapies
Definitions of Positive TST in Pediatrics

- Induration $\geq 10$ mm
  - Increased risk for disseminated disease
    - $< 4$ years of age
    - Chronic illness, immunosuppression, or malnutrition
  - High risk of exposure to TB disease
    - Born in high prevalence region
    - Travel to high prevalence region
    - Frequent exposure to high risk persons
      - Homeless, drug users, HIV, incarcerated
Definitions of Positive TST in Pediatrics

- Induration $\geq 15$ mm
  - Children $> 4$ years and adolescents without any risk factors
Tuberculin Skin Test (TST)

Advantages
- Well studied
- Treatment trials based on TST
- Cheap

Disadvantages
- 2 visits
- Lower specificity (BCG)
- Requires precise placement and interpretation
- Subjective error in interpretation
- Reduced sensitivity in immunocompromised patients
What Is An IGRA?

- Interferon-gamma release assay
- Measures ex-vivo IFN-γ production
IGRAs: Advantages

- Only one visit required
- Results often within 24 hours
- More reproducible results (compared with TST induration - often very subjective)
- Not affected by prior BCG vaccination
IGRAs: Limitations

- More labor-intensive
- More expensive
- Limited data for certain groups
  - Recently exposed to TB
  - Immunocompromised
  - Serial testing, e.g. health care providers
  - Young children
Straight from the AAP

“Some children who received BCG vaccine can have a false-positive TST result and LTBI is overestimated by the use of the TST in these circumstances.”

“The negative predictive value of IGRAs is not clear, but in general, if the IGRA result is negative and the TST is positive in an asymptomatic child, the diagnosis of LTBI is unlikely.”
AAP Revised Recommendations for Use of TST and IGRA in Children

- TST preferred / IGRA acceptable
  - Children < 5 years of age
AAP Revised Recommendations for Use of TST and IGRA in Children

- IGRA preferred, TST acceptable
  - Children $\geq 5$ yr who had BCG vaccine
  - Children $\geq 5$ yr unlikely to return for reading of TST
Patient # 37 on a Busy Monday

- A 5 year old child has had nasal congestion, yellow discharge, cough and intermittent low grade fever (Tmax 100.8) for 12 days. Past medical history is unremarkable. Immunizations are current.

- On exam he is non-ill appearing
  - Thick, yellow nasal discharge
  - Malodorous breath
  - Retracted TMs
  - Clear lungs
Patient # 37 on a Busy Monday

- You would:
  a. Treat with decongestants only
  b. Treat with high dose amoxicillin
  c. Treat with amox/clav (ES)
  d. Treat with cefdinir
Patient # 37 on a Busy Monday

- Acute bacterial sinusitis
- New IDSA guidelines published 2012
- Emphasis on accurate diagnosis:
  - Persistent / not improving (10 days)
  - Severe (> 3 days)
  - Worsening or “double-sickening” (> 3 days)

Acute Bacterial Rhinosinusitis

- **Antibiotic Recommendations from IDSA**
  - Amox/clav (recommended by IDSA)
    - 90 mg/kg/day divided 2X daily for children
      - 10-14 days
    - 2 g 2X daily for adults
      - 5-7 days
  - Oral cephalosporin for non-type 1 reaction to penicillin
  - Levofloxacin for type 1 hypersensitivity
Acute Bacterial Rhinosinusitis

- NOT recommended:
  - Amoxicillin
  - Trimethoprim-sulfamethoxazole
  - Doxycycline
  - Macrolides
    - Erythromycin
    - Clarithromycin
    - Azithromycin
Acute Bacterial Rhinosinusitis

AAP Guidelines 2013

- “Clinicians should not obtain imaging studies of any kind to distinguish acute bacterial sinusitis from viral URI, because they do not contribute to the diagnosis; however, a contrast-enhanced computed tomography scan of the paranasal sinuses should be obtained whenever a child is suspected of having orbital or central nervous system complications.”

