PNEUMONIA

• Caused by the inhalation or aspiration (as there is an average of 1 billion bacteria/mL saliva) >>
  hematogenous spread, of microorganisms to the bronchoalveolar units of the lungs→
  Inflammation=pneumonia, being either primary, or due to reactivation disease

Statistics:
• #1 lethal infectious disease in the U.S. →
  #6 cause of mortality†
• #1 lethal infectious disease in the world: Mycobacterium tuberculosis→tuberculosis
• #1 lethal nosocomial infectious disease: Hospital-acquired pneumonia→HAP
• #1 Intensive care unit–ICU infection: Hospital acquired pneumonia→HAP
• #1 lethal infectious disease in HIV patients: Pneumocystis jiroveci pneumonia‡
• #1 AIDS defining illness: Pneumocystis jiroveci pneumonia†

† Streptococcus pneumoniae mediated severe sepsis or septic shock remains associated w/ a 20% mortality

CLASSIFICATION/ RISK FACTORS/ ORGANISMS

COMMUNITY ACQUIRED PNEUMONIA–CAP
• Pneumonia developing in a relatively healthy person, either:
  • Out in the community
  • Within 48 hours of hospital or nursing home admission

Risk factors:
• Cigarette smoking
• Immunosuppression
  ◦ Advanced age
  ◦ Alcoholism
  ◦ Diabetes mellitus
  ◦ Hematologic malignancy
  ◦ HIV infection/ AIDS
  ◦ Malnutrition
  ◦ Medications
    − Chronic glucocorticoid use
    − Chemotherapy
    − Immunomodulating medications
  ◦ Renal dialysis

• Splenectomy or deficiency of the terminal complement components (C5C8) →
  ◦ Infection risk via encapsulated bacteria:
    − Escherichia coli
    − Haemophilus influenzae
    − Neisseria meningitides
    − Pseudomonas aeruginosa
    − Salmonella sp.
    − Streptococcus pneumoniae

Statistics:
• 4 million cases/ year in the U.S. →
  • 1 million hospitalizations

Organisms:
• No organism identified in >50% of cases
• Bacterial pneumonia
  ◦ Streptococcus pneumoniae→40%
  ◦ Haemophilus influenzae→15%, esp. in COPD patients
• Atypical organisms (see below)
  ◦ Anaerobes, esp. in alcoholics & others at aspiration risk
  ◦ Enterobacteriaceae, esp. in alcoholics & others at aspiration risk
    − Escherichia coli
    − Enterobacter cloacae
    − Klebsiella pneumoniae
    − Proteus mirabilis & vulgaris
    − Providencia rettgeri
    − Pseudomonas aeruginosa
    − Serratia marcescens
  ◦ Moraxella catarrhalis, esp. in COPD patients
  ◦ Staphylococcus aureus, esp. as a post-viral superinfection
Viral pneumonia
- Adenovirus
- Influenza virus
- Parainfluenza virus

Hospital Acquired Pneumonia (HAP)
- Pneumonia developing >48hrs of either hospital or nursing home admission

Pathophysiology:
- Actually a misnomer as the microorganisms typically responsible for hospital acquired pneumonia, cause pneumonia in moderate to severely ill patients, regardless of location, due in part to an illness-induced loss of the protective fibronectin coating of the oropharynx
  - Oropharyngeal colonization by the organisms typically responsible for hospital acquired pneumonia

Additional risk factors:
- Gastric pH
  - Medications
    - Antacids
    - Histamine 2 selective receptor blockers
    - Proton pump inhibitors
  - Pernicious anemia
  - Loss of the protective gastric acid coating
    - Gastroesophageal colonization by the organisms typically responsible for hospital acquired pneumonia

Organisms:
- Bacterial pneumonia - 95%
  - Enterobacteriaceae (esp. Klebsiella sp., & Enterobacter sp.)
    - Escherichia coli
    - Enterobacter cloacae
    - Klebsiella pneumoneae
    - Proteus mirabilis & vulgaris
    - Providencia rettgeri
  - Pseudomonas aeruginosa
    - Serratia marcescens
  - Atypical organisms (see below)
    - Acinetobacter sp.
    - Haemophilus influenzae
    - Staphylococcus aureus
    - Streptococcus pneumoneae
- Viral pneumonia
  - Cytomegalovirus-CMV
  - Influenza virus
  - Parainfluenza virus
- Fungal pneumonia
  - esp. Aspergillus sp.

Subclassifications

Aspiration Pneumonia
- Pneumonia developing in patients w/ a condition that predisposes to aspiration
  - Altered mental status
  - Dysphagia
  - Intubation
  - Neurologic deficits
  - ↓ cough reflex
  - Aspiration

Atypical Pneumonia
- A subacute form of pneumonia w/ a patchy interstitial infiltrate, for which no microorganism can be isolated using conventional sputum staining & cultures

Organisms:
- Atypical bacteria
  - Chlamyphilia pneumoneae (formerly Chlamydia pneumoneae)
  - Mycoplasma pneumoneae
PNEUMONIA

Legionella sp. (pneumophilia > bozemanii, micdadei) →
- Legionnaires’ disease

Acquisition:
- The organisms are associated with contaminated water supplies via vapor
  - Community sources
    - Air conditioners
    - Water cooling towers
  - Hospital sources
    - Showers
    - Sinks

- Legionnaires’ disease

Acquisition:
- The organisms are associated with contaminated water supplies via vapor
  - Community sources
    - Air conditioners
    - Water cooling towers
  - Hospital sources
    - Showers
    - Sinks

Atypical zoonotic bacteria—rare
Chlamydia psittaci →
- Psittacosis

Acquisition:
- The organism infects birds & many mammals →
  - High fecal concentrations, which when dried →
    - Human infection via aerosol inhalation of organisms

Coxiella burnetti →
- Q fever

Acquisition:
- The organism infects cattle, goats, & sheep →
  - High concentrations in feces, urine, unpasteurized milk, placental, & amniotic fluid, which when dried →
    - Human infection via aerosol inhalation of organisms

