Take Home Messages in Infectious Diseases

Paul E. Sax, M.D.
Brigham and Women’s Hospital
Harvard Medical School

Conflicts of Interest

• Consultant: Abbott, BMS, Gilead, GSK, Merck, Janssen, Viiv
• Grant Support: BMS, Gilead, Merck, Janssen

Take Home Messages in ID

• “Rapid-fire” review of content
• Focus on material of relevance to the board examination

Meningococcemia

• Rapid diagnosis and treatment essential
  — High dose penicillin
• Low Protein C level
• Contact tracing and prophylaxis — close contacts
  — Rifampin, ceftriaxone, ciprofloxacin
  — Ciprofloxacin resistance reported
• Vaccination (MCV4): A, C, Y, and W-135
  — All adolescents
  — Entering college students, military recruits, travelers to hyperendemic or endemic areas
  — Terminal complement deficiency (C5-9) or splenectomy

Suspected Bacterial Meningitis

• Pathogens: Strep pneumoniae, N meningitidis; rarely H influenzae, Listeria monocytogenes
• Treatment (start as soon as possible):
  — Most cases: ceftriaxone 2 gm IV q12h + vancomycin 500-750 mg IV q6h
  — Elderly or immunocompromised: add ampicillin 2 gm IV q4h
  — Recent neurosurgery: substitute meropenem 1 gm IV q8h for ceftriaxone
  — Narrow treatment once organism is identified
  — Adjunctive therapy: dexamethasone 0.15 mg/kg IV q6h x 2-4 days

Lyme Disease

• Seasonal: peaks in summer
• Characteristic rash – erythema migrans
• Early: fever, arthralgias, erythema migrans, Bell’s palsy, heart block
• Late: arthritis, other neurologic syndromes
• Treatment:
  — oral doxycycline (EM or Bell’s) or IV ceftriaxone (late, neuro disease, +/- cardiac)
• Tick attached for > 24 hours in endemic area: doxycycline 200 mg x 1 as prevention
### Lyme Disease – Key Take Homes

- **Diagnostic pitfalls**
  - Patient may not notice tick bite (ticks are TINY)
  - Central clearing ("bull’s eye) of rash not always present
  - Serologies frequently negative in early disease – no need to order if clinically suspect Lyme based on rash
- **Treatment pitfall**
  - Antibiotics not indicated for "seronegative" Lyme (fatigue only) or post-Lyme syndrome

### Other Tick-Borne Infections

- **Babesiosis**
  - Intra-erythrocytic parasites morphologically similar to malaria
  - Hemolytic anemia
  - Severity worse with older age, splenectomy
  - Treatment: atovaquone + azithro
- **Anaplasmosis/ehrlichiosis**
  - Fever, headache; low PLT +/- WBC
  - Treatment: doxycycline
- **RMSF**
  - Similar to anaplasma, only with petechial rash
  - Treatment: doxycycline

### Skin and Soft Tissue Infections

- **Non-purulent SSTI:** beta strep
- **Purulent SSTI:** Staph aureus, esp MRSA
- **Suspect MRSA** in any case of furunculosis ("boils"), esp with history of "spider bite", family/partner with similar
- **Management**
  - Incision and drainage critical
  - Antibiotics: TMP-SMX, tetracyclines, linezolid (watch for low plt), vancomycin – not beta lactams
  - TMP-SMX not active vs strep
  - Macrolide and clindamycin cross resistance in 50%

### Skin and Soft Tissue Infections

- **Special cases:**
  - DM with ulcer: Usual flora + GNR, anaerobes; use MRI to diagnose underlying osteomyelitis, with biopsy to get cultures/path
  - Bites: *P. multocida*, *Capnocytophaga* spp, mixed flora
  - Water: *Aeromonas*, *Vibrio* spp. (esp. with liver disease/splenectomy), *M. marinum*
  - Puncture wound through sneaker: *Pseudomonas aeruginosa*
  - Thorns: *Sporothrix schenckii*

### “D-Test”: Inducible Clindamycin Resistance

![Image of D-Test]

### Risk Factors for MRSA

- Prior use of antibiotics
- Reported "spider bite"
- History of MRSA
- Close contact with someone who has similar condition
- **But:** among patients with none of these factors, 48% still had MRSA

**“Surgical” Soft Tissue Infections**

- Systemic toxicity, rapid progression, severe pain or anaesthesia
- Crepitus, bullae, gas on plain film/CT
- Causes: gp A strep, clostridia, MRSA, mixed infections – depends on anatomic site
- Management
  - Broad spectrum antibiotics
  - Wide surgical debridement

