# Antibiotics Use in the ED

LW LIN

## Pathophysiology

- Mechanisms
  - Inhibition of cell wall synthesis
  - Inhibition of DNA synthesis
  - Inhibition of protein synthesis
  - Inhibition of RNA synthesis
  - Interference with folate metabolism
  - Production of free radicals

## Table 4. Brief Characteristics Of The Most Commonly Used Antibiotics.

| Class | Mechanism of Action | Metabolism and Excretion | Bacteria Covered |
|---|---|---|---|
| **Penicillins (natural)** (penicillin G, pen VK) | Bactericidal<br>Inhibit cell wall synthesis | Excreted in urine mostly in intact form | **Gram** (+), except staph<br>Some **anaerobes**<br>*N meningitides* |
| **Penicillinase-resistant penicillins** (methicillin, nafcillin, dicloxacillin) | Bactericidal<br>Inhibit cell wall synthesis | Excreted in bile and urine | **Gram** (+), used mostly for staph, but not MRSA |
| **Aminopenicillins** (ampicillin, amoxicillin) | Bactericidal<br>Inhibit cell wall synthesis | Some bile excretion, but mostly kidney | **Gram** (+), but not MRSA<br>Some **gram** (-), not *Pseudomonas*<br>Some **anaerobes** |
| **Aminopenicillins with beta-lactamase inhibitor** (ampi/sulbactam, amoxi/clavulanate) | | | Better staph coverage<br>Better **gram** (-) and **anaerobic** coverage |
| **Antipseudomonal penicillins** (ticarcillin azlocillin, mezlocillin, pipracillin) | Bactericidal<br>Inhibit cell wall synthesis | Excreted in bile and urine | **Gram** (+), but not staph<br>Some **gram** (-)<br>Some **anaerobes** |
| **Anti-pseudomonal penicillins with beta-lactamase inhibitor** (ticarcillin/clavulanate piperacillin/tazobactam) | | | Better staph coverage<br>Better **gram** (-) and **anaerobic** coverage |

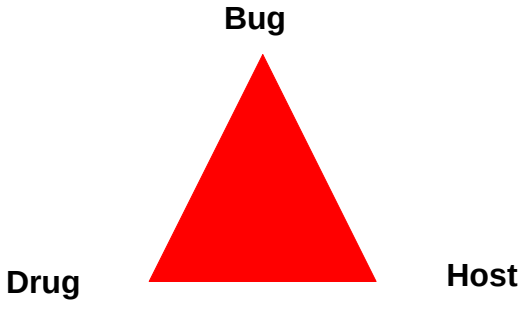

## Table 4. Brief Characteristics Of The Most Commonly Used Antibiotics.


| Class | Mechanism of Action | Metabolism and Excretion | Bacteria Covered |
|---|---|---|---|
| **Cephalosporins**<br>**1st-generation** (cephalexin, cefazolin, cephradine) | Bactericidal<br>Interfere with cell wall synthesis | Excreted mostly intact in urine | **Gram** (+), not MRSA<br>Some **gram** (-)<br>Some **anaerobes** |
| **2nd-generation** (cefuroxime, cefoxitin, cefotetan, cefaclor, cefprozil | | | **Gram** (+), not MRSA<br>**Gram** (-), not *Pseudomonas*<br>**Anaerobes** |
| **3rd-generation** (ceftriaxone, cefotaxime, ceftazidime, cefixime) | | | **Gram** (+), not MRSA<br>**Gram** (-), most are weak against *Pseudomonas*<br>Some **anaerobes** |
| **4th-generation** (cefepime) | | | **Gram** (+), not MRSA or enterococcus<br>**Gram** (-) |
| **Carbapenems** (imipenem, meropenem) | Bactericidal<br>Inhibit cell wall synthesis | Excreted mostly in urine | **Gram** (+), not MRSA<br>**Gram** (-)<br>**Anaerobes** |
| **Fluoroquinolones** (ciprofloxacin, ofloxacin, norfloxacin) | Bactericidal<br>Inhibit DNA gyrase | Some excreted by kidney, often metabolized in liver | Some **gram** (+), Staph but not MRSA<br>**Gram** (-)<br>Some atypicals |
| **Extended-spectrum fluoroquinolones** (levofloxacin, gatifloxacin, moxifloxacin) | | | **Gram** (+)<br>**Gram** (-)<br>**Atypicals**<br>Some **anaerobic** coverage |
| **Macrolides** (erythromycin, azithromycin, clarithromycin) | Bacteriostatic<br>Inhibit protein synthesis | Metabolized in liver, excreted in bile and minimally in urine | **Gram** (+), but not MRSA<br>Some **gram** (-)<br>**Atypicals**<br>Some **anaerobes** |

**Table 4. Brief Characteristics Of The Most Commonly Used Antibiotics (continued).**

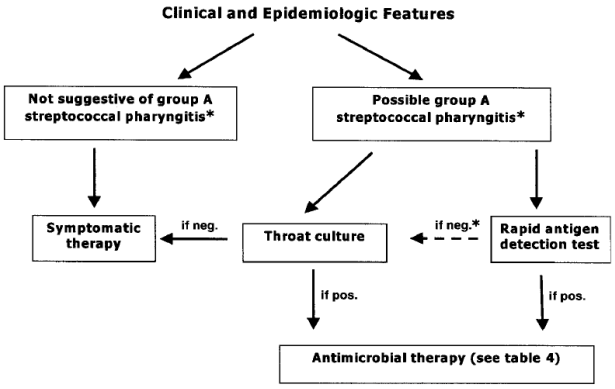
| Class | Mechanism of Action | Metabolism and Excretion | Bacteria Covered |
|---|---|---|---|
| **Aminoglycosides** (gentamicin, tobramycin, amikacin) | Bactericidal<br>Inhibit protein synthesis | Excreted unchanged in urine | Staph (combine with beta-lactams)<br>**Gram (-)** |
| **Tetracyclines** (tetracycline, doxycycline) | Bacteriostatic<br>Inhibit protein synthesis | Excreted mostly in urine | Some **gram (+)**<br>Some **gram (-)**<br>**Atypicals**<br>Some **anaerobes** |
| **Clindamycin** | Bacteriostatic<br>Inhibits protein synthesis | Metabolized mostly in liver and excreted in bile | **Gram (+)**, not MRSA<br>**Anaerobes** |
| **Vancomycin** | Bactericidal<br>Inhibits cell wall synthesis and inhibits RNA synthesis | Excreted in urine | **Gram (+)**<br>Some **anaerobes** |
| **Trimethoprim/ sulfamethoxazole** | Bacteriostatic<br>Folate antagonist/inhibits folate synthesis | Metabolized in liver, excreted in urine | Some **gram (+)**<br>Some **gram (-)**<br>Some **protozoans** |
| **Metronidazole** | Bactericidal<br>Toxic to cells by interfering with electron transport/producing free radicals | Metabolized in liver | **Anaerobes**<br>Some protozoans and parasites |
| **Chloramphenicol** | Bacteriostatic<br>Inhibits protein synthesis | Metabolized in liver, excreted by kidney | **Gram (+)**<br>**Gram (-)**<br>**Anaerobes**<br>***Rickettsia*** |
| **Nitrofurantoin** | Bacteriostatic or bacteriocidal depending on concentration | Metabolized in liver, excreted by kidney | **Gram (+)**<br>**Gram (-)**<br>Only in the lower urinary tract |