Note: The organism can also be acquired via direct contact w/ carcasses in slaughterhouses

OPPORTUNISTIC PNEUMONIA

- Pneumonia caused by a normally nonpathogenic microorganism (including latent organisms) in immunosuppressed patients

PULMONARY PATHOGENICITY

- Always pathogenic
  - The following organisms do not colonize the upper airways
  - Atypical organisms: Chlamyphilia pneumonia, Mycoplasma pneumoniae, Legionella sp.
  - Mycobacterium tuberculosis
  - Pathogenic fungi: Blastomyces dermatitides, Coccidioides immitis, Histoplasma capsulatum
  - Other fungi: Pneumocystis jiroveci
  - Certain viruses: Influenza virus, Parainfluenza virus, Respiratory syncytial virus

- Nonpathogenic
  - The following organisms lack the pathogenic potential to cause pneumonitis
    - Enterococcus sp.
    - Staphylococcus epidermidis

DIAGNOSIS

- Respiratory isolation w/ purified protein derivative-PPD placement if mycobacterial tuberculosis infection is suspected. Respiratory isolation is not needed for suspected mycobacteria other than tuberculosis-MOTT infection

General
- Inflammatory cytokines →
  - Anorexia →
  - Cachexia
  - Chills
  - Fatigue
  - Fever—75%
  - Headache
  - Malaise
  - Night sweats
  - Weakness

†Temperature may be normal in patients w/
- Chronic kidney disease, esp. w/ uremia
- Cirrhosis
- Heart failure
- Severe debility
...or those who are:
  • Intravenous drug users
  • Taking certain medications:
    ◦ Acetaminophen
    ◦ Antibiotics
    ◦ Glucocorticoids
    ◦ Nonsteroidal anti-inflammatory drugs—NSAIDs

Pulmonary
  • Bronchoalveolar inflammation
    ◦ Cough—85% ± sputum production—65%
    ◦ Pleurisy—30%, being thoracic pain exacerbated by either:
      − Deep inhalation (including coughing & sneezing)
      − Supine position
      − Thoracic palpation
    …& being relieved by leaning forward
  • Difficulty breathing= dyspnea—60%—
    − Respiratory rate > 16/ minute=tachypnea
    − Accessory muscle usage (sternocleidomastoid muscles for inspiration & abdominal muscles for expiration)
    − Speech frequently interrupted by inspiration=telegraphic speech
    − Purse lip breathing &/or grunting expirations—positive end−expiratory pressure—PEEP
    − Paradoxic abdominal motion: Negative intrathoracic pressure—fatigued diaphragm being pulled into the thorax—inspiratory inward motion of the anterior abdominal wall, rather than expected outward motion due to diaphragmatic contraction
  • Ventilation/ perfusion mismatch via:
    − ↑ Alveolar dead space: Alveolar ventilation through relatively underperfused capillaries
    − ↑ Vascular shunting: Capillary blood flow through relatively underventilated alveoli. Usually occurring, or exacerbated via ↑ venous return
    …→ ↓ diffusion of O₂ & CO₂→
      • Hypoxemia (SaO₂ ≤ 91% or PaO₂ ≤ 60 mmHg‡) on room air, w/ subsequent hypercapnia (PaCO₂ ≥ 45 mmHg) due to either:
        ◦ Respiratory muscle fatigue
        ◦ Alveolar hypoventilation
    …as CO₂ clearance is unimpaired (& may be ↑ in the dyspneic patient) as long as adequate ventilation (including lack of diffuse severe ventilation/ perfusion mismatching) is maintained, as:
      • CO₂ diffuses 20X as rapidly as O₂
      • Hypercapnia—
        ◦ Immediate brain stem respiratory center mediated stimulation of pulmonary ventilation, which may correct the hypercapnia, but not necessarily the hypoxia

Suggestive sputum findings:
  • Anaerobic sp.—
  ◦ Putrid odor due to the amines & fatty acids they produce
  • Streptococcus pneumoneae—
  ◦ Blood tinged sputum, termed ‘rusty sputum’
  • Klebsiella sp.—
  ◦ Thickened consistency w/ mucus & blood, termed ‘currant jelly sputum’

† Being exacerbated by the supine position→
‡ Systemic venous return→
† Vascular shunting→ dyspnea, being termed:
  − Orthopnea, if persistent
  − Paroxysmal nocturnal dyspnea if intermittent
  … causing the patient to either use multiple pillows or sleep in a chair
‡ Age adjusted normal PaO₂ = 101 − (0.43 X age)
COMPARATIVE THORACIC EXAMINATION FINDINGS

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Consolidation/empyema</th>
<th>Pleural effusion</th>
<th>Pneumothorax†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest expansion</td>
<td>≥</td>
<td>≥</td>
<td>≥</td>
</tr>
<tr>
<td>Auscultation</td>
<td>≥</td>
<td>≥</td>
<td>≥</td>
</tr>
<tr>
<td>Breath sounds w/ crackles, rhonchi, wheezes, &amp;/or egophony°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percussion</td>
<td>≥</td>
<td>≥</td>
<td>≥</td>
</tr>
<tr>
<td>Tactile or auscultatory fremitus</td>
<td>≥</td>
<td>≥</td>
<td>≥</td>
</tr>
</tbody>
</table>

Note: Outlining lung compression by all 3 etiologies→
- Atelectasis→
  - Signs of consolidation
† If via bronchopleural fistula, may be accompanied by:
  - Hemorrhax
  - Pyothorax=empyema
‡ Loss of intrapleural negative pressure→
  - Ipsilateral chest wall expansion→
    - Anteroposterior diameter→
      - Respiratory movement
° A patient's verbalization of the sound ‘E’ is heard as ‘A’
^ Best detected over the midclavicle w/ the patient sitting or standing. The ipsilateral breath sounds should guide you, as otherwise, you may be fooled by the contralateral side being relatively dull to percussion, assuming it to be the diseased lung
ⁿ Unless accompanied by a concomitant pleural effusion