**Endocarditis**

- Most common causes: oral streptococci, \textit{Staph aureus}
- High risk: known valvulopathy, prosthetic valve; role of dental work uncertain
- \textit{ECHO} can help make diagnosis
- Indications for surgery: \textbf{hemodynamic issues} (esp CHF), perivalvular complication, bad bug (fungi), uncontrolled embolic phenomena

**Prophylactic Antibiotics for Prevention of Endocarditis: What Cardiac Conditions?**

1. Prosthetic heart valve
2. Prior history of infective endocarditis
3. Congenital heart disease
4. Transplant valvulopathy

**Prophylactic Antibiotics for Prevention of Endocarditis: What Procedures?**

- Dental: gingival manipulation, perforation of mucosa
- Procedures breaching respiratory mucosa
- \textit{Infected skin/soft tissue}
- \textit{Not recommended for GU or GI procedures}

**Prevention of Infective Endocarditis, Circulation, May 7, 2007; circ.ahajournals.org**

**Herpes Zoster**

- Risk factors: increasing age, immunosuppression (cell-mediated – steroids, HIV, transplant)
- Prodrome precedes dermatomal skin eruption
- Most common complication: post-herpetic neuralgia
- Rx: oral acyclovir, valacyclovir, or famciclovir
- Zoster vaccine:
  - indicated for age > 60 (FDA approved but not yet recommended at 50), varicella immune
  - Contraindicated: some immunocompromised

**Diagnostic pitfalls**

- Pain may precede skin eruption – can lead to erroneous diagnoses (e.g., acute MI, appendicitis, cholecystitis, benign vertigo)
- Always consult ophthalmology for V1 zoster

**Treatment pitfalls**

- No proven benefit of treatment after 72 hours of rash
- Antivirals of no benefit in post-herpetic neuralgia

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Zoster Vaccine: Who’s Immunocompromised?

- Neoplasms affecting the bone marrow or lymphatic system
  - Post treatment: assess on case-by-case basis
- Acquired or congenital defects in cellular immune function
- HIV with symptoms or CD4 < 200/15%
- Immunosuppressive therapy
  - Prednisone ≥ 20 mg/d for ≥ 2 weeks
  - Recombinant human immune mediators and immune modulators (e.g. TNF blockers)

Varicella: Who Can be Considered Immune?

- History of chicken pox
- Healthcare-provider diagnosis of zoster
- Lab evidence of immunity
- Prior receipt of varicella vaccine (2 doses)
- US-born before 1980
  - Date of birth does not apply to immunocompromised, pregnant women, or healthcare workers

Respiratory Infections: Bronchitis

- Otherwise healthy: no treatment indicated
- Who to treat?
  - During documented pertussis outbreaks
  - Chronic bronchitis (M. pneumonia, B. pertussis)
  - Underlying lung disease (asthma, COPD, heavy tobacco use)

Pneumonia: Etiology

<table>
<thead>
<tr>
<th></th>
<th>OP (n=547)</th>
<th>IP (n=6152)</th>
<th>ICU (n=1415)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>64.4</td>
<td>48.3</td>
<td>39.7</td>
</tr>
<tr>
<td>S. pneumonia</td>
<td>4</td>
<td>20.3</td>
<td>22.5</td>
</tr>
<tr>
<td>H. influenza</td>
<td>4</td>
<td>6</td>
<td>5.3</td>
</tr>
<tr>
<td>M. pneumonia</td>
<td>19.3</td>
<td>3.9</td>
<td>1.9</td>
</tr>
<tr>
<td>C. pneumonia</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legionella spp.</td>
<td>0.9</td>
<td>3.4</td>
<td>5.9</td>
</tr>
<tr>
<td>S. aureus</td>
<td>1.8</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>GNR</td>
<td>3.2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>P. carinii</td>
<td>1.3</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>3.5</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>1.5</td>
<td>8.6</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Webster et al. AFC 2004;8:3-6

Pneumonia: Inpatient Treatment

- Broad spectrum
  - GNR (esp. in GU tract)
  - respiratory pathogens, incl. atypicals
  - (some) GPC, incl PCN resistant pneumococci
- Once-daily dosing (not ciprofloxacin)
- Generally well tolerated
- Few drug interactions
- Well-absorbed

Fluoroquinolones: Favorable Attributes
Fluoroquinolones: Some Problems

• Rising rates of resistance, especially with GNR and staph
• Adverse effects
  – Rash, allergy
  – Neuropsych
  – QT prolongation
  – Achilles tendon rupture and tendonopathy, cartilage erosions
  – Trovafloxacin, temafloxacin, grepafloxacin, sparfloxacin, gatifloxacin sagas
• Drug interactions: Mg, Ca, Al, Fe reduce absorption

Which Fluoroquinolone?

