Update on Infectious Diseases
(More than just “Bag Bugs and New Drugs”)

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Seven Timely “Hot Topics” in Infectious Diseases
(can we cover this in only one hour??)

- Skin and soft tissue infections.
- Community acquired pneumonia.
- Endocarditis.
- Seasonal and avian influenza.
- Meningitis.
- Sexually transmitted diseases.
- Antibiotic update.

Skin and Soft Tissue Infections
Skin and Soft Tissue Infections

- A patient comes to your office with a two day history of painful, tender boils that he thinks are "spider bites". His wife has had similar lesions in the past that occasionally drain yellow pus.
  - What is the diagnosis? How should he be treated? What about his wife?

Skin and Soft Tissue Infections: Bacteriology

- Cellulitis vs. Abscess (or both)
- Most common pathogens:
  - Staphylococcus aureus.
    - Methicillin-resistant strains (CA-MRSA).
      - Increasing prevalence in the community.
  - Beta hemolytic streptococci.
    - Group A, B, etc.

Bacteriology of Skin and Soft Tissue Infections (cont’d)

- Diabetic foot infections.
  - Mixed aerobic/anaerobic.
    - S. aureus, Group B strep, enterococcus, Bacteroides, gm negs, etc.
- Cat or dog bite/scratches.
  - Pasturella multocida, strep, staph, anaerobes.
- Human bites
  - Eikenella corrodens, strep, staph, anaerobes.
- Dirty, contaminated wounds.
  - Anaerobes, gram negative rods.
- Nodular lymphangitis.
  - Sporothrix schenckii (gardening), Nocardia, Mycobacterium marinum (seawater), Francisella tularensis, Leishmania.
Community Acquired Methicillin Resistant Staphylococcus aureus (CA-MRSA)

- Increasing prevalence in outpatients.
- Often presents as clusters of abscesses or “spider bites”.
- USA 300 strain prevalent.
  - Panton-Valentine leukocidin toxin.
- Enhanced transmissibility.
- Tendency for recurrence.
- Empiric rx of SSTI’s must cover for MRSA.
  - Drainage of abscess(es) may be more important than the correct antibiotic.

MRSA Skin and Soft Tissue Infection

Treatment of Skin and Soft Tissue Infections

- Drainage of abscesses most important.
- Empiric outpatient antibiotics:
  - 1st generation cephalosporin (Keflex®) or dicloxacillin.
    - Good for staph and strep (but NOT MRSA).
- If MRSA is a concern:
  - Clindamycin.
    - Good for PEN allergic patients, covers many strains of CA-MRSA.
  - TMP/SMX.
    - Covers MRSA, but NOT β-strep (?Add Keflex or amoxicillin).
- Bite wounds:
  - Augmentin®.

Other MRSA Treatment Options

- Tetracyclines: Not used in children.
- Rifampin: Not to be used alone, but may be added for “synergy”.
- Linezolid (Zyvox®): VERY expensive.
- Macrolides, Fluoroquinolones: Limited utility due to pre-existing or acquired resistance.
- Vancomycin:
  - Standard for severe MRSA infections.
  - Linezolid, daptomycin, tigecycline also options for severe disease when IV therapy warranted.
Preventing MRSA Transmission
- Keep wounds covered.
- Wash hands frequently (especially after touching infected skin or changing dressings).
- Dispose of used bandages in trash.
- Avoid sharing personal items.
- Is there a role for MRSA screening and decolonization if positive?
  - More data needed.
  - Nares cultures or rapid PCR testing.
  - Intranasal mupirocin 2% BID x 5 days.
  - Chlorhexidine showers and scrubs.

Emerging Multi-Drug Resistance in CA-MRSA
- Clusters of CA-MRSA isolates resistant to erythromycin, clindamycin, tetracycline, ciprofloxacin, and mupirocin\(^1\):
  - But most circulating strains of CA-MRSA are still sensitive to these alternate agents.
  - TMP/SMX resistance rare in MRSA USA300.