Cardiovascular
- Relative bradycardia w/ viral & atypical organisms (except Mycoplasma pneumoneae)
  
  Appropriate temperature-pulse relationship:
  - 102°F→110bpm. Thereafter, every 1°F↑→10bpm↑ (ex: 103°F→120bpm, 104°F→130bpm, etc…)
  
  Inclusion criteria:
  - The patient must be an adult w/ a temperature≥102°F, w/ both the pulse & temperature taken at the same time
  
  Exclusion criteria:
  - Dysrhythmia
  - Cardiac rate altering medication
  - Pacemaker mediated rhythm

Hematologic
- Inflammatory cytokines→
  - Leukocytosis
  - Leukopenia w/ either:
    - Viral infection
    - Severe Streptococcus pneumoneae infection
    - Pneumonia secondary to a cause of neutropenia
  - Acute phase proteins
    - Erythrocyte sedimentation rate=ESR (normal: 5mm/ decade aged + ≤10mm/h or ≤20mm/h)
    - C-reactive protein=CRP (normal: <2mg/ L), responding more acutely than ESR, as it rises within several hours & falls within 3 days upon partial resolution
    - Fibrinogen
    - Platelets→thrombocytosis
  - Lactate dehydrogenase=LDH, indicative of pneumonitis, being ↑↑ w/ Pneumocystis jiroveci pneumonia

Differentiating among inflammatory etiologies:
- Procalcitonin=PCT, a precursor of the hormone calcitonin, is ↑w/ bacterial, fungal, or parasitic sepsis, but not w/ localized infections, viral infections, or non-infectious causes of inflammation. Calcitonin is involved w/ calcium homeostasis, being produced by the C-cells of the thyroid gland. However, during non-viral sepsis, procalcitonin is released by extra-thyroid tissue, as patients lacking a thyroid gland continue to produce high levels, w/ no effect on plasma calcitonin level or activity
  - Elevated plasma levels occur @≥5hours of non-viral sepsis, w/ a half life of 24 hours
    - <0.1mg/L: Bacterial infection very unlikely
    - 0.1–0.25mg/L: Bacterial infection unlikely
    - 0.25–0.5mg/L: Bacterial infection likely
    - >0.5mg/L: Bacterial infection very likely
Suggestive extrapulmonary findings of atypical organisms:

- **Legionella sp.**
  - Cardiovascular: Relative bradycardia
  - Gastrointestinal: Abdominal pain, diarrhea, nausea ± vomiting
  - Hematologic: Hyponatremia

- **Mycoplasma pneumoneae**
  - Cardiovascular: Myopericarditis
  - Gastrointestinal: Hepatitis
  - Mucocutaneous: Erythema multiforme
  - Neurologic: Aseptic meningitis, encephalitis, peripheral neuropathy
  - Outer ear: Bullous myringitis
  - Hematologic: Hemolytic anemia, **cold agglutinins = 50%**

- **Coxiella burnetti**
  - Cardiovascular: Relative bradycardia
  - Gastrointestinal: Hepatitis

---

**Cold agglutinins** are acquired IgM erythrocyte cell membrane autoantibodies →

- Erythrocyte agglutination in capillaries at cold temperatures (<98.6°F=37°C) →
  - Extravascular hemolytic anemia
  - Ischemia (usually affecting the ears, fingers, nose, &/or toes), which resolves upon re-warming

**Etiologies:**

- Idiopathic
- Infections: Mycoplasma pneumoneae or Epstein-Barr virus (EBV)
- Neoplasms, esp. chronic lymphoid leukemia (CLL), lymphoma, or Waldenstrom's macroglobulinemia

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**IMAGING**

**Chest x ray**

**Findings:**

- A **new infiltrate** is the gold standard for the diagnosis of acute pneumonia, being either:
  - Interstitial
  - Lobar
  - Multilobar
- On a posteroanterior chest x ray, an infiltrate may obscure the border of the diaphragm &/or heart, allowing for localization
  - *Obscuration the diaphragm* w/ visualization of the heart border indicates a **lower lobe infiltrate**, being **located posteriorly** on lateral chest x ray
  - *Obscuration of the heart border* indicates the **lobe just above the lower lobe**, being **located anteriorly** on lateral chest x ray
- **Right middle lobe infiltrate**
- **Left upper lingular infiltrate**
- Pleural effusion (bacterial & mycoplasmal > viral), which if present, should undergo diagnostic + therapeutic thoracentesis
  - Requires ≥300mL of fluid to be visualized via posteroanterior chest x ray
  - Posteroanterior view: Blunting of the costophrenic angle
  - Lateral view: Blunting of the posterior diaphragm
  - w/ fluid usually tapering slightly up the lateral pleural wall, forming a **meniscus**, unless the effusion is accompanied by either:
    - Fluid loculation
    
  **Pathophysicsology:**
    - Current &/or previous pleural inflammation →
      - Outlining pleural layer fibrosis → **loculation of effusion** ± bulging into the lung
      - **Interlobal effusion:** Between the lung & chest wall
      - **Infrapulmonary effusion:** Between the lung & diaphragm
      - **Interlobular effusion:** Between 2 lung lobes, esp. the horizontal fissure
    - Pneumothorax, being almost always due to a bronchopleural fistula
    - ...→ loss of the meniscus
  - Requires ≥15mL of fluid to be visualized via decubitus chest x ray

