Update on Infectious Diseases
(Bugs in the News and More)
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Bugs in the News!

But Not Everyone is Paying Attention.....
2009 Top 10 Topics in Infectious Diseases

- Swine Flu, Bird Flu and Pandemic Flu.
- Seasonal Flu.
- MRSA.
- Increasing drug resistance.
- Community acquired pneumonia.
- Endocarditis.
- Meningitis.
- Antibiotic update.
- Sexually transmitted diseases.
- HIV.

Influenza: Swine, Avian and Seasonal

ID Question #1

- Which is a true statement regarding the current swine flu (H1N1) outbreak?
  1. The virus is resistant to oseltamivir (Tamiflu).
  2. This virus is H5N1 avian flu that jumped species.
  3. This is the same strain seen in 1918.
  4. The virus has a unique assortment of genes and seems to spread easily person-to-person.
  5. “Huh? Is there a swine flu outbreak?”

• This little piggy shoulda stayed home....
ID Question #1–answer

- (4) The virus has a unique assortment of genes and, unlike other swine influenza strains, spreads readily person-to-person.
  - Preliminary tests suggest swine, avian, and human genetic components.
- New virus; uncertain if humans have immunity from prior exposure to related viruses.
  - Seasonal vaccine likely does not offer any protection.
- Spreading globally.
  - WHO pandemic level 6.
- Most cases mild-moderate; mortality in US low so far.
  - ?Higher mortality initially in Mexico.
- Susceptible to oseltamivir and zanamivir.
- Unclear as to future directions.

2009 Swine influenza A (H1N1) Outbreak

Facts so far (as of 7/3/09):
- 33,902 confirmed US cases in all states and territories with 170 deaths (CDC).
- 89,921 confirmed worldwide cases; 382 deaths (WHO).
  - 10,262 confirmed cases from Mexico; 119 deaths.
- Most cases reported in developed countries with good surveillance systems
  - Many more cases likely undiagnosed and not yet confirmed.
- Most cases in young people (<25 yrs).
  - Highest mortality in ages 30-50 yrs and compromised hosts.
  - Increased infection rates in young persons suggests possible cross immunity in older persons from prior related infections.

Influenza Activity – 2008-9

New Human Influenza A (H1N1)
Number of laboratory confirmed cases and deaths

Status as of 9 May 2009
45/30 CET

The Influenza A (H1N1) virus has been declared a public health emergency. The World Health Organization has called on all countries to do what they can to contain the spread of this new strain of the flu virus.

As reported by National Focal Points

Map produced: 3 May 2009 12:07 CET
Avian influenza A (H5N1) Pandemic Level 3

<table>
<thead>
<tr>
<th>Inter-pandemic phase</th>
<th>New virus in animals, no human cases</th>
<th>Pandemic alert</th>
<th>No or very limited human-to-human transmission</th>
<th>Evidence of increased human-to-human transmission</th>
<th>Efficient and sustained human-to-human transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk of human cases</td>
<td>1</td>
<td>Pandemic</td>
<td>2</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
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2009 Swine influenza A (H1N1) Outbreak

- Level of panic in population.
  - Media frenzy.
  - Cautious government reaction.
  - Packed ER’s & MD offices, excessive flu testing.
  - School closures, social distancing, surgical masks.
  - Risk of over-prescribing antivirals.

Patient Zero?

- Edgar Hernandez (age 5).
  - First confirmed case of H1N1.
- LaGloria, Mexico (pop 3000).
  - Near Mexico City.
  - 72 pig farms in surrounding area.
  - Feb 2009, 1300 residents became ill with flu-like symptoms.
Hmm... How Could This Happen?

What next?
Is this finally “the big one,” the long predicted influenza pandemic?

Possible scenarios:

• Outbreak stabilizes and fizzles out.
  – Unlikely in view of current trends.
• Outbreak progresses and continues to spread worldwide over the next several months.
  – Southern hemisphere flu season beginning.
  – Virus may re-emerge in northern hemisphere in late summer and fall, possibly more severe, with increasing infections and mortality.
  • Similar to 1918 and 1957.
Avian Influenza (H5N1)

- Migratory aquatic birds responsible for spread.
  - Transmission to domestic fowl → humans.
  - Poultry infections widespread (>49 countries)
- Current outbreak = H5N1 subtype.
  - Prior outbreaks of avian flu: H7N7, H1N1.
- Disease in humans.
  - Fever, cough, SOB, 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 ⇒ pandemic strain.

H5N1 Human Cases
(as of 6/2/09)

- 433 human cases, 262 deaths.
- Since Jan 2003, human cases in 15 countries:
  - East Asia and the Pacific:
    - Cambodia, China, Indonesia, Thailand, Lao People's Democratic Republic, Vietnam, Pakistan, Bangladesh, Myanmar.
  - Europe and Eurasia:
    - Azerbaijan, Turkey.
  - Near East, Africa:
    - Djibouti, Egypt, Iraq, Nigeria.