**Community Acquired Pneumonia**

- A patient presents with a 3 day history of cough, fever, pleuritic chest pain and yellow sputum.
  - What diagnostic tests should be ordered?
  - What are the common causes?
  - How should the patient be treated?
  - Should he be hospitalized or managed as an outpatient?

**Etiology of CAP***

<table>
<thead>
<tr>
<th>Outpatients</th>
<th>Non-ICU Inpt.</th>
<th>ICU Inpatient</th>
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<tbody>
<tr>
<td>S. pneumoniae</td>
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<tr>
<td>M. pneumoniae</td>
<td>M. pneumoniae</td>
<td>Legionella spp</td>
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<td>H. influenzae</td>
<td>H. influenzae</td>
<td>H. influenzae</td>
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<tr>
<td>C. pneumoniae</td>
<td>C. pneumoniae</td>
<td>Gm neg rods</td>
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<tr>
<td>Respiratory viruses</td>
<td>Legionella spp</td>
<td>S. aureus</td>
</tr>
<tr>
<td>Respiratory viruses</td>
<td>Viruses</td>
<td>* Increasing MRSA and drug resistant S. pneumoniae (DRSP).</td>
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</table>

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**Community Acquired Pneumonia**

- 5 million cases CAP per year in US.
  - 6th leading cause of death.
- Common symptoms: Cough, dyspnea, sputum production, pleuritic chest pain.
- “Typical” vs. “atypical” organisms.
  - S. pneumoniae, H. influenzae, S. aureus, K. pneumoniae, etc.
  - M. pneumoniae, L. pneumophila, Legionella sp, viruses, etc.

**Heated Discussions Between IDSA and ATS on CAP on Treatment Guidelines**
Hospitalize vs. outpatient therapy?
- CURB-65 severity criteria.
  - Confusion. Uremia (BUN > 19), Resp rate > 30, BP < 90/60, age > 65.
  - If score ≤ 1, OK for outpatient rx.
  - If score > 1, hospitalize.

Med-surg vs. ICU admission

Empiric Treatment Guidelines

CAP Diagnostic Studies

- CBC.
- Chest X-ray.
- Sputum culture?
  - Yes for severe CAP.
  - Controversial for mild dz in outpts, since yield is low.
- Blood cultures?
  - Controversial, since yield is low (<10%).
  - But: Blood cxs before antibiotics are a quality measure as part of in-hospital CAP initiative.
- Other studies:
  - Urinary pneumococcal and Legionella antigen.
  - Serologies.
  - Mycoplasma, Legionella, etc.

CAP Empiric Treatment

Outpatient therapy
- Previously healthy, no risk for Pseudomonas:
  - Macrolide (azithromycin, clarithromycin, or erythromycin).
    - Doxycycline (less preferred).
- Co-morbid conditions (DM, chronic heart, lung or kidney dz, EtOH, immunosuppressed, recent antibiotics).
  - Respiratory fluoroquinolone (levofloxacin, moxifloxacin, gemifloxacin), or
  - β-lactam (Augmentin®) + macrolide.

CAP Empiric Treatment

Inpatient therapy
- Non-ICU admission.
  - Respiratory fluoroquinolone (levofloxacin, moxifloxacin, gemifloxacin), or
  - β-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam, ertapenem) + macrolide.
- ICU admission.
  - β-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam) + azithromycin or fluoroquinolone.
- ICU admission with Pseudomonas risk.
  - Anti-pseudomonal, anti-pneumococcal β-lactam (piperacillin-tazobactam, ceftepime, imipenem, meropenem) + ciprofloxacin or levofloxacin.
  - ALSO: Add vancomycin or linezolid if risk for MRSA.
Other Important Points

- Influenza vaccine.
- Pneumococcal vaccine.
- Smoking cessation counseling.
- Respiratory hygiene measures.

Endocarditis & SBE Prophylaxis

Endocarditis Prophylaxis

- **A patient known to have mitral valve prolapse is scheduled for dental work. In the past, she has taken antibiotics to prevent endocarditis.**
  - Under what circumstances should a patient take antibiotics before dental work?
  - What is the optimal antibiotic regimen?