<table>
<thead>
<tr>
<th>Fluoroquinolone</th>
<th>GNR</th>
<th>GPC</th>
<th>Metabolism</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>***</td>
<td>*</td>
<td>Renal</td>
<td>Do not use for CAP</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>**</td>
<td>**</td>
<td>Renal</td>
<td>More QT prolongation</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>*</td>
<td>***</td>
<td>Hepatic</td>
<td>Anaerobe coverage; no activity vs. Pseudomonas</td>
</tr>
</tbody>
</table>

Pneumonia Case – Take 1

• A 27 year old woman is admitted with fever (103°F), cough, and RLL infiltrate. What treatment would you begin?
  1. Levofloxacin or moxifloxacin
  2. Ceftriaxone + azithromycin
  3. Something else

Pneumonia Case – Take 2

• A 27 year old woman is admitted with fever (103°F), cough, and RLL infiltrate. She reports hemoptysis and a 10 lb weight loss over 3 months. She is from Pakistan, has a pos PPD (“from BCG”). What treatment would you begin?
  1. Levofloxacin or moxifloxacin
  2. Ceftriaxone + azithromycin
  3. Something else

Tuberculosis: Prevention

• Positive PPD: Ignore BCG history! No age cutoff!
  – 5 mm: immunosuppressed, known exposure, CXR w/ healed TB (not just a granuloma)
  – 10 mm: IVDU, foreign born, NHR, DM, cancer, inc Cr, gastrectomy
  – 15 mm: Low risk patients
• Alternative: Interferon gamma release assay (IGRA)
• No “gold standard” for screening tests
• Preventive therapy: INH x 9 mos; alt RIF x 4 mos; weekly INH + rifapentine X 12 doses
**Tuberculosis: Treatment**

- Most cases of active TB are in foreign-born; HIV and anti-TNF therapy are major medical risks
- Consider TB in any case of chronic pneumonia
- Non-pulmonary: sterile pyuria, lymphadenitis, monoarticular arthritis, spine disease
- Rx: INH, rifampin, pyrazinamide, ethambutol (4 drugs)

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**Tuberculosis**

- Diagnostic pitfalls
  - PPD or IGRA may be negative in patients with impaired immune function or overwhelming (miliary) disease
  - Sputum smears neither sensitive or specific
- Treatment pitfalls
  - Monitor for hepatotoxicity – stop all meds if symptoms or ALT/AST > 3-5X ULN
  - Don’t give single-drug preventive therapy to someone with active TB

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**Infectious Diarrhea**

- Community-acquired, symptoms < 14 days
  - Rotavirus – young children; seasonal peak in winter
  - Norovirus – familial clusters and outbreaks in winter
  - Major gram-negative bacterial pathogens: salmonella, shigella, campylobacter, E. coli
  - Entamoeba histolytica – acute colitis, with fever and dysentery
- Nosocomial: C difficile
- Chronic: Parasitic (esp protozoan) pathogens – giardia by far the most common

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**Infectious Diarrhea: Clinical Presentations**

<table>
<thead>
<tr>
<th>Small amounts of watery diarrhea</th>
<th>Rotavirus, norovirus, ETEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile/inflammatory diarrhea syndromes</td>
<td>Shigella, campylobacter, salmonella</td>
</tr>
<tr>
<td>Bloody diarrhea</td>
<td>Shigella 15%, campylobacter 6%, salmonella 6%, EHEC 3%</td>
</tr>
<tr>
<td>Profuse watery diarrhea</td>
<td>Vibrio, ETEC</td>
</tr>
<tr>
<td>Abdominal pain, fever</td>
<td>Campylobacter, yersinia</td>
</tr>
</tbody>
</table>

ETEC = enterotoxigenic E. coli; EHEC = enterohemorrhagic E. coli (O157:H7)

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**Infectious Diarrhea: When Should Antibiotics be Given?**

- Moderate-severe illness, awaiting results of diagnostic testing
- Immunocompromised
- Age > 50
- Suspected travel-related diarrhea (most is ETEC)
- Any diagnosis of shigella
- Generally not given for EHEC

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**Clostridium difficile** Associated Disease (CDAD)

- Causative organism of antibiotic-associated colitis
- Risk factors: antibiotics, hospitalization, comorbid illness, age, H2/PPI therapies
- Hypervirulent strain causing disease in those with fewer or no risk factors

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**CDAD: Diagnostic Approach**