# How to choice antibiotics wisely?



# 1. Prescribe antibiotics for patients only when necessary

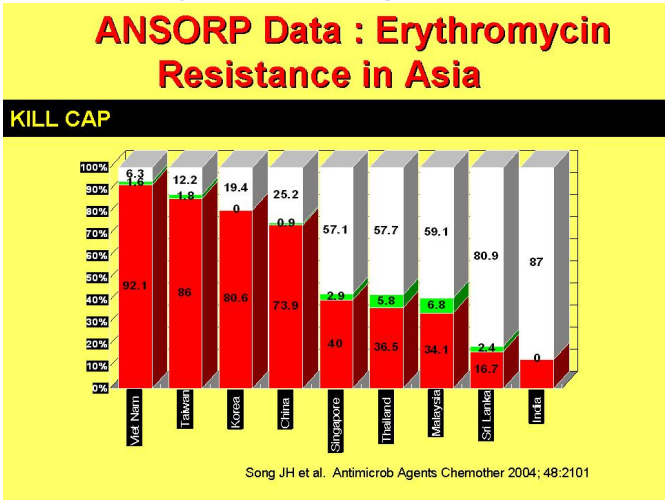
- Bacterial vs viral infection




# 2. Make a reasonable guess as to the possible pathogens

| Site of Infection | Pathogen |
|---|---|
| Dental/odontogenic infections | Streptococcus, anaerobes, staphylococcus |
| Pharyngitis | Group A streptococcus, group C streptococcus, group G streptococcus |
| Otitis media | *S pneumoniae, H influenzae, M catarrhalis* |
| Sinusitis | *S pneumoniae, H influenzae, M catarrhalis*, group A streptococcus, anaerobes |
| Bronchitis (acute exacerbation of chronic bronchitis) | *S pneumoniae, H influenzae, M catarrhalis* |
| Pneumonia | **Newborns**: Group B streptococcus, enterobacteriaceae, *Listeria, Chlamydia*<br>**Age less than 5**: *S pneumoniae, H influenzae, S aureus, M pneumoniae*<br>**Age 5-18**: *S pneumoniae, M pneumoniae, Chlamydia*<br>**Adults**: *S pneumoniae, M pneumoniae, Chlamydia, M catarrhalis, H influenzae* |
| UTI | Enterobacteriaceae (*E coli*), *S saprophyticus, Proteus* sp, *Klebsiella*, enterococci |
| PID | *N gonorrheae, C trachomatis*, anaerobes, enterobacteriaceae |
| Intraabdominal infections | Enterobacteriaceae, enterococci, *Bacteroides fragilis*, clostridia |
| Gastrointestinal (bacterial diarrhea) | *Shigella, Salmonella, E coli, Campylobacter jejuni, Yersinia enterocoltica* |
| Skin | **Cellulitis**: *S aureus, Streptococcus pyogenes*, group A streptococcus<br>**Bite wounds**: *S viridans, Pasteurella multocida, S aureus, Eikenella corrodens*<br>**Diabetic foot**: Aerobic cocci and bacilli, anaerobes |
| Meningitis | **Neonates**: Group B streptococcus, *E coli, Listeria*<br>**Age 1-50**: *S pneumoniae, N meningitidis, H influenzae*<br>**Older than 50**: *S pneumoniae, Listeria*, enterobacteriaceae |
| Endocarditis | **Native valves not IVDU**: *S viridans*, staphylococci, enterococci<br>**IVDU**: *S aureus*<br>**Artificial valve**s: *Staphylococcus epidermidis, S aureus, S viridans* |

# 3. Be aware of the susceptibility patterns in your hospital/community




# 4. Take into account previous antibiotic treatment

| Specific pathogen for pneumonia | Patient risk factor |
|---|---|
| Drug-resist Streptococcus pneumonia (DRSP) | Age > 65 years [OR 1.2-3.8] |
| | B-lactam use within 3 months [OR 2.8] |
| | Alcoholism [OR 5.2] |
| | Immunosuppression |
| | Multiple medical comorbidities |
| | Exposure to child in a day care center |
| Enteric gram-negatives | Nursing home resident |
| | Cardiopulmonary disease (esp COPD) |
| | Multiple medical comorbidities |
| | Recent antibiotic use |
| Pseudomonas aeruginosa | Structural lung disease ( esp bronchiectasis) |
| | Corticosteroid therapy (>10 mg prednisone daily) |
| | Broad-spectrum antibiotic use . 7 d in past 1 month |
| | Malnutrition |

## 5. Take into consideration important host factors

- The site of infection (tissue penetration)
- Peripheral WBC
- Age and underlying disease (hepatic and renal dysfunction)
- Duration of hospitalization (community or nosocominal infection)
- Severity of the patient illness

## 6. Understand property of antibiotics

- Bactericidal vs baceriostatic
  - Important property for **endocarditis**, **meningitis**, **osteomyelitis**, or in **neutropenic** patients.
  - Clindamycin, which covers *Streptococcus viridans* and *Staphylococcus aureus*, does not adequately treat endocarditis.
- Augmentin vs Cefmetazole, Clindaymcin vs metronidazole, Ertapenem vs Imipenem
- Excretion: Ceftriaxone vs Cefotaxime

## 7. Use the fewest drugs possible

- Cover infections that may be caused by multiple organisms, eg, PID
- Cover simultaneous infections at multiple sites, as in a nursing home patient who has concomitant pneumonia, UTI, and infected decubiti.
- Advantage of the synergy that exists between certain antibiotics, eg. the use of penicillin with aminoglycosides to treat enterococcus endocarditis.
- Treat critical patients with an unknown source of infection.
- Use combination therapy only when necessary, especially since it has the potential to increase side effects and is more expensive

## 8. Switch to narrower-spectrum antibiotic coverage with 3 days

- Broad-spectrum antibiotics can and should be used for infections with multiple etiologic agents, like chronic diabetic foot infections or peritonitis, or for patients with infections at multiple sites.
- Board-spectrum antibiotic may increase bacterial resistance.