Countries with Confirmed Human Cases of H5N1 since 2003 (as of 5/09)

H5N1 Vaccine

- H5N1 vaccine produced by Sanofi Pasteur and 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.
We Can All Sleep Better Tonight

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

Seasonal Influenza: Clinical Features

• Physical exam: fever, weakness, mild upper respiratory tract inflammation, rare crackles 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

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.

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

Yearly Notable Seasonal Flu Events

• 2008-9: Widespread resistance of seasonal H1N1 to oseltamivir (Tamiflu).
• 2007-8: Circulating H3N2 and B strains were not well matched with vaccine components.
  – Less effective protection rates.
• 2004-5: Vaccine shortage due to Serratia contamination of a Chiron plant in England.
  – Vaccine shortages and limited availability.
Influenza Vaccine Shortage 2004-5

TO OUR PATIENTS

WE WILL NOT BE RECEIVING ANY FLU VACCINE.
WE ARE SORRY FOR ANY INCONVENIENCE THIS MAY HAVE CAUSED.
PLEASE CALL YOUR LOCAL PHARMACY OR DEPT OF HEALTH.

2008-9: No Vaccine Shortage

Newsweek
FluFever
The Vaccine Crisis
Who Should Get Shots?
The Scary Future Of Winter Bugs
Skin and Soft Tissue Infections

- ID Question #3
- 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.
  - *Pasteurella 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...
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.

Counseling Prevention of 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 mupirocin1.
  - But most circulating strains of CA-MRSA are still sensitive to these alternate agents.
  - TMP/SMX resistance rare in MRSA USA300.

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Community Acquired Pneumonia

• ID Question #4
  • *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?

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, C. pneumoniae, Legionella sp., viruses*, etc.
Etiology of CAP*

Outpatients
- S. pneumoniae
- M. pneumoniae, H. influenzae, C. pneumoniae
- Respiratory viruses

Non-ICU Inpt.
- S. pneumoniae
- M. pneumoniae
- H. influenzae
- C. pneumoniae
- Legionella spp
- Viruses

ICU Inpatient
- S. pneumoniae
- Legionella spp
- H. influenzae
- Gm neg rods
- S. aureus

* Increasing MRSA and drug resistant S. pneumoniae (DRSP).

IDSA/ATS Consensus Guidelines on Management of CAP
Mandell et al. Clinical Infectious Diseases 2007; 44:S27-S72

- 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, ceftazidime, 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

• ID Question #5
• 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>
</thead>
<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>
</tbody>
</table>
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).
  - Toxic shock syndrome (group A strep, S. aureus).
  - 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.
  - Kernig's, Brudzinski 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 mengococcal 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, coccidiodes serology, etc.

Empiric Antibiotic Therapy for Bacterial Meningitis

<table>
<thead>
<tr>
<th>Age</th>
<th>Etiology</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-23 months</td>
<td>S. pneumoniae, N. meningitidis, H. influenzae, group B strep</td>
<td>Ampicillin + 3rd gen cephalosporin</td>
</tr>
<tr>
<td>2-50 yrs</td>
<td>S. pneumoniae, N. meningitidis (H. influenzae less common)</td>
<td>Vancomycin + 3rd gen cephalosporin</td>
</tr>
<tr>
<td>&gt;50 yrs</td>
<td>S. pneumoniae, N. meningitidis, Listeria monocytogenes, 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).
ID Question #7

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).

- 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.

**MDR & XDR Tuberculosis**

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

**Primary MDR TB**

**United States, 1993–2007**

*Updated as of April 23, 2008.*

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
Primary MDR TB in U.S.-born vs. Foreign-born Persons, United States, 1993–2007*

XDR TB Case Count defined on Initial DST† by Year, 1993–2007*

Antibiotic Update

*Updated as of April 23, 2008.
Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.

†Drug susceptibility test.
*Reported incident cases as of April 23, 2008.
Extensively drug-resistant TB (XDR TB) is defined as resistance to isoniazid and rifampin, plus resistance to any fluoroquinolone and at least one of three injectable second-line anti-TB drugs.

FIGURE Number of reported cases of extensively drug-resistant tuberculosis (XDR TB)* — United States, 1993–2006

* XDR TB defined as resistance to at least isoniazid, rifampin, any fluoroquinolone, and at least one second-line injectable drug (kanamycin, amikacin, or capreomycin).
†Excludes New York City.
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.
- Potential side effects: Tendinitis.

Carbapenems

- Very broad spectrum with gm(+), gm(-), anaerobic coverage.
  - ESBL producing GNR’s.
  - Most cover Pseudomonas (not ertapenem).
- 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.