**Indications:**

- Pleural effusion present on posteroanterior chest x ray, in order to check for loculation
- Hilar &/or mediastinal lymphadenopathy
- Cavitary lesions, usually via:
  - Bacteria, esp. anaerobes, Klebsiella sp., Pseudomonas aeruginosa, or Staphylococcus aureus
  - Mycobacterial sp.
- w/ air fluid levels occurring mostly in those caused by bacteria
Suggestive radiographic findings:
- **Bacterial pneumonia**: Dense & asymmetric infiltrate
  - *Atypical pneumonia*: Patchy interstitial infiltrate
- **Viral & Pneumocystis jiroveci pneumonia**: Diffuse, symmetric, interstitial infiltrate
- **Aspiration pneumonia**: Infiltrate in a lung lobe that is dependent in the recumbent position
  - Supine position →
    - Superior segment of the right lower lobe
    - Posterior segment of the right upper lobe
- **Post-obstructive pneumonia**: The right middle lobe is the most common site of obstruction
  - Being that a right middle lobe pneumonia may signify a post-obstructive process, radiographic resolution must be ensured via repeat imaging @ 6weeks after treatment completion

Outcomes:
- Radiographic resolution upon adequate treatment
  - 50% within 2weeks
  - 25% @ 2−6weeks
  - 25% @ >6weeks

Limitations:
- False negative chest x ray is possible in the following circumstances:
  - Within 24hours of infection
  - Within 48hours of Pneumocystis jiroveci infection~30%
  - Severe neutropenia
  - Severe dehydration

### SPUTUM STUDIES
- Sputum must be transported to the laboratory for testing within 2hours of collection
- If tuberculosis is suspected, **3 consecutive early morning sputum samples** must be obtained for acid fast bacillus staining
- There is **no serologic test for Pneumocystis jiroveci**, & the organism **has not been grown in culture**

### SPUTUM ACQUISITION
**Induced sputum**
- **Indications:**
  - Nonproductive cough
  - Suspected Pneumocystis jiroveci pneumonia, as the presence of neutrophils in expectorated sputum prevents the detection of typical cysts
- **Procedure:**
  - A nebulized hypertonic saline solution is inhaled by the patient in order to induce a deep cough

**Procedure acquired sputum**
- **Indications:**
  - Immunosuppressed patients
  - Poor response to medical treatment
  - Possible Pneumocystis jiroveci pneumonia
  - Possible mycobacterial infection not otherwise diagnosed
  - Unable to produce useful sputum
- **Protected bronchoalveolar lavage**=BAL
  - **Procedure:**
    1. A bronchoscope is passed through the upper respiratory tract & wedged into a distal airway. In order to prevent upper airways contamination, the bronchoscope contains a dual catheter device in which one catheter is housed within a larger outer catheter, which is plugged at its distal end w/ a dissolvable material such as gelatin
    2. The inner catheter is advanced, knocking off the distal plug, allowing for advancement into the lower airways, w/ subsequent lavage w/ ≥120mL of isotonic saline
    3. ≤25% of the instilled volume is aspirated back into the catheter, which is retracted into the outer catheter, w/ the entire device retracted through the bronchoscope
  - **Threshold for a positive culture result**
    - $10^6$ CFU/ mL
• Protected specimen brushings—PSB
  Procedure:
  1. A bronchoscope is passed through the upper respiratory tract & wedged into a distal airway. In order to prevent upper airways contamination, the bronchoscope contains a dual catheter device in which one catheter is housed within a larger outer catheter, which is plugged at its distal end w/ a dissolvable material such as gelatin.
  2. The inner catheter is advanced, knocking off the distal plug, allowing for advancement of a brush into the lower airways.
  3. Once the brushing is obtained, the brush is retracted into the inner catheter, which is retracted into the outer catheter, w/ the entire device retracted through the bronchoscope.
  4. The brush is then placed in 1mL transport medium.

  Threshold for a positive culture result:
  • \(10^3\) CFU/ mL

• CFU=colony forming units=cultures

SPUTUM SCREENING
  Criteria for an appropriate sputum sample:
  • **Indicating derivation from the lower airways:**
    - \(<10\) epithelial cells/ lpf (X100)
    - \(\geq 1\) macrophage(s) on any magnification
  • **Indicating derivation from an inflammatory area**
    - \(\geq 25\) neutrophils/ lpf (X100)
  • **Indicating necrotizing pneumonia**
    - Elastin fibers on a 40% KOH preparation

• lpf=low power field

SPUTUM & PLEURAL FLUID STUDIES
  • For pleural fluid cultures, 2 sets of aerobic & anaerobic culture mediums are recommended, w/ each bottle inoculated w/ \(\geq 10\)mL of pleural fluid

• **Gram stain & culture**
  Indications:
  • Possible bacterial infection (all patients)
  Note: The finding of **gram negative diplococci** (at times found within polymorphonuclear cells) is typically associated w/ Neisseria sp. (gonorrhoeae or meningitides). However, the genus Neisseria is one of several in the family Neisseriaceae, containing the organism Moraxella Catarrhalis, w/ similar microscopic findings.

• **Fungal stains & cultures**
  Indications:
  • Possible fungal infection (including Pneumocystis jiroveci, not grown in culture)

  Visualized Pneumocystis jiroveci
  • Trophic forms, being 1~4μm in diameter, within foamy exudates via:
    - Gram–Weigert stain
    - Modified Papanicolaou stain
    - Wright–Giemsa stain
  • Cystic forms, being 8μm in diameter, w/ intracystic bodies via:
    - Calcofluor white
    - Cresyl echt violet stain
    - Gomori methenamine silver stain
    - Toluidine blue O

• **Acid fast bacillus**—AFB stain
  Indications:
  • Suspected Mycobacterium tuberculosis infection
  Mechanism:
  • Auramine stained mycobacteria, visualized by fluorescence microscopy, resist acid/ alcohol decolorization=acid/ alcohol fast bacilli=AFB
  Outcomes/ limitations:
  • Stain positive indicates possible active disease, as M. kansasii & M. avium intracellulare=MAI look identical to M. tuberculosis
• **Mycobacterial culture**
  
  **Indications:**
  - Definitive proof of active tuberculosis & infectivity, as 50% of culture positive patients are AFB stain negative
  - To test for antimicrobial susceptibilities
  