# 9. Consider drug toxicity

**Table 12. Safety Of Selected Antibiotics In Pregnancy.**

| Generally Safe | Unsafe |
|---|---|
| Penicillins | Aminoglycosides |
| Cephalosporins | Imipenem |
| Macrolides (except clarithromycin) | Quinolones |
| | Tetracyclines |
| | Sulfonamides (third trimester) |

| Antibiotic | Adverse Reactions |
|---|---|
| Aminoglycosides | Renal failure, hearing loss |
| Clindamycin | Pseudomembranous colitis* |
| Imipenem | Seizures |
| Macrolides | Vomiting, abdominal cramping |
| Penicillins | Allergic reactions, rash, diarrhea |
| Quinolones | Affect cartilage growth†, GI upset, CNS effects especially in the elderly, hypoglycemia‡ |
| Sulfonamides | Allergic reactions, rash, leukopenia, CNS effects |
| Tetracyclines | Phototoxicity, affect growing bones |
| Vancomycin | Renal failure, "red man syndrome" (RMS) |

*Although the first entity famous for this was clindamycin, many antibiotics were subsequently found to cause this problem.
†Shown in animal studies, used in the third world with no report of cartilage problems.
‡Often described in elderly patients on long-acting, oral hypoglycemic agents, particularly with concomitant renal insufficiency

# 10. Pick the least expensive drug

| **Antibiotic** (Generic/**Brand**)* | **Cost to Pharmacist for 10 Days of Treatment**† |
|---|---|
| Amoxicillin/**Amoxil** | $2.21/**$6.48** |
| Amoxicillin/clavulanate/ **Augmentin** | **$72.65** |
| Azithromycin/**Zithromax** | **$40.54** |
| Cephalexin/**Keflex** | $4.41/**$63.35** |
| Clarithromycin/**Biaxin** | **$70.44** |
| Clindamycin/**Cleocin** | $39.42/**$71.42** |
| Doxycycline/**Vibramycin** | $1.7/**$39.69** |
| Erythromycin | $7.17 |
| Fluoroquinolones:<br>Ciprofloxacin/**Cipro**<br>Levofloxacin/**Levaquin**<br>Gatifloxacin/**Tequin** | <br>**$70.98**<br>**$73.07**<br>**$73.33** |
| Penicillin V | $2.31 |
| Trimethoprim-sulfamethoxazole DS/**Bactrim DS** | $1.79/**$25.65** |

# Issues in CAP

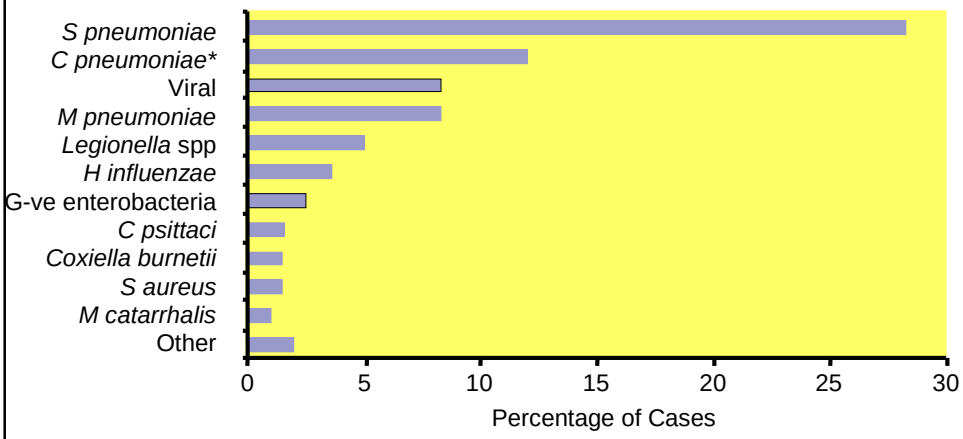
**Diagnosis:**

- Failure to differentiate etiology clinically and radiologically
- No study has reliably shown a correlation between clinical symptoms and/or chest radiograph and etiology.

**Etiology:**

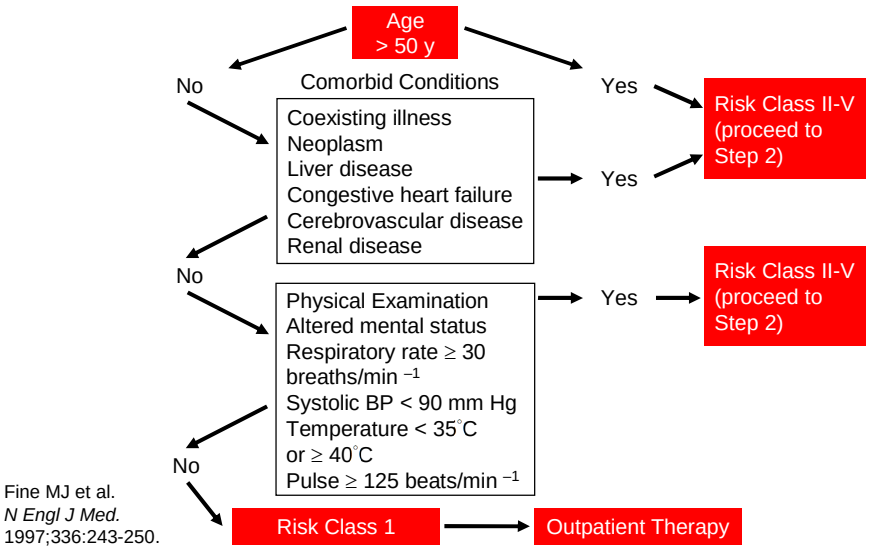
- Not defined in 50% of patients

# Bacteriology of Hospitalized CAP




Data from 26 prospective studies (5961 adults) from 10 countries.
*Data from 6 studies; Woodhead, Mass, 1998.

# Prediction Rule to Identify Low-Risk Patients




Fine MJ et al.
*N Engl J Med.*
1997;336:243-250.

# Prediction Rule: Scoring System for Step 2

| Characteristic | Points Assigned |
|---|---|
| **Demographic factor** | |
| Age | |
| Male | Age (years) |
| Female | Age-10 (years) |
| Nursing home resident | +10 |
| **Comorbid illness** | |
| Neoplasm | +30 |
| Liver disease | +20 |
| Congestive heart failure | +10 |
| Cerebrovascular disease | +10 |
| Renal disease | +10 |
| **Physical examination** | |
| Altered mental status | +20 |
| Respiratory rate ≥ 30 breaths/min $^{-1}$ | +20 |
| Systolic blood pressure < 90 mm Hg | +20 |
| Temperature < 95°F (35°C) or ≥ 104°F (40°C) | +15 |
| Pulse ≥ 125 beats/min $^{-1}$ | +10 |

Fine MJ et al. *N Engl J Med*. 1997;336:243-250.

# Prediction Rule: Scoring System for Step 2

| Characteristic | Points Assigned |
|---|---|
| **Laboratory and radiographic findings** | |
| Arterial pH < 7.35 | +30 |
| BUN ≥ 30 mg/dL $^{-1}$ (11 mM) | +20 |
| Sodium < 130 mM | +20 |
| Glucose > 250 mg/dL $^{-1}$ (14 mM) | +10 |
| Hematocrit < 30% | +10 |
| $Po_2$ < 8.0 kPa (60 mm Hg) (room air) | +10 |
| Pleural effusion | +10 |

BUN = blood urea nitrogen.
Fine MJ et al. *N Engl J Med.* 1997;336:243-250.