- “Amoxicillin with or without clavulanate is the first-line treatment of acute bacterial sinusitis.”
Taking a Good History

- 8 year old boy has had fever (to 104 degrees) for 2 days
- Malaise and myalgias
- Now presents with new skin findings
Taking a Good History

Exam reveals:
- Talkative, not acutely ill in appearance
- Multiple petechiae and purpura, mainly on extremities
- Clear lungs, normal heart exam
- Warmth over knees, tenderness to ROM
Taking a Good History

The pediatrician suspected the correct diagnosis on the basis of which part of the history:

a) Social History
b) Family History
c) Immunization History
d) Medication History
e) Review of Systems
Taking a Good History

The pediatrician focused on what aspects of the Social History:

a) Travel
b) Exposure to ill contacts
c) Pets in the home
d) Self-injurious behaviors
e) Flooring in the home
Rat Bite Fever

- Two bacterial etiologies
  - *Streptobacillus moniliformis*
  - *Spirillum minus*
- Fever, chills, achiness
- Maculopapular skin lesions, petechiae, purpura
- Arthritis
- Occasional cardiac and CNS involvement
- 10% fatality if untreated
- Our patient did fine with penicillin TX
3 day old infant born at 36 5/7 weeks to 33 y.o. Mexican-American mom
- Late fall, southeastern PA
- Prenatal I.D. labs were negative, but HIV and GC/CT unknown
- Gestational diabetes
- Delivered by cesarean section because of poor BPP, Apgars 3 and 8
- On DOL 2 in well baby nursery at OSH, he developed respiratory distress
- Metabolic acidosis, LFTs abnormal (ALT 200)
- CBC showed platelets of 88k and WBC of 4700
- Intubated and transferred to CCHS
It’s Always on Board Exams
and Sometimes You See It in Real Life

What antimicrobials would you start?

A) Ampicillin and gentamicin
B) Ampicillin, gentamicin and acyclovir
C) Ampicillin and cefotaxime
D) Vancomycin and piperacillin / tazobactam
It’s Always on Board Exams
and Sometimes You See It in Real Life

- Additional lab results:
  - Creatinine 1.5
  - CSF protein 919, WBC 3050 with segs, lymphs and monocytes
  - CSF Gram stain showed Gram positive rods (\( ? \) Lactobacillus sp.)
  - Blood culture from OSH grew:
It’s Always on Board Exams
and Sometimes You See It in Real Life

- Additional lab results:
  - Creatinine 1.5
  - CSF protein 919, WBC 3050 with segs, lymphs and monocytes
  - CSF Gram stain showed Gram positive rods (? Lactobacillus sp.)
  - Blood culture from OSH grew:

- *Listeria monocytogenes*
It’s Always on Board Exams: 
*Listeria monocytogenes*

- Gram positive rod (sometimes Gram variable, often misidentified)
- Usually associated with foodborne illness
- In pregnancy it is associated with
  - Spontaneous abortion
  - Fetal death
  - Preterm delivery
- Early and late onset neonatal infection is associated with
  - Sepsis
  - Papular rash (“granulomatosis infantisepticum”)
  - Meningitis (usually late onset, associated with 25% mortality rate)
- Treatment of choice: amp and gent
It’s Always on Board Exams: 
*Listeria monocytogenes*

- **Our patient:**
  - Prolonged mechanical ventilation
  - EEG severely abnormal – burst suppression pattern
    - Keppra, fosphenytoin, phenobarbital
  - Poor feeding
  - ? Imaging
- **Age 5 weeks – pyloric stenosis**
17 y.o. previously healthy male presented in August with 5 day history
- Fever / chills
- Headache / photophobia
- Myalgias
- Vomiting

Became dehydrated, required fluid administration, and was admitted to AIDHC
Figuring It Out

PMH:
- Negative. No meds. Imms UTD.