Bacterial Endocarditis

- Endothelial valve injury with bacterial infection.
  - Valvular destruction, local extension of infection.
  - Metastatic infection from bacteria.
  - Embolization.
  - Immune complex mediated injury.
- Subacute vs. acute presentation.
  - Often depends on organism.
**Bacteriology of Endocarditis**

- *S. aureus.*
  - Increasing incidence of MRSA.
- Viridans group streptococci.
- Coagulase negative staph.
- Strep bovis.
- HACEK group.
- “Culture negative”.
  - Abiotrophia, Bartonella, Coxiella, Chlamydia, Legionella, etc, unknown causes.
- Fungi.

**Duke Criteria for Endocarditis**

- Definite:
  - Histopathology, or
  - Major criteria = ECHO, blood culture (+), new regurgitant murmur.
  - Minor criteria = predisposing condition, temp >38, serology, vascular findings, “soft” pos ECHO.
  - Need 2 major, 1 major + 3 minor, 5 minor.
- Possible:
  - 1 major and 1-2 minor, or 4 minor.

**2007 AHA Guidelines on Prevention of Infective Endocarditis (IE)**


- Major revision compared to previous recommendations.
- Rationale for change:
  - Most cases of IE are NOT attributable to invasive procedures, but are the result of randomly occurring bacteremias.
  - Widespread prophylaxis may prevent exceedingly small number of cases of IE, if any at all.
  - Risk of antibiotics exceeds the benefits.
  - Maintenance of optimal oral health and hygiene may reduce IE incidence more than antibiotics.

**Candidates for Antibiotic Prophylaxis = “High Risk Persons”**

- Only those with highest risk of adverse outcomes from endocarditis.
  - Indwelling prosthetic heart valve.
  - Previous episode of IE.
  - Congenital heart disease (CHD).
    - Unrepaired cyanotic CHD.
    - Six months after repair of CHD.
    - Repaired CHD with residual defects.
  - Cardiac transplantation with valvulopathy.
Procedures Which Require Antibiotic Prophylaxis in **High Risk Persons Only**

- All dental procedures that involve manipulation of gingival tissue or the periapical region of tooth or perforation of oral mucosa.
- Invasive respiratory procedure.
- Surgical procedure of infected skin or soft tissues.
- Prophylaxis is NOT recommended for any GI or GU procedure.

**Antibiotic Regimens for Dental Procedure to Prevent IE**
(Single dose 30-60 min before procedure)

<table>
<thead>
<tr>
<th>Oral:</th>
<th>Amoxicillin 2 gm PO</th>
</tr>
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<tbody>
<tr>
<td>Oral (allergic to penicillin):</td>
<td>Cephalexin 2 gm or clindamycin 600 mg or azithromycin 500 mg PO</td>
</tr>
<tr>
<td>Unable to take PO:</td>
<td>Ampicillin 2 gm IV, or cefazolin or ceftriaxone 1 gm IM or IV</td>
</tr>
<tr>
<td>Unable to take PO allergic to penicillin:</td>
<td>cefazolin or ceftriaxone 1 gm, or clindamycin 600 mg IM or IV</td>
</tr>
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**Influenza: Seasonal and Avian**
Clarification of Terms

• Seasonal flu
  – Contagious respiratory illness caused by influenza viruses.
• Avian flu (Bird Flu)
  – Human infection caused by avian influenza viruses (which occur naturally among birds).
• Pandemic flu
  – Global outbreak (pandemic) of serious illness that spreads easily from person to person.
  – (Currently, there is no pandemic flu.)

Seasonal Influenza

• Respiratory illness.
  – Mild to severe disease.
• Each year 5-20% of population affected.
• Pattern of global spread predictable.
• >200,000 hospitalizations/year in US.
• 36,000 deaths/year in US.
• Elderly and young children at highest risk for complications and death.