  **Outcomes:**
  - Culture negative indicates latent or no infection
  - Culture positive (which may require 2 months) is definitive proof of active tuberculosis & infectivity, being greatly ↑ if concomitantly stain positive

• **Sputum polymerase chain reaction-PCR**
  
  **Indications:**
  - To identify the mycobacterial species found via either acid-fast bacillus- AFB stain &/or culture
  - Suspected atypical organism
    - Chlamyphilia pneumoneae
    - Legionella sp.
    - Mycoplasma pneumoneae
  - Suspected Pneumocystis jiroveci pneumonia
  
  **Outcomes:**
  - Mycobacteria:
    - Stain positive samples: Sensitivity & specificity >95%
    - Stain negative samples: Specificity >95%, sensitivity 40-77%

• **Direct fluorescent antibody-DFA staining**
  
  **Procedure:**
  - The patients sputum, serum, or cerebrospinal fluid is incubated w/ fluorescent dye (fluorescein or rhodamine)-labeled IgG antibodies against organism surface antigens, w/ subsequent washing. Matching serum antigens→
    - Post-wash trophozoite or cyst visualization via an ultraviolet light microscope
  - Being termed ‘direct’ as the antibody binds directly to the antigen
  
  **Indications:**
  - Suspected Legionella sp. infection
  - Suspected Pneumocystis jiroveci pneumonia
  
  **Outcomes:**
  - Legionella pneumophilia sensitivity: 20-80% (specificity: 98%)
  
  **Limitations:**
  - False positive:
    - Anti-Legionella sp. antibodies may cross react w/ Pseudomonas aeruginosa & Francisella tularensis

• **Cytology**
  
  **Indications:**
  - Suspected malignancy mediated post-obstructive pneumonia

---

**BLOOD & EFFUSION STUDIES**

• **Cultures**
  
  **Indications:**
  - All patients requiring hospital admission
  
  **Procedure:**
  - 2 sets of aerobic & anaerobic culture mediums, w/ each bottle inoculated w/ ≥10mL of fluid
  
  **Outcomes:**
  - Community acquired pneumonia-CAP sensitivity
    - Streptococcus pneumoneae: 5-20%
    - Others: 10-45%
  - Hospital acquired pneumonia-HAP sensitivity: 10%
  
  **Limitations:**
  - Careful, as source may be contaminated via:
    - Concomitant infection
    - Intravascular line/catheter, or lack of aseptic technique→
      - Skin organism contamination
URINE STUDIES

• Urine antigen assay

  Indications:
  • Suspected Streptococcus pneumoniae
  • Suspected atypical pneumonia

  Mechanism:
  • Detects:
    ◦ *Streptococcus pneumoniae C polysaccharide*, found in the cell wall, being common to all serotypes, w/ the results available at 15 minutes
    ◦ *Legionella pneumophila serogroup 1 antigen*, accounting for 70% of Legionella sp. infections

  Outcomes:
  • *Streptococcus pneumoniae*
    ◦ Sensitivity 75%, specificity 95%
  • *Legionella pneumophila serogroup 1*
    ◦ Sensitivity 65% during week 1 & 100% by week 2
    ◦ Specificity 100%

OTHER STUDIES

• Human Immune Deficiency virus—HIV serology

  Indications:
  • Ages 15–55 years

PROGNOSIS/ TRIAGE

<table>
<thead>
<tr>
<th>COMMUNITY ACQUIRED PNEUMONIA PROGNOSIS &amp; TRIAGE SCORE</th>
<th>Score</th>
<th>30 day mortality</th>
<th>Suggested Triage</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤70</td>
<td>&lt;1%</td>
<td>Outpatient</td>
<td></td>
</tr>
<tr>
<td>71–90</td>
<td>3%</td>
<td>Brief inpatient—general medicine ward</td>
<td></td>
</tr>
<tr>
<td>91–130</td>
<td>8%</td>
<td>Inpatient—general medicine ward</td>
<td></td>
</tr>
<tr>
<td>&gt;130</td>
<td>30%</td>
<td>Inpatient—intensive care unit—ICU</td>
<td></td>
</tr>
</tbody>
</table>

• 25% of patients will require hospitalization, w/ an overall 25% inpatient mortality rate

Indications to admit regardless of score:
• Altered mental status
• Hypotension
• Hypoxemic respiratory failure
• Suppurative disease (empyema, lung abscess)
• Metastatic disease (endocarditis, meningitis, osteomyelitis)

Point calculation:
• Gender: ♂ age, ♀ age –10
• 10: Nursing home resident
• Comorbidities
  ◦ 10: Heart failure
  ◦ 10: Cerebrovascular disease
  ◦ 10: Renal failure
  ◦ 20: Chronic liver disease (hepatitis, cirrhosis)
  ◦ 30: Malignancy†
• Physical examination
  ◦ 10: Tachycardia ≥125
  ◦ 15: Temperature ≤35°C or ≥104°F=40°C
  ◦ 20: Altered mental status
  ◦ 20: Tachypnea of ≥30/ minute
• Hematologic
  ◦ 10: Glucose ≥250mg/ dL
  ◦ 10: Hematocrit <30%
  ◦ 10: Hypoxemic respiratory failure
  ◦ 20: Blood urea nitrogen—BUN ≥30mg/ dL
  ◦ 20: Sodium <130mEq/ L
  ◦ 30: Arterial pH <7.35
• Other
  ◦ 10: Pleural effusion

†Active or in remission, being diagnosed within 1 year to the pneumonia (except basal or squamous cell cancers)
TREATMENT