SH:
- Resides in southeastern PA – semirural
- Known tick exposure
- Recent mission to Dominican Republic
  - Drank bottled water, ate unwashed fruit
  - Swam in fresh water
  - No contact with animals
  - Used mosquito precautions
  - No travel vaccines or prophylaxis
Figuring It Out

- Physical examination
  - 38.6 / 115 / 115/87 / pulse ox 100%
  - Photophobia, no conjunctivitis or papilledema
  - Heart, lungs and abdomen normal
  - Neuro exam unremarkable
  - Musculoskeletal exam normal
  - Skin without rashes or lesions
Figuring It Out: Initial Lab Results

- **CBC:**
  - WBC 11,400 with neutrophil predominance
  - Platelets 145,000 with normal H/H
- Creatinine 2.5, BUN 35
- Bilirubin 1.9
- AST 63, ALT 79
- CPK normal
- UA: Moderate bilirubin and 50-100 WBC
Figuring It Out

- Hospital course:
  - Remained febrile
  - Additional lab tests sent
  - Chloroquine for 1.5 days (smears negative)
  - Hospital day 2
    - Conjunctival suffusion
    - Abdominal pain, hepatosplenomegaly
  - Intravenous doxycycline
  - Defervescence within 48 hr
Figuring It Out: What is in S.E. PA in the Summer?

- Lyme disease
- Ehrlichiosis / Anaplasmosis
- Enteroviruses
- Non-seasonal
  - Epstein-Barr virus
  - Adenoviruses
Table 2. Incubation period for common infections in returning traveler.²,³

<table>
<thead>
<tr>
<th>Incubation Period</th>
<th>&lt;10 days</th>
<th>11-21 days</th>
<th>&gt;1 month</th>
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<tbody>
<tr>
<td>Dengue fever</td>
<td>Malaria</td>
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<td>Yellow fever</td>
<td>Hepatitis</td>
<td>Tuberculosis</td>
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<tr>
<td>Diarrheal illnesses</td>
<td>Typhoid</td>
<td>Hepatitis</td>
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<tr>
<td>Rickettsial Infections</td>
<td>Leptospirosis</td>
<td>HIV</td>
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<tr>
<td>Influenza</td>
<td>Rickettsial</td>
<td>Schistosomiasis</td>
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<tr>
<td>Viral hemorrhagic fevers</td>
<td>Protozoan Infection</td>
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Figuring It Out: What is on Hispaniola?

- Malaria
- Dengue
- Typhoid fever
- Non-typhoid enteric pathogens
  - Salmonella
  - Shigella
- Hepatitis A
- Leptospirosis
Figuring It Out: Differential Diagnosis

- Ehrlichiosis / Anaplasmosis
- Malaria
- Dengue
- Leptospirosis
Leptospirosis

- **Etiology:** *Leptospira ictohemorrhagiae*
- Contact with animal urine, often from swimming
- **Early phase**
  - Fever, headache, myalgias, conjunctivitis
- **Late phase**
  - Immune mediated meningitis
  - Severe (Weil’s) disease
    - Liver and kidney involvement, hemorrhage
- **Treatment:** Penicillin G
  - Doxycycline
  - 3rd generation cephalosporins
Serendipity?

- 12 year old male
- Presented in October with 6 days of worse, periumbilical pain and fever to 103 (F)
- At OSH concern for appendicitis → CT
  - Normal appendix
  - Several liver lesions
- Admitted to AIDHC
Serendipity?

- Fever lasted 4 days
- Drenching night sweats
- No respiratory symptoms
- No known lymph node swelling
- No jaundice
- No nausea, vomiting or diarrhea
- Small for age but no weight loss
- Abdominal pain improved after CT
Serendipity? Social History

- Resides in rural Maryland with parents and 2 sisters
- They own dogs, cats, chickens, goats, rabbits, pig and a cockatoo
  - Cleans the pens
  - “Always wears gloves”
- No tobacco exposure
- Attends public school
Serendipity? Physical Exam