- Suspect CDAD in anyone with new diarrhea in the hospital or with recent Abx
- Lab clues for severe disease: leukocytosis, hypoalbuminemia
- Start empiric therapy awaiting results of stool studies – usually a stool ELISA

**CDAD: Treatment**

<table>
<thead>
<tr>
<th>Positive test, symptoms resolve off antibiotics</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild disease</td>
<td>Oral metronidazole or vancomycin</td>
</tr>
<tr>
<td>Moderate-severe disease</td>
<td>Oral vancomycin</td>
</tr>
<tr>
<td>Severe disease with ileus</td>
<td>IV metronidazole, vancomycin enemas, IVIG, colectomy</td>
</tr>
<tr>
<td>Multiple relapses</td>
<td>Oral vancomycin taper, probiotics</td>
</tr>
</tbody>
</table>

**Vaccination: MMR**

- Live virus vaccines; can be given to HIV+ if not severely immunosuppressed
- Measles
  - All born after 1956; revaccinate if first series was between 1963-1967
- Mumps: recent outbreak in immunized persons
- Rubella
  - Fever, rash, joint pain in young women
  - Avoid in pregnancy, but not an indication for TAB

**Vaccination: Influenza**

- Indications
  - Age > 50, CRF, DM, cardiac dz, pulm dz, HIV, immunosuppressed, nursing home residents
  - Health care workers, household contacts of at risk patients
- Inactivated: avoid in egg allergy
- Live attenuated, intranasal vaccine
  - Contraindications: >50yo, pregnancy, egg allergy, h/o GBS, immunocompromised, recent resp illness (72h), or those w/cardiac, pulmonary, metabolic, or renal dz

**Vaccination: Rabies**

- Pre-exposure
  - Occupational risk, some travelers
  - Boost when titer <0.5 IU/ml or <1:5
- Domestic animals (dogs, cats, ferrets)
  - Healthy: Observe x 10 days; vaccinate if rabies develops
  - Acting rabid: immediate vaccination
- Skunks, raccoons, bats, foxes, coyotes: immediate vaccination
- What to do post-exposure
  - Rabies immune-globulin and vaccinate D0, 3, 7, 14 (also 28?)
  - If previously vaccinated: vaccinate D0 and 3, no rabies immune globulin
- Rodents, livestock, rabbits: No vaccination

**Tropical Medicine/Parasitology**

- **Causes of fever**
  - Malaria: “the mime”; early severe most likely P falciparum, late relapse P vivax
  - Dengue: rash with capillary fragility
  - Rickettsial infections with eschar: rx doxycycline
- **Causes of GI illness**
  - Most common parasitic cause of chronic diarrhea: Giardiasis
  - Bloody diarrhea: Shigella, E histolytica
- **Eosinophilia:** Worms (e.g. strongyloides, schistosomiasis)
Tropical Medicine/Parasitology

- Diagnostic pitfalls
  - Many fevers in returning travelers are from common causes (STDs, influenza, drugs)!
  - Post-travel “irritable bowel” – subjective complaints, but no weight loss, no identifiable pathogen

- Treatment pitfalls
  - Failure to prescribe malaria prophylaxis to a person “visiting home” since she/he lived there as a child without being on malaria preventive rx

Tropical Medicine/Parasitology

- Eosinophilia: r/o strongyloides before giving steroids!

- Diarrhea:
  - "ETEC", salmonella, shigella, campylobacter;
  - Chronic diarrhea with weight loss: giardia or other protozoan
  - E histolytica vs non-pathogenic protozoa

STDs: Ulcers

- Herpes, herpes, herpes
  - Primary episode most severe
  - Recurrence rates variable
  - Most transmission from asymptomatic shedding
  - Chronic suppressive therapy reduces outbreaks and transmission
  - Recognize unusual presentations: discharges, irritation, sacral radiculitis, recurrent meningitis (differentiate from HSV encephalitis)

STDs: Ulcers

- Syphilis
  - Stages of the disease: primary (chancre), secondary (rash), latent, tertiary (neuro)
  - Diagnostic tests
    - Screening: RPR, VDRL – false-positives
    - Confirmatory: FTA-ABS, MHA-TP, TP-PA
    - Indications for CSF examination
  - Treatment is penicillin
    - Benzathine IM for primary, secondary, latent
    - IV for neurosyphilis
    - PCN allergy: doxycycline or desensitize

STDs: Non-ulcerative

- Gonorrhea
  - Treat with ceftriaxone – not FQ or azithromycin
  - Always also treat chlamydia

- Chlamydia
  - 75% of women and 50% of men asymptomatic
  - Most sexually-active women: routine screening recommended
  - Rx: azithromycin preferred, even in pregnancy