Seasonal Influenza: Clinical Features

• Incubation period: 1-4 days
• Symptoms often of abrupt onset.
  – Fever, chills, myalgias, anorexia, H/A, extreme fatigue.
• Fever lasts 2-3 days, up to 38-40° C.
• Nonproductive cough, sore throat, upper respiratory congestion.
• Nausea, vomiting, and diarrhea
  – More common in children
• Physical exam: fever, weakness, mild upper respiratory tract inflammation, rare cracks on lung examination.
• Uncomplicated: major symptoms gone in a few days; cough, weakness, and malaise up to 2 weeks.
• Routine lab: non-specific; thrombocytopenia and leukopenia in fulminant cases
• CXR: usually clear
Seasonal Influenza: Diagnosis

- Clinical presentation.
  - Local epidemiology.
- Laboratory testing
  - EIA rapid screen.
    - Directigen assay (>70% sensitivity; >90% specificity).
    - Nasopharyngeal swab, nasal aspirates, throat swab.
  - PCR
  - IFA
  - Viral culture
  - Serology

2007-8 Seasonal Influenza Activity

How Effective is the Flu Vaccine?

- Healthy adults <65 yrs.
  - 70-90% effective if strain well matched.
    - 40-60% effective if strains not well matched.
- Chronically ill adults >65 yrs.
  - 30-60% effective under ideal conditions.
  - Less effective if strain not well matched.

What Was Different About the 2007-8 Flu Season?

- H3N2 and B strains were not well matched with vaccine components
  - Vaccine only 44% effective (70-90% when strains well matched).
- Circulating H3N2 strain resistant to amantadine and rimantadine.
  - Oseltamivir (Tamiflu®) & zanamivir (Relenza®) still recommended.
  - But: 11% H1N1 strains resistant to oseltamivir.
Who Should Get Vaccinated?
ACIP Recommendations

- All persons at high risk for influenza-related complications and severe disease, including
  - children aged 6–59 months,
  - pregnant women,
  - persons aged ≥50 years,
  - persons of any age with certain chronic medical conditions; and
- persons who live with or care for persons at high risk, including
  - household contacts who have frequent contact with persons at high risk and who can transmit influenza to those persons at high risk and
  - health-care workers

Avian Influenza
Avian Influenza

- Current avian influenza = H5N1 subtype.
  - Prior outbreaks of avian flu: H7N7, H1N1.
- Virus spread by migratory aquatic birds.
  - Transmission to domestic fowl -> humans.
  - Poultry infections widespread (>49 countries).
  - H5N1 detected in mute swans in Michigan.
- Disease in humans.
  - Fever, cough, S0B, lymphopenia, pneumonia.
  - Mortality rate = 50%.
  - Rare person to person transmission (NEJM 1/27/05).
  - BUT: Swine, quail or humans could be "mixing hosts" with other influenza strains \( \Rightarrow \) pandemic strain.
  - Oseltamivir (Tamiflu®) may be effective, but higher doses and durations may be required.

H5N1 Human Cases
(as of 4/30/08)

- 382 human cases, 241 deaths.
- Since Jan 2003, human cases in 14 countries:
  - East Asia and the Pacific:
    - Cambodia, China, Indonesia, Thailand, Lao People’s Democratic Republic, Vietnam, Pakistan, Myanmar.
  - Europe and Eurasia:
    - Azerbaijan, Turkey.
  - Near East, Africa:
    - Djibouti, Egypt, Iraq, Nigeria.

Countries with Confirmed H5N1 in Birds

Countries with Confirmed Human Cases of H5N1 since 2003 (as of 4/08)
Vaccine for Avian Influenza

- Vaccines produced and stockpiled (Sanofi Pasteur, Novartis).
- Inactivated human H5N1 isolate.
  - Two doses one month apart for persons 18-64 yrs.
  - Immunogenic in studies.
    - Protective against pandemic strain.
- Not commercially available.
  - Stockpiled by WHO and US government.
    - WHO states 100 million two dose courses available immediately.
    - Global production capability by 2010 = 4.5 billion courses.
Fever and a Skin Rash: Meningitis

• A 22 year old college student presents with fever to 103, confusion, headache, stiff neck, and diffuse petechial skin rash.
  – What is the most worrisome diagnosis?
  – What else is in the differential diagnosis?
  – What diagnostic tests are required?
  – How should he be managed?