• **Empiric intravenous antibiotics**
  - If treatment is initially begun with intravenous medication, the switch to PO medication should be attempted upon clinical improvement (fever resolution & clinical stabilization) X 24 hours, if an acceptable PO medication is available, & the patient is able to take PO medication.
  - **Organism-narrowed therapy** should be initiated promptly upon stain, culture, & sensitivities results.
  - The following antibiotics achieve equivalent plasma levels via PO or intravenous administration in persons with a functioning gastrointestinal tract:
    - Chloramphenicol
    - Doxycycline
    - Minocycline
    - Most fluoroquinolones
    - Trimethoprim/ Sulfamethoxazole
  - **Consider treating for possible Pneumocystis jiroveci pneumonia** in patients with either:
    - HIV/ AIDS
    - Chronic glucocorticoid or immunomodulating medication treatment

Bactericidal antibiotics

• **Cell wall synthesis inhibitors**
  - β-lactam medications:
    - Carbapenems
    - Cephalosporins
    - Monobactams
    - Penicillins
    - Vancomycin

• **DNA synthesis inhibitors**
  - Fluoroquinolones
  - Linezolid, in part
  - Metronidazole
  - Rifampin
  - Quinupristin & Dalfopristin

• **Aminoglycosides**

Treatment duration:

• **Community & hospital acquired pneumonia: 5−10 days**
  - Treatment length is based on response & complications
• **Pneumocystis jiroveci pneumonia: 3 weeks**
• **Tuberculosis:** See section

• Azithromycin X 5 days can be considered equivalent to a 10 day course due to its prolonged biological half-life

COMMUNITY ACQUIRED PNEUMONIA

OUTPATIENT TREATMENT

<table>
<thead>
<tr>
<th>MACROLIDES</th>
<th>M</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin (Zithromax)</td>
<td>L</td>
<td>500mg PO q24hours</td>
</tr>
</tbody>
</table>

**Mechanism:**

- Affects the ribosomal 50S subunit
- Transfer RNA translocation

**Side effects:**

- Gastrointestinal
  - Diarrhea
  - Nausea ± vomiting
- Neurologic
  - Headache
- Transient deafness
- Hematologic
  - Eosinophilia

OR
### Tetracyclines

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline (Adoxa)</td>
<td>LK</td>
<td>200mg PO q12hours X 3 days loading dose, then 100mg PO q12hours</td>
</tr>
</tbody>
</table>

**Mechanism:**
- Affects the ribosomal 30S subunit → Ribosomal binding to transfer RNA

**Side effects:**
- **Gastrointestinal**
  - Acute hepatic fatty necrosis
  - Gastroenteritis → Abdominal pain
  - Clostridium difficile pseudomembranous colitis
- **Genitourinary**
  - Acute tubular necrosis
- **Mucocutaneous**
  - Photosensitivity
- **Neurologic**
  - Fetus to age 10 years → Tooth staining
  - Bone growth

### Fluoroquinolones: Nationally, <1% of pneumococcal isolates are resistant to fluoroquinolones

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatifloxacin (Tequin)</td>
<td>K</td>
<td>400mg PO/ IV q24hours</td>
</tr>
<tr>
<td>Levofloxacin (Levaquin)</td>
<td>KL</td>
<td>500mg PO/ IV q24hours</td>
</tr>
<tr>
<td>Moxifloxacin (Avelox)</td>
<td>LK</td>
<td>400mg PO/ IV q24hours</td>
</tr>
</tbody>
</table>

**Mechanism:**
- DNA gyrase=topoisomerase action → Bacterial DNA synthesis

**Side effects:**
- **General**
  - Hypersensitivity reactions
- **Cardiovascular**
  - QT interval → Torsades de pointes
- **Gastrointestinal**
  - Gastroenteritis → Diarrhea
  - Nausea ± vomiting
  - Clostridium difficile pseudomembranous colitis
- **Mucocutaneous**
  - Phototoxicity
- **Musculoskeletal**
  - Tendinopathy → Tendon rupture risk
- **Neurologic**
  - Dizziness
  - Drowsiness
  - Headache
  - Restlessness
  - Seizures
- **Materno–fetal**
  - Fetal & child tendon malformation (including breast fed) → Tendon rupture risk

**Interactions**
- False positive urine assay for opiates
# PNEUMONIA

## INPATIENT TREATMENT

### FLUOROQUINOLONES: Nationally, <1% of pneumococcal isolates are resistant to fluoroquinolones

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>Gender</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatifloxacin (Tequin)</td>
<td>M♀</td>
<td>400mg PO/ IV q24hours</td>
</tr>
<tr>
<td>Levofloxacin (Levaquin)</td>
<td>KL♀</td>
<td>500mg PO/ IV q24hours</td>
</tr>
<tr>
<td>Moxifloxacin (Avelox)</td>
<td>LK♀</td>
<td>400mg PO/ IV q24hours</td>
</tr>
</tbody>
</table>

OR THE COMBINATION OF

### CEPHALOSPORINS: 3rd-4th generation

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>Gender</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime (Claforan)</td>
<td>KP</td>
<td>2g IV/ IM q12hours</td>
</tr>
<tr>
<td>Ceftriaxone (Rocephin)</td>
<td>KB</td>
<td>2g IV/ IM q24hours</td>
</tr>
</tbody>
</table>

**Mechanism:**
- A β-lactam ring structure which binds to bacterial transpeptidase→
  - ↓Transpeptidase function→
    - ↓Bacterial cell wall peptidoglycan cross-linking→↓cell wall synthesis→osmotic influx of extracellular fluid→↑intracellular hydrostatic pressure→cell rupture→cell death=bactericidal
  - ↑Bacterial autolytic enzymes→
    - Peptidoglycan degradation

### Certain bacteria produce β-lactamase→
- Cleavage of this essential structural component of cephalosporins & certain penicillins (as the other β-lactam medications differ sufficiently to prevent ring cleavage)→
  - Antibiotic inactivation. This process may be antagonized by the concomitant administration of β-lactamase inhibitors (Clavulanic acid=clavulanate, Sulbactam, or Tazobactam)→renewed susceptibility

### MACROLIDES

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>Gender</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin (Zithromax)</td>
<td>LP</td>
<td>500mg PO/ IV q24hours</td>
</tr>
</tbody>
</table>