Vaginitis

- Bacterial vaginosis (40-50%)
  - grayish-white discharge, pH>4.5 pos whiff-amine test, clue cells on wet mount

- Vulvovaginal candidiasis (20-25%)
  - pH 4-4.5, organism on a wet mount or KOH prep

- Trichomoniasis (15-20%)
  - elevated pH, motile trichomonads on wet mount
### Urinary Tract Infections

- Acute cystitis in healthy women
  - *E. coli* in 80%
  - Treat without culture unless resistance suspected
  - Recommended: T/S or nitrofurantoin or fosfomycin
  - Avoid quinolones due to "collateral damage"
  - Avoid beta-lactams since they eradicate lactobacillus
- Pyelonephritis: ciprofloxacin
- Prostatitis: ciprofloxacin, with long course for chronic infection

### Asymptomatic Bacteriuria

- Treatment generally not indicated, including for:
  - Elderly
  - Diabetics
  - Patients with urinary catheters
  - Patients with pyuria
- Exceptions
  - Pregnant women
  - Patients about to undergo urologic procedures
  - Possible exception: Patients about to undergo any surgery

### HIV: Testing

- ELISA screening test done followed by Western blot
- CDC criteria for Western blot interpretation
  - positive: at least 2/3 of p24, gp41, or gp120/160
  - negative: no bands
  - indeterminate: any HIV band, but not meeting criteria for positive – may be lab artifact or seroconversion in progress
- Highly sensitive and specific for established infection
- All reactive rapid HIV tests must be followed by standard testing

### HIV: Acute (Primary) Infection

- Mononucleosis-like syndrome – may include fever, sore throat, rash, oral/genital ulcers, hepatitis, diarrhea, meningitis
- HIV antibody negative; HIV RNA ("viral load") high-titer positive – very contagious
- False-positive HIV RNA at low levels may occur
- Treatment controversial

### HIV: Treatment

- **Who gets treatment?**
  - All patients with symptomatic HIV disease
  - All patients with CD4 < 500, even if asymptomatic
  - All pregnant women
  - All with hepatitis B
- **Who doesn’t get treatment?**
  - Controversial
  - CD4 > 500 – treat if patient is “ready”
**Most Commonly-Used Antiretroviral Agents, 2012**

<table>
<thead>
<tr>
<th>Combination</th>
<th>Class</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>zidovudine + lamivudine (Combivir)</td>
<td>NRTI combination</td>
<td>Anemia, fatigue, nausea</td>
</tr>
<tr>
<td>tenofovir + emtricitabine (Truvada)</td>
<td>NRTI combination</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>abacavir + lamivudine (Epzicom)</td>
<td>NRTI combination</td>
<td>Abacavir hypersensitivity*</td>
</tr>
</tbody>
</table>

*All patients should be tested for HLA-B*5701 before receiving abacavir!

**HIV: Post-exposure Prophylaxis**

- “Rule of 3’s” for blood-borne pathogens
- Obtain baseline serologies in person who sustained injury
- Initiate PEP while results of testing of source patient are pending
- Use 2 or 3 drugs x 28 days if source patient positive
- High rates of discontinuation for side effects

**HIV: OI Prophylaxes**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Indication</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>CD4&lt;200, prior PCP, thrush</td>
<td>TMP-SMX</td>
</tr>
<tr>
<td>TB</td>
<td>PPD&gt;5 mm or exposure to active case</td>
<td>INH</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>CD4&lt;100, positive toxo antibody</td>
<td>TMP-SMX</td>
</tr>
<tr>
<td>M avium complex</td>
<td>CD4&lt;50</td>
<td>azithromycin</td>
</tr>
<tr>
<td>S pneumoniae</td>
<td>CD4&gt;200</td>
<td>pneumococcal vaccine</td>
</tr>
</tbody>
</table>

**HIV: Vaccines**

- Indicated:
  - Annual influenza
  - Hepatitis A and B if susceptible
  - Pneumococcal (if CD4 > 200)
  - Other non-HIV related vaccines, if indicated
- Avoid live virus vaccines (varicella, zoster, Yellow Fever, MMR) if CD4 < 200

**Non-HIV Immunocompromised Hosts**

- Splenectomy: Overwhelming infection from encapsulated organisms (esp pneumococcus); Vibrio spp; babesiosis
- Steroids: increased routine bacterial infections as well as certain OIs (Listeria, aspergillus, PCP, strongyloides)
  - Risk higher with longer dose/duration (> 1 month)
- TNF-alpha inhibitors: disseminated mycobacterial and fungal infections (e.g., histoplasmosis)
Thank you and good luck!

(... but you won’t need it!)