Fever and Skin Rash

• Life threatening infections:
  – Meningococcal infection.
  – Pneumococcal sepsis.
  – Rickettsia infection (RMSF, typhus).
  – Hemorrhagic fevers (Dengue, Lassa, Marburg, Ebola, Rift Valley Fever).
  – Other causes of sepsis.

• Non-life threatening infections:
  – Enteroviruses.
  – Measles.
  – Rubella.
  – Herpes simplex virus.
  – Varicella-zoster virus.
  – Syphilis.
  – Disseminated gonococcal infection.
  – Primary HIV infection.
Bacterial Meningitis

- Bacterial infection and inflammation of the leptomeninges (tissue surrounding brain and spinal cord).
- Fever, headache, stiff neck, altered mental status.
  - Kernigs, Brudzinsky signs specific but NOT sensitive.
- CSF analysis, blood cultures, CT scan.
- Begin rx ASAP if meningitis suspected.
  - Increased mortality with delay in rx.
- Antibiotic prophylaxis indicated for close contacts of pts with meningococcal and H. flu.
  - Ciprofloxacin or rifampin.

Initial Management of Suspected Bacterial Meningitis

- Hospitalization mandatory.
- IV antibiotics should be started ASAP.
- CBC, chemistries, blood cultures.
- CT scan before LP (?)
- Lumbar puncture for CSF analysis.
  - OP, cell count and diff, protein, glucose, gm stain and culture.
  - HSV-DNA, VDRL, enterovirus culture, CRAG, fungus cx, AFB cx, coccidioides serology, etc.

Empiric Antibiotic Therapy for Bacterial Meningitis

**Tunkel et al. Clinical Infectious Diseases 2004; 39: 1267-84.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Etiology</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-23 months</td>
<td><em>S. pneumoniae</em>, <em>N. meningitidis</em>, <em>H. influenzae</em>, group B strep</td>
<td>Ampicillin + 3rd gen cephalosporin</td>
</tr>
<tr>
<td>2-50 yrs</td>
<td><em>S. pneumoniae</em>, <em>N. meningitidis</em> (<em>H. influenzae</em> less common)</td>
<td>Vancomycin + 3rd gen cephalosporin</td>
</tr>
<tr>
<td>&gt;50 yrs</td>
<td><em>S. pneumoniae</em>, <em>N. meningitidis</em>, <em>Listeria monocytogenes</em>, gm neg rods</td>
<td>Vancomycin + 3rd gen cephalosporin + ampicillin</td>
</tr>
</tbody>
</table>

Steroids for Meningitis

- Shown to reduce long term morbidity and mortality.
  - Especially in children and adults with AMS.
- Rationale: Inflammatory cytokines play major role in clinical manifestations.
  - Internal components of lysed bacteria very inflammatory.
- Ideally, give 1st dose of steroids BEFORE (or at same time) as 1st dose of antibiotic.
- Dose: dexamethasone 0.15 mg/kg q6hrs for 2-4 days.
  - May reduce CSF vancomycin penetration (?add rifampin).
Let’s Talk About SEX!

Sexually Transmitted Diseases

- A sexually active patient complains of genital “sores” and a genital discharge. He/she has had 4 different partners over the past 6 months. He/she wants to be tested “for everything”.
  - Which infections are most common?
  - What diagnostic tests should be ordered?
  - What is optimal treatment for STD’s?

Prevalence of STD’s in the US

- HPV 20 million
- Chlamydia 3 million
- Hepatitis B 1.25 million
- HIV 1.2 million
- Genital Herpes 50 million

References:
Genital Herpes

**Primary**
- Tender vesicles.
- Shallow ulcerations.
- Local pain & itching.
- Dysuria.
- Urethral discharge.
- Cervicitis/vaginal discharge.
- Inguinal adenopathy.
- Systemic symptoms
  - Fever, headache, myalgias, meningismus.

**Recurrent**
- Prodrome may be present.
- Milder clinical illness.
  - Local symptoms only.
  - Less extensive distribution.
  - Frequency variable.
  - Emotional burden.
  - ?? Predisposing factors.