# Prediction Rule: Risk Categories

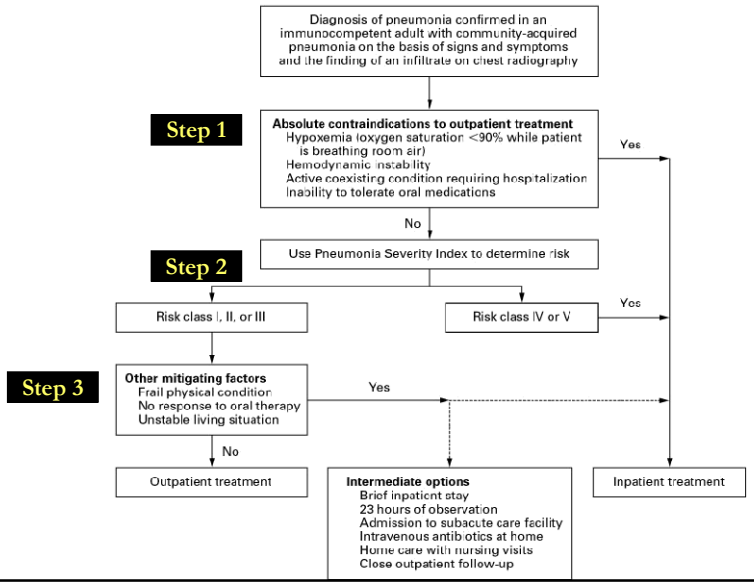
| Total Points | Class | Mortality % | How to Treat |
|---|---|---|---|
| | 1 | 0.1-0.4 | Outpatient |
| ≤ 70 | 2 | 0.6-0.7 | Outpatient |
| 71-90 | 3 | 0.9-2.8 | Brief hospital observation |
| 91-130 | 4 | 8.5-9.3 | Inpatient |
| ≥ 130 | 5 | 27.0-31.1 | Inpatient ICU |

Risk categories according to 2 validation cohorts (38,039 inpatients and 2287 in- and outpatients).
Fine MJ et al. *N Engl J Med*. 1997;336:243-250.

# ATS Severe Pneumonia Criteria

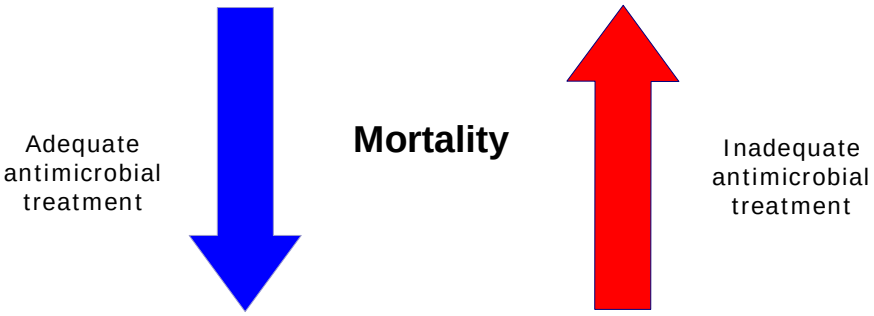
- Major criteria (1 of 2)
  - Mechanical ventilation requirement
  - Septic shock
- Minor criteria (at least 3)
  - Respiratory rate ≥ 30 breaths/min
  - PaO2/FiO2 ratio ≤ 250
  - Multilobar infiltrates
  - Confusion/disorientation
  - Uremia (BUN level ≥ 20 mg/dL)
  - Leukopenia (WBC count < 4000 cells/mm3)
  - Thrombocytopenia (platelet count <100,000 cells/mm3)
  - Hypothermia (core temperature <36℃)
  - Hypotension requiring aggressive fluid resuscitation

# 3-tiered Approach (2003 IDSA Guideline)



## Importance of Adequate and Appropriate Antimicrobial Treatment

- Selection of drug-resistant microorganisms
- Ongoing bacterial proliferation and inflammation




Ewig et al, Thorax 2002; 57:366

## Risk Factors for Gram-Negative Pneumonia

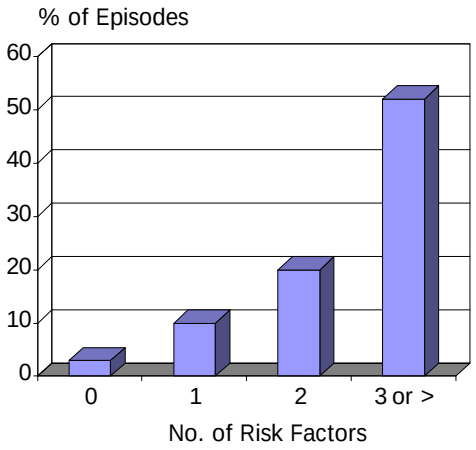
- 559 consecutive hospitalized patients with CAP
- 60 patients (11%) had CAP due to GNB

| Risk Factor | OR (95% CI) | p Value |
|---|---|---|
| Probable aspiration | 2.3 (1.02-5.2) | .04 |
| Previous hospital admission | 3.5 (1.7-7.1) | <.001 |
| Previous use of antibiotics | 1.9 (1.01-3.7) | .049 |
| Pulmonary comorbid illness | 2.8 (1.5-5.5) | .02 |

Arancibia F, et al. Arch Intern Med 2002; 162:1849-58

## Incidence of GNB According to Number of Risk Factors Present

- 559 consecutive hospitalized patients with CAP
- 60 patients (11%) had CAP due to GNB
- 4 risk factors identified in MV analysis:
  - Probable aspiration
  - Previous hospital admission
  - Previous antibiotic Rx
  - Presence of pulmonary comorbidity




**Arancibia, F. et al. Arch Intern Med 2002;162:1849-1858.**

## Outpatient

| Previously healthy without ATB use within 3 m | Presence of comorbidities, use ATB within 3 m, high rate of DRSP |
|---|---|
| Macrolide (level I evidence) | RFQ (moxifloxacin, gemifloxacin, levofloxacin [750 mg]) ( level I evidence) |
| Doxycyline (level III evidence) | $\beta$-lactam **plus** macrolide (level I evidence) |

## Inpatient - Ward

| |
|---|
| RFQ<br>( level I evidence) |
| β-lactam **plus** macrolide<br>(level I evidence) |

## Inpatient - ICU

| Pseudomonas(-) | Pseudomonas(+) |
|---|---|
| β-lactam + RFQ<br>(level I evidence) | APPsA+Cipro/APsQ |
| β-lactam+ azithromycin<br>(level II evidence) | APPsA+AG+APsFQ |
| | APPsA+AG+Azithromycin |

## Classification of Fluoroquinolones

G(-):
**Pseudomonas**

- First generation: Ciproxin
- Second generation: Cravit
- Third generation: Avelox

G(+):
**Pneumococcus**
**Anaerobes**
**Atypical pathogens**

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## Criteria for Determining Discharge

- Patient's vital signs are stable for 24-hour period
  - BT≦37.8℃, RR ≦24, HR ≦100, SBP≧90, and SpO2≧90% in room air or at baseline with COPD
- Patient is able to take oral antibiotics.
- Patient is able to maintain adequate hydration and nutrition.
- Patient's mental status is normal (or at baseline level).
- Patient has no other active clinical or psychosocial problems requiring hospitalization.