- T – 36.4, HR – 66, R – 20, BP 109/70
- Alert, smiling, in no distress
- Small for age
  - < 5th percentile for weight
- Normal, including abdominal exam
- Subsequently, 2x3 cm mass noted in right axilla
Serendipity? Lab Results

- WBC 10.0, normal diff, Hg 12.7, platelets 458k
- C-reactive protein normal
- CMP normal
- LDH normal
- AFP normal
- HCG negative
Serendipity? W/U for Infections

- Blood cultures (aerobic / anaerobic) negative
- EBV PCR negative
- CMV EBV negative
- Brucellosis antibodies negative
- Histoplasma antibodies negative
Serendipity? Additional Imaging

- Abdominal US – 3 hypoechoic lesions
- Abdominal MRI – multiple liver lesions
  - “Highly suspicious for metastatic process”
- PET scan – Hypermetabolic activity in 4 hepatic lesions, right axillary and subpectoral regions, and likely LUQ abnormality
- CT neck and thorax – focal haziness in RLL, two 2 mm nodules in LLL and RML, and mildly enhanced soft tissue lesion in right axilla, normal neck, liver lesions as previously noted
Tissue is the Issue

- Bone marrow biopsies – normal
- Lymph node
  - Florid follicular hyperplasia
  - Nodal and perinodal granulomatous inflammation
  - Few foci of associated necrosis
  - Multiple special stains negative
    - Gram
    - Silver
    - Acid fast
    - Warthin-Starry
- Routine, fungal and AFB cultures (-)
Cat Scratch Disease

- Nodal presentation in 90%
  - Inoculation lesion in 61%
- “Atypical” presentations in 10%
  - Fever of unknown origin
  - Osteomyelitis
  - Hepatosplenic granulomas
  - Encephalitis
  - Ocular disease
  - Henoch-Schönlein purpura

- If treatment required → azithromycin
  - Also TMP-SMX, RIF, and gentamicin
Gastroenteritis – Not!

- 16 year old girl has 24 hour history of febrile illness beginning with vomiting and diarrhea
- This morning, when getting off toilet, she became dizzy and fell, though no LOC
- After the mother called for an appointment, she developed rash and her eyes looked red
- In your office, vital signs included
  - Temp – 102.6
  - HR – 100
  - Resp – 28
  - BP – 94/58
Gastroenteritis – Not!

- Assuming you take a complete history, you would particularly want to know:
  a) Menstrual history
  b) Exposure to ticks
  c) History of sore throat and swollen cervical nodes
  d) Recent travel
You decide to admit her to the hospital. After appropriate cultures, empiric antibiotic therapy would be

a) Ceftriaxone
b) Doxycycline
c) Penicillin and clindamycin
d) Vancomycin and clindamycin
Gastroenteritis – Not!

- Patient required multiple fluid boluses and was briefly on a dopamine infusion
- She ultimately improved and was discharged home on clindamycin
- When you see her back the following week, her exam was basically normal except for:
Gastroenteritis – Not!

- Staphylococcal TSS
  - Mediated by TSST-1
  - MSSA >> MRSA
  - Menstrual – 50%
  - Non-menstrual
    - Often minor cutaneous infection
- Usually begins with GI symptoms
TSS: Clinical Findings

- Fever ≥ 102 (F)
- Rash – erythroderma, followed by desquamation
- Hypotension
- Multisystem organ involvement (3 or more):
  - GI – Vomiting and diarrhea
  - Muscular – elevated CPK
  - Mucous membrane
  - Renal
  - Hepatic
  - Hematologic
  - CNS
TSS: Treatment

- Fluids
- Management of end organ dysfunction
- Inotropic support if required
- Vancomycin or anti-staphylococcal beta-lactam
  - PLUS clindamycin
Scary Sounding, But Often They Do OK

- 3 day old term infant noted on DOL 1 to have significant rash, resulting in admission to NICU
- Maternal I.D. labs negative except for GBS, for which she received appropriate antibiotics
- Vaginal delivery with meconium stained fluid but no chorioamnionitis
- Mildly depressed at birth, but responded to stimulation
- Blood culture obtained, started on ampicillin and gentamicin
Scary Sounding, But Often They Do OK