Diagnosis of HSV Infection

- Virus culture.
- DNA detection.
  - PCR.
  - More sensitive than culture.
- Antigen detection.
  - DFA stain, IP stain.
- Cytology.
  - Tzanck, PAP.
- Antibody detection.

HSV Serology

- Older techniques (IF, CF, neut) unreliable due to HSV-1 & HSV-2 cross-reactivity.
- IgM assays are **not useful** for diagnosis.
  - HSV IgM detected during recurrences.
- Glycoprotein G based assays.
  - HerpeSelect ELISA HSV 1 & 2.
  - HerpeSelect Immunoblot HSV 1 & 2.
  - HSV-2 ELISA (Trinity Biotech).
  - Point of care tests:
    - Biokit HSV-2, SureVue HSV-2
2006 CDC HSV Rx Guidelines

1st Episode (7-10 days rx)

- Acyclovir
  - 400 mg TID.
  - 200 mg 5x/day.
- Valacyclovir
  - 1000 mg BID.
- Famciclovir
  - 250 mg TID.

Recurrent Episode*

- Acyclovir
  - 400 mg TID or 800 mg BID x5 days.
  - 800 mg TID x2 days.
- Valacyclovir
  - 500 mg BID x3 days.
  - 1 gm daily x 5 days.
- Famciclovir
  - 125 mg BID x5 days.
  - 1 gm BID x1 day.

* Higher doses/durations recommended for HIV (+)

2006 CDC HSV Rx Guidelines for Suppressive Rx

- Acyclovir 400 mg BID
- Famciclovir 250 mg BID
- Valacyclovir 500 mg daily
  - If <10 outbreaks/yr
  - Valacyclovir 1 gm daily
    - If ≥ 10 outbreaks/yr

* Higher doses recommended for HIV (+)

Suppressive Valacyclovir Reduces Risk of HSV Transmission to Partner

Placebo

Valacyclovir 500 mg once daily

2.2% (16/741)

75% reduction

P=0.01
RR: 0.25 (95% CI: 0.08, 0.74)

0.5% (4/743)


Human Papillomavirus (HPV)

Genital Warts

Cervical Cancer
1.4 million new cases of low-grade cervical dysplasia (CIN 1)

1 million new cases of genital warts

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**Efficacy of HPV4 Vaccine in the Per-Protocol Analysis Population**

- 16- to 26-year-old females naive to the relevant vaccine type at enrollment and through 30 days Postdose 3
- Over a period of 2 to 4 years

<table>
<thead>
<tr>
<th>End Point: HPV 6/11/16/18-related</th>
<th>Vaccine Group</th>
<th>n</th>
<th>Placebo Group</th>
<th>n</th>
<th>Efficacy (95% CI)</th>
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<tbody>
<tr>
<td>CIN 2/3 or AIS</td>
<td>8,487</td>
<td>0</td>
<td>8,460</td>
<td>53</td>
<td>100% (93–100)</td>
</tr>
<tr>
<td>CIN 3 or AIS‡</td>
<td>8,487</td>
<td>0</td>
<td>8,460</td>
<td>32</td>
<td>100% (88–100)</td>
</tr>
</tbody>
</table>

- The efficacy of vaccine against HPV 16- and 18-related VIN 2/3 or VaIN 2/3 was 100%.

*Analysis of CIN 2/3 and AIS endpoints included protocol 205.
*Defined by FIGO as Stage 0 cervical cancer; FIGO = International Federation of Gynecology and Obstetrics.

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**Advisory Committee on Immunization Practices (ACIP) Statement (6/29/06)**

- HPV vaccine should be routinely given to all girls 11-12 years old.
- Clinicians should allow for vaccination of girls beginning at nine years old.
- Clinicians should allow for vaccination of girls and women 13-26 years old.
- The vaccine should be administered before onset of sexual activity, but females who are sexually active should still be vaccinated.
  - ACIP consists of 15 members appointed by the Secretary of the Department of Health and Human Services (HHS). They advise the director of CDC and Secretary of HHS on control of vaccine-preventable disease and vaccine usage.
Syphilis: Chancre