## Nosocomial Pneumonia

- Second most common nosocomial infection
  15-20%
- Most common infection in ICU
- Most common nosocomial infection related to death
- Crude mortality of VAP – 50%-70%
- Attributable mortality – 30%

## Hospital-acquired pneumonia

- HAP is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission

## Ventilator-associated pneumonia

- VAP refers to pneumonia that arises more than 48-72 hours after endotracheal intubation
- Some patients may required intubation after developing severe HAP and should be managed as VAP

## Healthcare-associated pneumonia

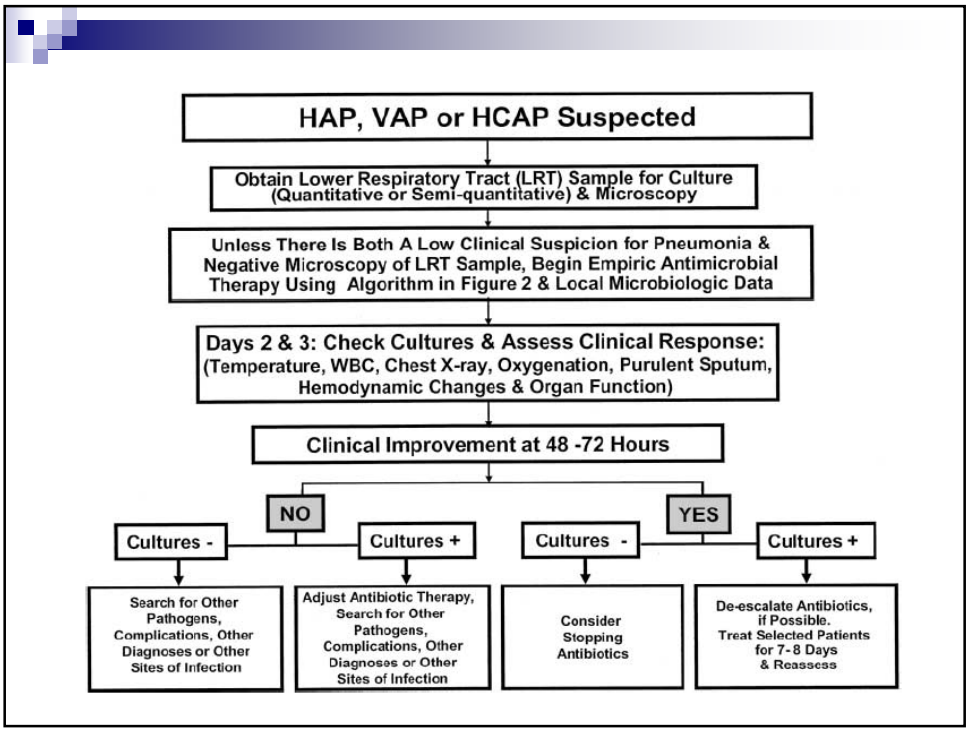
- HCAP includes any patient who was
  - Hospitalized in an acute care hospital for 2 or more days within 90 days of the infection
  - Resided in a nursing home or long-term care facility
  - Received recent intravenous antibiotic therapy, chemotherapy or wound care with the past 30 days of the current infection
  - Attended a hospital or hemodialysis clinic

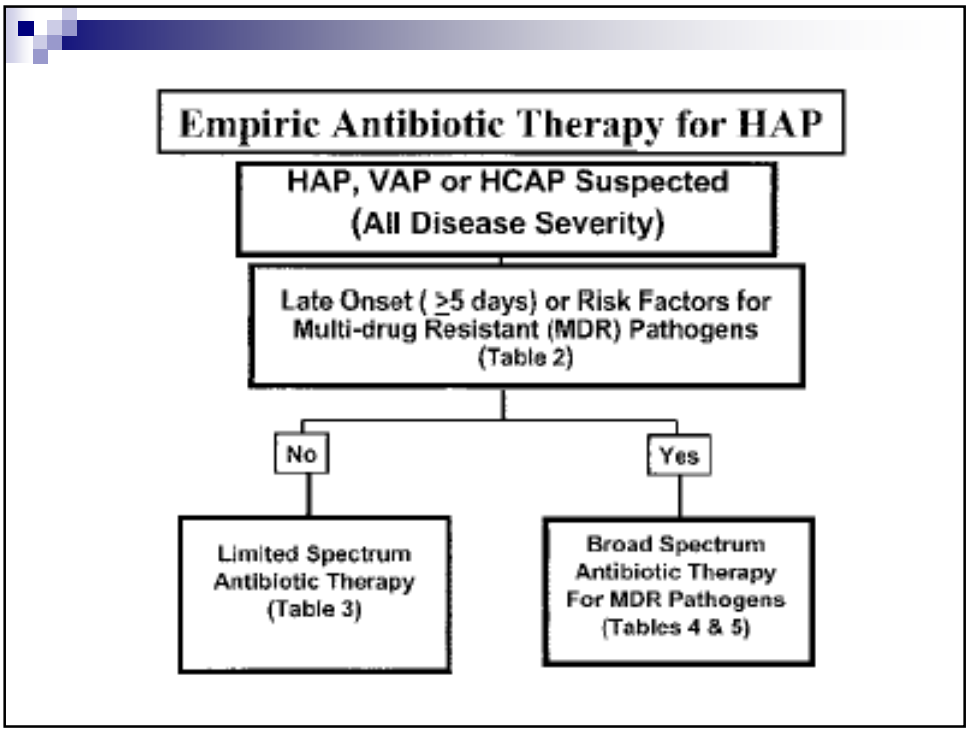
# Drug-resistant bacteria for VAP

- Duration of MV≧7 days (OR 6.0)
- Prior antibiotic use (OR 13.5)
- Prior use of broad-spectrum drugs, 3rd cephalosporin, FQ, carbapenem (OR 4.1)

**TABLE 2. RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS CAUSING HOSPITAL-ACQUIRED PNEUMONIA, HEALTHCARE-ASSOCIATED PNEUMONIA, AND VENTILATOR-ASSOCIATED PNEUMONIA**

- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP:
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic dialysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy


HAP, VAP or HCAP Suspected
Obtain Lower Respiratory Tract (LRT) Sample for Culture (Quantitative or Semi-quantitative) & Microscopy
Unless There Is Both A Low Clinical Suspicion for Pneumonia & Negative Microscopy of LRT Sample, Begin Empiric Antimicrobial Therapy Using Algorithm in Figure 2 & Local Microbiologic Data
Days 2 & 3: Check Cultures & Assess Clinical Response: (Temperature, WBC, Chest X-ray, Oxygenation, Purulent Sputum, Hemodynamic Changes & Organ Function)
Clinical Improvement at 48 -72 Hours
NO
YES
Cultures -
Cultures +
Cultures -
Cultures +
Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection
Adjust Antibiotic Therapy, Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection
Consider Stopping Antibiotics
De-escalate Antibiotics, if Possible. Treat Selected Patients for 7-8 Days & Reassess


Empiric Antibiotic Therapy for HAP
HAP, VAP or HCAP Suspected (All Disease Severity)
Late Onset ( ≥5 days) or Risk Factors for Multi-drug Resistant (MDR) Pathogens (Table 2)
No
Yes
Limited Spectrum Antibiotic Therapy (Table 3)
Broad Spectrum Antibiotic Therapy For MDR Pathogens (Tables 4 & 5)