**Gastrointestinal**
- *Clostridium difficile* pseudomembranous colitis (esp. 3rd generation)

## HOSPITAL ACQUIRED PNEUMONIA—HAP, BRONCHIECTASIS, OR CYSTIC FIBROSIS

- **2 OF THE FOLLOWING** in order to provide double coverage for possible *Pseudomonas aeruginosa* infection. **DO NOT** use 2 β-lactam ring containing antibiotics (penicillins, cephalosporins, carbapenems, monobactams) concomitantly, due to lack of either additive or synergistic effects

- **Remember to cover for atypical organisms in any patient from the community**, regardless if treating as a hospital acquired pneumonia due to a concomitant underlying moderate to severe illness

### PENICILLINS

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>Gender</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin–Tazobactam (Zosyn)</td>
<td>KP</td>
<td>4.5g IV q6hours</td>
</tr>
<tr>
<td>Ticarcillin–clavulanic acid (Timentin)</td>
<td>KP</td>
<td>50mg/ kg IV q4hours</td>
</tr>
</tbody>
</table>

**Mechanism:**
- A β-lactam ring structure which binds to bacterial transpeptidase→
  - ↓Transpeptidase function→
    - ↓Bacterial cell wall peptidoglycan cross-linking→↓cell wall synthesis→osmotic influx of extracellular fluid→↑intracellular hydrostatic pressure→cell rupture→cell death=bactericidal
• Bacterial autolytic enzymes →
  ◦ Peptidoglycan degradation

• Certain bacteria produce β-lactamase →
  ◦ Cleavage of this essential structural component of cephalosporins & certain penicillins (as the other β-lactam medications differ sufficiently to prevent ring cleavage) →
    − Antibiotic inactivation. This process may be antagonized by the concomitant administration of β-lactamase inhibitors (Clavulanic acid = clavulanate, Sulbactam, or Tazobactam) → renewed susceptibility

• When uricosuric medications (Probenecid, Sulfinpyrazone) are administered concomitantly w/ a β-lactam medication, they competitively inhibits its active secretion by the renal tubules →
  ◦ Plasma levels

Side effects:
General
  • Hypersensitivity reactions ≤10%
    ◦ Anaphylaxis = 0.5% →
    ◦ Death = 0.002% (1:50,000)
    ◦ Acute interstitial nephritis
    ◦ Dermatitis
    ◦ Drug fever
    ◦ Hemolytic anemia
      ... having cross-hypersensitivity to other β-lactam medications (cephalosporins, carbapenems), except monobactams (ex: Aztreonam)

CEPHALOSPORINS: 3rd-4th generation

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefipime (Maxipime)</td>
<td>K P</td>
<td>2g IV q8hours</td>
</tr>
<tr>
<td>Ceftazidime (Ceptaz, Fortaz)</td>
<td>K P</td>
<td>2g IV q8hours</td>
</tr>
</tbody>
</table>

FLUOROQUINOLONES

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofoxacin (Levaquin)</td>
<td>KL ?</td>
<td>750mg IV q24hours</td>
</tr>
</tbody>
</table>

CARBAPENEMS

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipinem−Cilastatin (Primaxin)</td>
<td>K ?</td>
<td>500mg IV q6hours</td>
</tr>
<tr>
<td>Meropenem (Merrem)</td>
<td>K P</td>
<td>1g IV q8hours</td>
</tr>
</tbody>
</table>

Mechanism:
• A β-lactam ring structure which binds to bacterial transpeptidase →
  ◦ Transpeptidase function →
    − | Bacterial cell wall peptidoglycan cross-linking → | cell wall synthesis → osmotic influx of extracellular fluid → | intracellular hydrostatic pressure → | cell rupture → | cell death = bactericidal

• When uricosuric medications (Probenecid, Sulfinpyrazone) are administered concomitantly w/ a β-lactam medication, they competitively inhibits its active secretion by the renal tubules →
  ◦ Plasma levels

Side effects:
General
  • Hypersensitivity reactions
    ◦ Anaphylaxis
    ◦ Acute interstitial nephritis
    ◦ Dermatitis
    ◦ Drug fever
    ◦ Hemolytic anemia
      ... having cross-hypersensitivity to other β-lactam medications (penicillins, cephalosporins), except monobactams (ex: Aztreonam)

Cardiovascular
  • Venous inflammation = phlebitis

Gastrointestinal
  • Gastroenteritis →
  ◦ Diarrhea
  ◦ Nausea ± vomiting
  ◦ Clostridium difficile pseudomembranous colitis
Neurologic
- **Seizures** (Imipenem > Meropenem), esp. w/
  - ↑Age
  - Renal failure
  - Seizure history

<table>
<thead>
<tr>
<th>Imipenem dosage</th>
<th>Seizure occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mg q6hours</td>
<td>0.2–1%</td>
</tr>
<tr>
<td>1g q6hours</td>
<td>10%</td>
</tr>
</tbody>
</table>

**AMINOGLYCOSIDES**

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M</th>
<th>Dosing†</th>
<th>Peak</th>
<th>Trough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin (Amikin)</td>
<td>K</td>
<td>15mg/ kg IV q24hours</td>
<td>&gt;30μg/ mL</td>
<td>&lt;5μg/ mL</td>
</tr>
<tr>
<td>Gentamycin (Garamycin)</td>
<td>K</td>
<td>7mg/ kg IV q24hours</td>
<td>&gt;6μg/ mL</td>
<td>&lt;2μg/ mL</td>
</tr>
<tr>
<td>Tobramycin (Nebcin)</td>
<td>K</td>
<td>7mg/ kg IV q24hours</td>
<td>&gt;6μg/ mL</td>
<td>&lt;2μg/ mL</td>
</tr>
</tbody>
</table>

- Peak levels are obtained 30 minutes after the dose, w/ trough levels being obtained at the end of the dosing interval. Plasma peak & trough levels are directly related to clinical efficacy & toxicity respectively
- †Patients receiving an aminoglycoside for synergy w/ a β-lactam medication versus Enterococcus sp. should receive thrice daily dosing