<table>
<thead>
<tr>
<th>Year</th>
<th>American Indian/AK Native</th>
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<th>Black</th>
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<td>1</td>
<td>5</td>
<td>10</td>
<td>14</td>
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</table>
Rx of Syphilis

- **Early:**
  - Primary, secondary, early-latent
    - Benzathine Pen-G 2.4 million U IM
      - Alt: Doxycycline 100mg BID for 14 days.
      - Ceftriaxone 1 gm IM/IV x 8-10 days.
      - Azithromycin 2 gm PO x1 dose.
        - BUT recent reports of in vitro resistance and azithromycin treatment failures!
  - Late latent:
    - Benzathine Pen-G 2.4 million U IM weekly x 3
    - Alt: Doxycycline 100mg BID for 28 days.
- **Neurosyphilis:**
  - Penicillin-G 18-24 million U/d IV for 10-14 days.
  - Ceftriaxone not recommended in HIV due to frequent treatment failures.

**Neisseria gonorrhoeae**

Gonococcal Isolate Surveillance Project (GISP) — Penicillin, tetracycline, and ciprofloxacin resistance among GISP isolates, 2006

Note: PenR=penicillinase producing N. gonorrhoeae and chromosomally mediated penicillin-resistant N. gonorrhoeae; TetR=chromosomally and plasmid mediated tetracycline-resistant N. gonorrhoeae; QRNG=ciprofloxacin resistant N. gonorrhoeae.
Intermediate resistance have ciprofloxacin MICs of 0.125 - 0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.

Note: Resistant isolates have ciprofloxacin MICs > 1 µg/ml. Isolates with intermediate resistance have ciprofloxacin MICs of 0.125 - 0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.

**Guidelines for Rx of Gonorrhea**

**Low risk of resistance**
- Cefixime 400 mg
- Cefpodoxime 400 mg
- Ceftriaxone 125 mg IM*
- Ciprofloxacin 500 mg*
- Ofloxacin 400 mg*
- Levofloxacin 250 mg*

**CA, HI, PI, SE Asia, MSM, etc**
- Cefixime 400 mg
- Cefpodoxime 400 mg
- Ceftriaxone 125 mg IM*
- Alternatives:
  - Spectinomycin 2 gm IM
  - Azithromycin 2 gm (four 500 mg tabs)* with test of cure.
  - Cipro*, Oflox*, or Levo* with test of cure.

Plus Azithromycin 1 gm, or Doxycycline 100 mg BID x 7 days
* OK for pharyngeal infection

**Tuberculosis**
Tuberculosis

• A family of six immigrated to the US from SE Asia and are referred to you. The grandmother has apical fibrotic scarring on CXR and mild cough. Two children have positive PPD skin tests but no symptoms and normal CXR’s.
  – What do you do? Are they contagious? What tests and therapies do you recommend?

Tuberculosis

• Worldwide endemic infection.
  – Leading cause of death worldwide from a single infection (higher than AIDS and malaria).
• Synergistic disease in HIV(+) population.
• Increasing resistance worldwide.
  – Multi-drug resistance (MDR).
    • Resistant to INH and rifampin.
  – Extensively drug resistance (XDR).
    • Resistant to INH, rifampin, quinolones and ≥ one injectable agent (capreomycin, kanamycin, or amikacin).

Tuberculosis

• Pulmonary infection in >85% cases.
  – Classic symptoms: Fever, night sweats, cough, hemoptysis, weight loss.
  – CXR abnormalities.
    • Apical infiltrates common.
    • Miliary pattern in disseminated disease.
• Extrapulmonary disease.
  – Lymphadenitis.
  – Pleura, renal, GI tract, pelvic, CNS, etc.

Tuberculosis

• Diagnosis:
  – AFB stain and culture.
  • DNA probe for rapid diagnosis.
  • Susceptibility testing routine.
• Latent TB Infection (LTBI)
  – Tuberculin skin test (TST) with purified protein derivative (PPD)
    • Limitations: False negatives, false positives
  – QuantiFERON Gold blood assay.
Treatment of Tuberculosis

• Active disease:
  – Multiple drugs needed.
  – INH, RIF, EMB, PZA for 2 months; then (if sensitive to all) INH & RIF for 4 more months.
  – Other options available if side effects, toxicity, resistance, etc.
  – Daily observed therapy (DOT) recommended.