## Empiric Antibiotic Therapy
## No risks for MDR pathogens
## Early Onset

- Potential Pathogen
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - MSSA
  - Antibiotic-sensitive enteric GNB
    - *E. Coli*
    - *K. peumoniae*
    - *Enterobacter* species
    - *Proteus* species
    - *Serratia marcescens*
- Recommended Antibiotic
  - Ceftriaxone
  - Levofloxaxin, moxifloxacin, or ciprofloxacin
  - Ampicillin/sulbactam
  - Ertapenem

## Empiric Antibiotic Therapy
## Risks for MDR Pathogens
## Late Onset

- Potential Pathogens
  - Pathogens listed in previous slide and MDR pathogens
    - *Pseudomonas aeruginosa*
    - *K. pneumoniae* (ESBL)
    - *Acinetobacter* species
    - MRSA
  - *Legionella pneumophila*
- Combination Antibiotic Therapy
  - Antipseudomonal cephalosporin
    - (cefepime, ceftazidime)
  - Antipesudomonal carbepenem
    - (imipenem, meropenem)
  - β-Lactam/β-lactamase inhibitor
    - (piperacillin-tazobactam)

    plus
  - Antipseudomonal FQ
    - (ciprofloxacin, levofloxacin)
  - Aminoglycoside
    - (amikacin, GM, tobramycin)

    plus
  - Linezolid or vancomycin

TABLE 5. INITIAL INTRAVENOUS, ADULT DOSES OF ANTIBIOTICS FOR EMPIRIC THERAPY OF HOSPITAL-ACQUIRED PNEUMONIA, INCLUDING VENTILATOR-ASSOCIATED PNEUMONIA, AND HEALTHCARE-ASSOCIATED PNEUMONIA IN PATIENTS WITH LATE-ONSET DISEASE OR RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS

| Antibiotic | Dosage* |
|---|---|
| Antipseudomonal cephalosporin | |
| Cefepime | 1–2 g every 8–12 h |
| Ceftazidime | 2 g every 8 h |
| Carbepenems | |
| Imipenem | 500 mg every 6 h or 1 g every 8 h |
| Meropenem | 1 g every 8 h |
| β-Lactam/β-lactamase inhibitor | |
| Piperacillin–tazobactam | 4.5 g every 6 h |
| Aminoglycosides | |
| Gentamicin | 7 mg/kg per d† |
| Tobramycin | 7 mg/kg per d† |
| Amikacin | 20 mg/kg per d† |
| Antipseudomonal quinolones | |
| Levofloxacin | 750 mg every d |
| Ciprofloxacin | 400 mg every 8 h |
| Vancomycin | 15 mg/kg every 12 h‡ |
| Linezolid | 600 mg every 12 h |

* Dosages are based on normal renal and hepatic function.
† Trough levels for gentamicin and tobramycin should be less than 1 μg/ml, and for amikacin they should be less than 4–5 μg/ml.
‡ Trough levels for vancomycin should be 15–20 μg/ml.

# Neutropenic Fever

- Endogenous flora account for approximately 80% of infections patients.
  - Gut (eg, *Escherichia coli,Enterobacter,* anaerobes)
  - Skin (eg, *Staphylococcus,Streptococcus*)
  - Respiratory tract (eg, *Streptococcus pneumoniae, Klebsiella, Corynebacterium, Pseudomonas*)
  - Opportunistic colonization (eg, by *Clostridium difficile, Mycobacterium, Candida, Aspergillus*).

# Neutropenic fever

- Definition
  - A single temperature measurement ≥ 38.3°C or a sustained temperature ≥ 38°C (≥ 100.4°F) for more than 1 hour
  - In a patient with an ANC of either < 500 cells/ $\mu$L or < 1000 cells/ $\mu$L, with a predicted nadir of < 500 cells/ $\mu$L over the subsequent 48 hours.

## Factors Associated With Low Risk For Severe Infection In Patients With Neutropenic Fever

- Absolute neutrophil count ≥ 100 cells/mm³
- Absolute monocyte count ≥ 100 cells/mm³
- Normal results on chest radiograph
- Normal hepatic and renal function
- Neutropenia duration < 7 days
- Neutropenia expected to resolve in < 10 days
- No IV catheter site infection
- Early evidence of bone marrow recovery
- Malignancy in remission
- Peak temperature < 39.0°C (< 102.2ºF)
- Normal results on neurologic examination
- Not ill-appearing
- No abdominal pain
- No concomitant comorbidities (eg, shock, hypoxia, deep organ infection, vomiting, diarrhea)

## MASCC Risk Index For Patients With Neutropenic Fever

| Patient Clinical Factors | Score[a,b] |
|---|---|
| Severity of illness | |
| No symptoms or mild symptoms | 5 points |
| Moderate symptoms | 3 points |
| No hypotension | 5 points |
| No chronic obstructive pulmonary disease | 4 points |
| Solid tumor *or* no fungal infection | 4 points |
| No dehydration | 3 points |
| Outpatient at onset of fever | 3 points |
| Age < 60 years | 2 points |

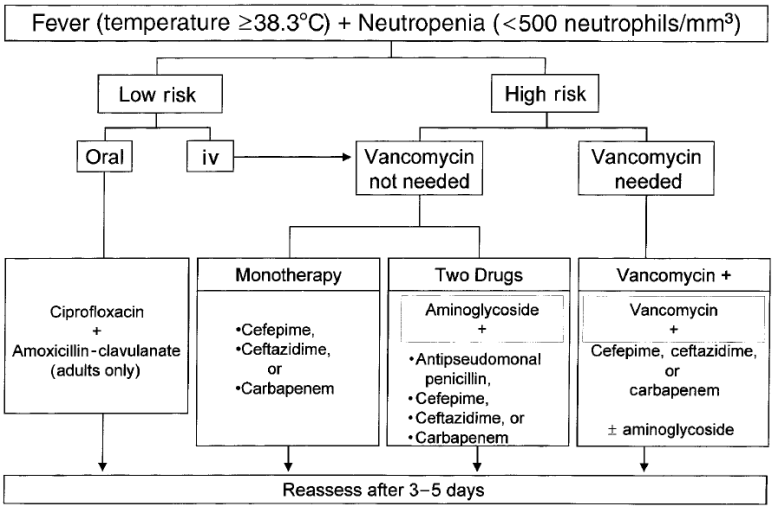
[a]Validated in individuals older than 16.

- A score ≥ 21 indicates that the patient is likely at low risk for significant bacterial illness.