- What did he have:
  - A) Neonatal HSV
  - B) Congenital varicella
  - C) Congenital candidiasis
  - D) Pustular melanosis
Scary Sounding, But Often They Do OK
Scary Sounding, But Often They Do OK

Congenital Cutaneous Candidiasis

- Usually present on DOL 1
- Papules, pustules, vesicles
- Often with palm / sole involvement
  - Helps differentiate from erythema toxicum
- Funisitis is typical
- Term infants usually do not have invasive infection
  - Topical antifungals often suffice
- Preterm infants often have blood stream invasion and systemic illness
  - Systemic antifungal therapy required
Congenital Cutaneous Candidiasis

- Normal CBC
- Negative blood culture
- Negative urine culture
- CXR – questionable mild infiltrate
- Ophthalmologic exam – normal

Treated with brief course of fluconazole and did well
15 year old female has a 1 week history of fever, fatigue, achiness and left sided abdominal pain

Throat pain was worst symptom

PMH – Gilbert’s

Admitted overnight (elsewhere) for IV hydration

Hg 9.3, platelets 138, T. bili 5.9, AST 192, ALT 185

Monospot negative

Admitted through ED to AIDHC
Ubiquitous, Uncanny, Understandable

- T – 36.8, P – 82, R – 20, BP – 106/51
- General: alert, NAD
- Skin: jaundiced, no rashes or lesions
- HEENT: icteric conjunctivae, pharynx erythematous, absent tonsils
- Neck: bilateral tender lymph nodes
- Lungs: clear bilaterally
- Heart: grade 1-2/6 SEM, normal rhythm, S1 and S2
- Abdomen: mildly tender epigastrium, liver and spleen each 4 cm below costal margin
- Musculoskeletal: normal
CBC: Hg 8.9, platelets 205, WBC 15.8 (29 segs, 15 bands, 46 lymphs, 8 monos, 2 atypical lymphs)

Reticulocytes: 11.1%

ESR 78, CRP 4.0

CMP: T. bili 5.5, AST 226, ALT 279

Rapid HIV: negative

Respiratory viral panel: rhino/entero

Throat culture: negative for GAS

Blood culture: negative

Abdominal US: hepatosplenomegaly, sludge in GB
Ubiquitous, Uncanny, Understandable

- Remained febrile, but generally stable
- H/H dropped to nadir of 7.3/20
- 4th hospital day – atypical lymphs 23%
Ubiquitous, Uncanny, Understandable

- What did she have:
  a) Ehrlichiosis
  b) EBV-associated autoimmune hemolytic anemia
  c) Typhoid fever
  d) Leptospirosis
Diagnosis of EBV Infection

- CBC
  - Atypical lymphocytosis
- Heterophile (Monospot)
  - Highly specific
  - Variably sensitive
- EBV-specific antibodies
  - IgM to VCA
  - IgG to VCA
  - EBNA
- PCR to detect EBV genome
Months following EBV infection

Titer

Heterophile

IgG to VCA

IgM to VCA

Anti-EA

Anti-EBNA

R

D
Complications of EBV Infection in Normal Hosts

- Neurologic:
  - Encephalitis
  - Myelitis
  - Facial palsy
  - Guillain-Barré
  - Metamorphopsia

- Splenic rupture

- Secondary infections

- Hematologic:
  - HLH
  - ITP
  - AHA
EBV-Induced Autoimmune Hemolytic Anemia

- Occurs in 0.5 – 3% of IM cases
- Usually in 2\textsuperscript{nd} or 3\textsuperscript{rd} week
- Usually associated with cold agglutinins (IgM) often with anti-i specificity
- Recovers completely over 1 – 2 months
- More severe cases are treated with corticosteroids with excellent response
Fusobacterium necrophorum pneumonia in EBV infection