• LTBI:
  – Recommendations for who to treat depends on co-morbidities, risk of reactivation, etc.
  – INH 300 mg/day for 9 months.

XDR TB

• Resistant to INH, rifampin, quinolones and ≥ one injectable agent (capreomycin, kanamycin, or amikacin).
• XDR strains detected in at least 17 countries (including US).
  – Estimated 10% MDR TB is XDR.
• 2005 XDR outbreak in HIV (+) pts in S. Africa.
  – 53 patients; 55% had not been treated previously.
  >95% mortality.
• Rx = Early detection, proper isolation, optimal treatment, DOT.
**Antibiotic Update**

(Good News and Bad News)

- Fewer new drugs and fewer new drug classes over time.
- Increasing resistance.
- Increasing incidence of MDRO’s (multi-drug resistant organisms).
  - MRSA.
  - VRE.
  - ESBL producing gram neg rods.

**Antibiotic Classes**

- Penicillins
- Cephalosporins
- Quinolones
- Macrolides
- Tetracyclines
- Carbapenems
- Oxazolidines
- Aminoglycosides
- Miscellaneous antibacterial agents
- Antifungals
Penicillins

- Penicillin G.
- Ampicillin, amoxicillin.
- Nafcillin, oxacillin, dicloxacillin.
  - Staph aureus, strep (not MRSA or enterococcus).
- Combination with β-lactamase inhibitors.
  - Staph, strep, enterococcus, some gm negs, anaerobes.
  - Augmentin® (amoxicillin + clavulanic acid).
  - Unasyn® (ampicillin + sulbactam).
  - Zosyn® (piperacillin + tazobactam).
  - Timentin® (ticarcillin + clavulanate).

Cephalosporins

- No coverage for enterococcus or MRSA.
- 1st generation: Staph, strep, some gm negs.
  - Cefazolin, cefalexin.
- 2nd generation: Adds anaerobes and/or more gm negs.
  - Cefuroxime, cefoxitin, cefotetan.
- 3rd generation: More gm negs, good CSF penetration.
  - Ceftriaxone, cefotaxime.
  - Ceftazadime (covers pseudomonas, but not S. aureus).
- 4th generation: (pseudomonas AND S. aureus)
  - Cefepime

Fluoroquinolones

- Broad spectrum coverage.
- Excellent PO absorption.
- Increasing resistance.
  - Levofloxacin.
  - Gemifloxacin.
  - Ciprofloxacin.
    - Unreliable activity against S. pneumoniae.
      - Should NOT be used for CAP.
  - Moxifloxacin.
    - Poor urinary excretion.
      - Should NOT be used for UTI’s

Carbapenems

- Very broad spectrum with gm(+), gm (-), anaerobic coverage.
  - ESBL producing GNR’s.
  - Most cover Pseudomonas.
- Imipenem/cilastatin.
- Meropenem.
- Ertapenem.
- Doripenem.
Antifungals

• Amphotericin-B:
  – Lipid-based preparations.
  – Broad spectrum, but IV only and nephrotoxic.
• Azoles:
  – Fluconazole, ketoconazole, itraconazole.
  – Voriconazole, posaconazole.
  • Aspergillus activity.
• Echinocandins:
  – Active against all strains of Candida.
  – Caspofungin, anidulofungin, micafungin.

Miscellaneous Agents

• Azithromycin.
  – Long half life macrolide.
  – Excellent choice for CAP, Chlamydia.
• Vancomycin.
  – Glycopeptide with gm(+) coverage.
  – Oral therapy for C. difficile colitis.
• Linezolid.
  – Oxazolidine with gm(+) coverage.
  – MRSA and VRE.
• Daptomycin.
  – Gm(+) coverage including MRSA.
  – Not effective for pulmonary infections.
• Tigecycline.
  – Broad spectrum including gm(-)’s, anaerobes, MRSA.