## Indications For Vancomycin In Patients With Neutropenic Fever

- Hypotension
- Preliminary cultures showing gram-positive flora
- Known history of methicillin-resistant Staphylococcus aureus or $\beta$-lactam-resistant pneumococci
- Prior prophylaxis with a fluoroquinolone or trimethoprim/sulfamethoxazole
- Probable catheter-related infection

# Clinical Pathway For Neutropenic fever




# Intra-abdominal infection

- Stomach and duodenum
  - Sterile or Gram(+) organisms, lactobacilli, and Candida
- Proximal small bowel
  - Gram(-) organisms, acute lethality
- Distal small bowel and colon
  - Anaerobes, abscess formation
- Colonization resistance
  - Anti-anaerobic activity can promote E.coli, Candida, and VRE growth

# Classification

- Primary peritonitis
  - Spontaneous bacterial peritonitis
  - Monomicrobial
- Secondary peritonitis
  - Polymicrobial
- Tertiary peritonitis
  - Persist or recur at least 48 hrs after the apparently adequate management of primary or secondary peritonitis
  - Mortality >50%

# Microbiology of Peritonitis

| Primary Peritonitis | Secondary Peritonitis | Tertiary Peritonitis |
|---|---|---|
| Gram-negative bacteria | Gram-negative bacteria | Gram-negative bacteria |
| *Eschecheri coli* | *E. coli* 32–61% | *Pseudomonas* |
| *Klebsiella* | *Enterobacter* 8–26% | *Enterobacter* |
| | *Klebsiella* 6–26% | *Acinetobacter* |
| | *Proteus* 4–23% | |
| Gram-positive bacteria | Gram-positive bacteria | Gram-positive bacteria |
| *S. aureus* | *Enterococci* 18–24% | *Enterococci* |
| *Enterococci* | *Streptococci* 6–55% | Coagulase-negative |
| | *Staphylococci* 6–16% | *Staphylococci* |
| | Anerobic bacteria | |
| | *Bacteroides* 25–80% | |
| | *Clostridium* 5–18% | |
| | Fungi 2–15% | Fungi |
| | | *Candida* |

# Health care–associated infection

- Community-onset infection includes cases involving patients with at least 1 of the following health care risk factors:
  - (1) presence of an invasive device at time of admission;
  - (2) history of MRSA infection or colonization;
  - (3) history of surgery, hospitalization, dialysis, or residence in a long-term care facility in the 12 months preceding the culture date.
- Hospital-onset infection includes cases involving patients with positive culture results from a normally sterile site obtained >48 h after hospital admission.
  - These patients might also have 1 of the communityonset risk factors.

# Concepts in the management of IA infection

- Source control
  - Drainage
  - Debridement
  - Definitive management

| | |
|---|---|
| Peritonitis | Inflammation of the peritoneal lining of the abdominal cavity |
| Abscess | Collection of tissue fluid, neutrophils, and bacteria enclosed in a fibrin capsule |
| Fistula | Abnormal communication between two epithelially lined surfaces |
| Sinus | Cavity communicating with an epithelially lined surface |
| Drainage | Conversion of an abscess to a controlled sinus or fistula |
| Debridement | Physical removal of infected or necrotic solid tissue |

## Clinical Factors Predicting Failure of Source Control for Intra-abdominal Infection

Delay in the initial intervention (>24 h)
High severity of illness (APACHE II score ⩾15)
Advanced age
Comorbidity and degree of organ dysfunction
Low albumin level
Poor nutritional status
Degree of peritoneal involvement or diffuse peritonitis
Inability to achieve adequate debridement or control of drainage
Presence of malignancy

**NOTE.** APACHE, Acute Physiology and Chronic Health Evaluation.

## Extra-biliary Intra-abdominal Infection

| | Community-acquired infection in adults | |
|---|---|---|
| Regimen | Mild-to-moderate severity: perforated or abscessed appendicitis and other infections of mild-to-moderate severity | High risk or severity: severe physiologic disturbance, advanced age, or immunocompromised state |
| Single agent | Cefoxitin, ertapenem, moxifloxacin, tigecycline, and ticarcillin-clavulanic acid | Imipenem-cilastatin, meropenem, doripenem, and piperacillin-tazobactam |
| Combination | Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a] | Cefepime, ceftazidime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a] |

# Biliary Infection in Adults

| Infection | Regimen |
|---|---|
| Community-acquired acute cholecystitis of mild-to-moderate severity | Cefazolin, cefuroxime, or ceftriaxone |
| Community-acquired acute cholecystitis of severe physiologic disturbance, advanced age, or immunocompromised state | Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam, ciprofloxacin, levofloxacin, or cefepime, each in combination with metronidazole[a] |
| Acute cholangitis following bilio-enteric anastamosis of any severity | Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam, ciprofloxacin, levofloxacin, or cefepime, each in combination with metronidazole[a] |
| Health care–associated biliary infection of any severity | Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam, ciprofloxacin, levofloxacin, or cefepime, each in combination with metronidazole, vancomycin added to each regimen[a] |

[a] Because of increasing resistance of *Escherichia coli* to fluoroquinolones, local population susceptibility profiles and, if available, isolate susceptibility should be reviewed.

# Health Care–Associated Complicated Intra-abdominal Infection

| Organisms seen in health care–associated infection at the local institution | Regimen | | | | |
|---|---|---|---|---|---|
| | Carbapenem[a] | Piperacillin-tazobactam | Ceftazidime or cefepime, each with metronidazole | Aminoglycoside | Vancomycin |
| <20% Resistant *Pseudomonas aeruginosa*, ESBL-producing Enterobacteriaceae, *Acinetobacter*, or other MDR GNB | Recommended | Recommended | Recommended | Not recommended | Not recommended |
| ESBL-producing Enterobacteriaceae | Recommended | Recommended | Not recommended | Recommended | Not recommended |
| *P. aeruginosa* >20% resistant to ceftazidime | Recommended | Recommended | Not recommended | Recommended | Not recommended |
| MRSA | Not recommended | Not recommended | Not recommended | Not recommended | Recommended |

**NOTE.** ESBL, extended-spectrum β-lactamase; GNB, gram-negative bacilli; MDR, multidrug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*. "Recommended" indicates that the listed agent or class is recommended for empiric use, before culture and susceptibility data are available, at institutions that encounter these isolates from other health care–associated infections. These may be unit- or hospital-specific.

[a] Imipenem-cilastatin, meropenem, or doripenem

# UTI

| First Choice | Second Choice |
|---|---|
| **Uncomplicated Infection (Cystitis)**<br>Usual duration of treatment is 3 days | Trimethoprim/sulfamethoxazole: 1 tab DS (160 mg TMP) PO BID X 3 days[†]<br><br>Fluoroquinolone[†]:<br>ciprofloxacin 500 mg PO BID<br>levofloxacin 250 mg PO QD<br>gatifloxacin 200 or 400 mg PO QD x 3 days<br><br>1st-generation cephalosporin[¶]:<br>cephalexin 500 mg PO QID<br><br>Nitrofurantoin 100 mg PO QID x 7 days[¶] |
| **Pyelonephritis Outpatients** | Fluoroquinolone*[§]:<br>ciprofloxacin 500 mg PO BID<br>levofloxacin 250 mg PO QD<br>gatifloxacin 200 or 400 mg PO QD x 7 days<br><br>Cephalosporin[‖]:<br>cephalexin 500 mg PO QID x 14 days<br><br>Amoxicillin/clavulanic acid 875/125 mg PO q12 or 500/125 mg PO q8 x 14 days[‖]<br><br>Trimethoprim/sulfamethoxazole*[†‖] |
| **Hospitalized Patients[#]** | Fluoroquinolone*:<br>levofloxacin 500 mg IV QD<br>gatifloxacin 400 mg IV QD<br><br>Ampicillin/sulbactam 3.0 gm IV q6 + gentamicin*<br><br>Beta-lactam/beta-lactamase inhibitor[¶]: ticarcillin/clavulanate 3.1 gm IV q6, piperacillin/tazobactam 3.375 gm q6 or 4.5 gm q8 IV<br><br>Carbapenem*[¶]: imipenem 0.5 gm IV q6 or meropenem 1.0 gm IV q8 |

# Endocarditis

| | First Choice | Second Choice |
|---|---|---|
| **Native Valves IVDU** | Nafcillin or oxacillin 2.0 gm IV q4 + gentamicin 1.0 mg/kg IM/IV q8 | Vancomycin 15 mg/kg IV q12 |
| **Non-IVDU** | Penicillin G 20 mu IV QD or ampicillin 12 gm IV QD + nafcillin or oxacillin 2.0 gm IV q4 + gentamicin 1.0 mg/kg IM/IV q8 | Vancomycin 15 mg/kg IV q12 + gentamicin 1.0 mg/kg IM/IV q8 |
| **Prosthetic Valves** | Vancomycin 15 mg/kg IV q12 + gentamicin 1.0 mg/kg IM/IV q8+ rifampin 600 mg PO QD | |

*Empiric treatment before culture results available.

# Meningitis

| | First Choice | Second Choice |
|---|---|---|
| **Newborns** | Ampicillin + cefotaxime (dosage varies by age of patient and weight) | Ampicillin + gentamicin |
| **Patients 2 Mos-60 Yrs** | Ceftriaxone 2 gm IV q12 or cefotaxime 2.0 gm IV q4-6 + /- vancomycin 500-750 mg IV q8* +/- rifampin* | Meropenem¶ 1.0 gm IV q8+ /-vancomycin 500-750 mg IV q8* |
| | **Peds**: Ceftriaxone 80-100 mg/kg div dose q12-24 +/- vancomycin 15 mg/kg IV q6 | **Peds**: Meropenem 40 mg/kg IV q8 + vancomycin 15 mg/kg IV q6 |
| **Patients older than 60 or immune compromised** | Ceftriaxone 2.0 gm IV q12 or cefotaxime 2.0 gm IV q6 +/- vancomycin* + ampicillin 2.0 gm IV q4† +/- gentamicin† | Meropenem 1.0 gm IV q8 +/- vancomycin* |

# Cellulitis

| | First Choice | Second Choice |
|---|---|---|
| **Outpatients** | Dicloxacillin 500 mg PO q6<br><br>Amoxicillin/clavulanic acid 500 mg PO TID* | Macrolide:<br>Azithromycin 500 mg PO initial dose then 250 mg PO QD x 4 days<br><br>1st-generation cephalosporin: cephalexin 500 mg PO QID x 7-10 days |
| **Hospitalized Patients** | Nafcillin or oxacillin 2.0 gm IV q4<br><br>Carbapenem¶:<br>Imipenem/Cilastin 0.5 gm IV q6 or meropenem 1.0 gm IV q8<br><br>Beta-lactam/beta-lactamase inhibitor† | Macrolide IV<br><br>1st-generation cephalosporin IV<br><br>Fluoroquinolone + clindamycin or metronidazole‡: |
| **Bite Wounds** | | |
| **Mild** | Amoxicillin/clavulanic acid 500 mg PO TID* | Fluoroquinolone + clindamycin<br>or trimethoprim/sulfemethoxazole |
| **Severe** | Ticarcillin/clavulanate 3.1 gm IV q6<br>Ampicillin-sulbactam 3.0 gm IV q6 | Fluoroquinolone + clindamycin<br>or trimethoprim/sulfemethoxazole |
| **Diabetic Foot** | | |
| **Mild infection previously untreated** | 1st-generation cephalosporin: cephalexin 500 mg PO QID x 14 days<br><br>clindamycin: 300 mg PO qid or 450-900 mg IV q8 | Amoxicillin/clavulanic acid 875/125 mg PO q12 or 500/125 mg q8 |
| **Severe¥** | Beta-lactam/beta-lactamase inhibitor:<br>ampicillin/sulbactam 3.0 gm IV q6<br>piperacillin/tazobactam 3.375 gm IV q6 or 4.5 gm IV q8<br><br>Cefoxitin or cefotetan<br><br>Fluoroquinolone + clindamycin or metronidazole | Carbapenem:<br>Imipenem Cilastin 0.5 gm IV q6 meropenem 1.0 gm IV q8<br><br>Nafcillin or oxacillin 2.0 gm IV q4 + gentamicin 1.0 mg/kg IM/IV q8 + metronidazole 500 mg IV q6 |

# PID

| | First Choice | Second Choice |
|---|---|---|
| **Outpatients*** | Ofloxacin 400 mg PO BID or levofloxacin 400 mg PO qd + metronidazole 500 mg PO BID<br><br>Ceftriaxone 125 mg IM/IV x 1 dose + doxycycline 100 mg PO BID x 14 days† | Azithromycin‡ |
| **Hospitalized patients** | Cefotetan 2 gm IV q12 or cefoxitin 2 gm IV q12 + doxycycline 100 mg IV/PO q12<br><br>Clindamycin 900 mg IV q8 + gentamicin 2 mg/kg IV loading dose then 1.5 mg/kg IV q8h, or 4.5 mg/kg x 1 dose, then doxycycline 100 mg PO BID X 14 days§ | Ofloxacin 400 mg IV q12 + metronidazole 500 mg IV q8<br><br>Ampicillin/sulbactam 3 gm IV q6 + doxycycline 100 mg IV/PO q12<br><br>Ciprofloxacin 200 mg IV q12 + doxycycline 100 mg IV/PO q12 + metronidazole 500 mg IV q8<br><br>Azithromycin‖ + metronidazole |

**(1) A previously healthy young woman presents with fever, dysuria, and flank pain. The most likely pathogen causing her symptoms is:**

a. *S pneumoniae*

b. *H influenzae*

c. *S aureus*

d. *B fragilis*

e. *E coli*

**(2)A young woman presents with a high fever andappears to be toxic. Her history is noteworthy only for a splenectomy due to a car accident 10 years previously. The pathogens that you would have to especially consider and treat for are:**

a. gram-negative organisms: *E coli*, *K pneumoniae*

b. encapsulated organisms: *S pneumoniae, H influenzae*

c. anaerobes: *Bacteroides fragilis*, *Clostridium welchii*

d. pneumocystis, *Cryptococcus*, and toxoplasma

e. *S aureus* and *S pyogenes*

**(3)potential long-term side effect of using broad spectrum antibiotics is:**

a. genetic mutations in the human race

b. bankruptcy of the pharmaceutical companies

c. emergence of resistant organisms

d. lack of adequate coverage leading to chronic infection

e. poor patient compliance

**(4)First-generation cephalosporins cannot be used to treat meningitis because:**

a. they do not adequately penetrate the blood-brain barrier

b. the most likely pathogens are resistant to them

c. they are bacteriostatic drugs

d. their side effects are usually not tolerated

e. they are extremely expensiv

**(5)Which class of antibiotics should generally be avoided in young children?**

a. penicillins

b. aminoglycosides

c. macrolides

d. sulfonamides

e. tetracyclines