**Dose adjustment based on creatinine clearance (mL/ minute)**

- 40–59: q36hours
- 20–39: q48hours

**Obesity dosage adjustment:**
- †Ideal weight† + 0.4 (actual weight – ideal weight) = adjusted weight
- †♂: 50kg + 2.3kg per inch > 5’
- †♀: 45.5kg + 2.3kg per inch > 5’

**Mechanism:**
- Affects the ribosomal 30S subunit →
  - ↓Initiation complex function
  - Misreading of messenger RNA

**Side effects:**

**Genitourinary**
- **Nephrotoxicity†** (Gentamicin > Tobramycin > Amikacin > Neomycin), w/ renal failure usually @ ≥1 week via acute tubular necrosis
  - Risk factors:
    - ↑Age
    - Cirrhosis
    - Hypovolemia
    - Hypokalemia
    - Hypomagnesemia
    - Renal failure

**Neurologic**
- **Ototoxicity‡, being dose related & irreversible** →
  - High frequency sound loss
  - Risk factors:
    - Concomitant use w/ other ototoxic medications such as loop diuretics
    - Renal failure
    - Use >2 weeks
  - Neuromuscular blockade via:
    - ↓Presynaptic acetylcholine release
    - Postsynaptic sensitivity to acetylcholine

†Early signs of nephrotoxicity include:
- ↓Ability to concentrate the urine (noted via ↓specific gravity)
- Cylindrical urinary casts
- Proteinuria

‡Audiometry is required to document ototoxicity, as the hearing loss occurs above the frequency range of normal human conversation

**Monitoring:**
- Obtain baseline & serial audiometry w/ treatment >2 weeks
ALTERNATIVE OPTIONS FOR BETA LACTAM HYPERSENSITIVITY

MONOBACTAMS

**Indications:**
- Consider for regimen incorporation, as it is the only β-lactam based medication which can be administered to patients w/ hypersensitivity syndrome to the β-lactam structure. **But, it is only active against gram negative organisms**

**Generic (Trade) M ♀ Dose**

Aztreonam (Azactam) K P 2g IV q6hours

**Mechanism:**
- A β-lactam ring structure which binds to bacterial transpeptidase→
  - ↓Transpeptidase function→
    - ↓Bacterial cell wall peptidoglycan cross-linking→↓cell wall synthesis→osmotic influx of extracellular fluid→↑intracellular hydrostatic pressure→cell rupture→cell death=bactericidal
- ↑Bacterial autolytic enzymes→
  - Peptidoglycan degradation

- When uricosuric medications (Probenecid, Sulfinpyrazone) are administered concomitantly w/ a β-lactam medication, they competitively inhibits its active secretion by the renal tubules→↑Plasma levels

ADDITONAL TREATMENT

VANCOMYCIN

**Indications:**
- Suspected *methicillin resistant Staphylococcus aureus* MRSA via:
  - History of colonization/ infection
  - Recent hospitalization or nursing home residence
  - Recent invasive procedure
  - Severe mucositis

**M ♀ Dose**

<table>
<thead>
<tr>
<th>K</th>
<th>1g IV q12hours, to be administered over 1 hour</th>
<th>30-40 μg/mL</th>
<th>&gt;5μg/mL</th>
</tr>
</thead>
</table>

- Peak levels are obtained 30minutes after the dose, w/ trough levels being obtained at the end of the dosing interval. Plasma peak & trough levels are directly related to toxicity & clinical efficacy respectively

**Mechanism:**
- Direct cell wall peptidoglycan binding→
  - ↓Transpeptidase function→
    - ↓Bacterial cell wall peptidoglycan cross-linking→↓cell wall synthesis→osmotic influx of extracellular fluid→↑intracellular hydrostatic pressure→cell rupture→cell death=bactericidal

- Vancomycin resistant enterococci–VRE & staphylococci–VRS have developed

**Side effects:**
- **General**
  - Rapid intravenous administration (over <1hour)→
    - Intrinsic hypersensitivity syndrome→
      - Face, neck, &/or upper thoracic angioedema, termed ‘red man syndrome’. Occurrence does not prevent continued use, unless accompanied by an anaphylactoid reaction

- **Cardiovascular**
  - Venous inflammation=phlebitis ± thrombus formation

- **Otolaryngology**
  - Ototoxicity

- **Hematology**
  - Thrombocytopenia

CLINDAMYCIN (Cleocin)

**Indications:**
- Suspected:
  - Aspiration pneumonia
  - Lung abscess
  - Empyema

**M ♀ Dose**

<table>
<thead>
<tr>
<th>L</th>
<th>900mg IV q8hours or 450mg PO q6hours</th>
</tr>
</thead>
</table>

**Mechanism:**
- Affects the ribosomal 50S subunit→
  - Peptid bond formation
PNEUMONIA

Side effects:
Gastrointestinal
• Clostridium difficile pseudomembranous colitis
• Gastroenteritis →
  ♦ Diarrhea
  ♦ Nausea ± vomiting
Mucocutaneous
• Dermatitis

METRONIDAZOLE (Flagyl)

Indications:
• Suspected:
  ♦ Aspiration pneumonia
  ♦ Lung abscess
  ♦ Empyema

M ♀ Dose
KL P–U in 1st trimester 1g IV loading dose, then 500mg IV/ PO q8hours

Mechanism:
• DNA binding →
  ♦ DNA strand breakage

Side effects:
General
• Disulfuram–like reaction to alcohol
  ♦ Avoid alcoholic beverages during, & for 48 hours after completion of treatment
• Headache
Gastrointestinal
• Nausea ± vomiting = 10%
  • Taste changes = dysgeusia (esp. metallic taste)
Genitourinary
• Dark urine, being common, but harmless
Neurological
• Aseptic meningitis
• Incoordination = ataxia
• Peripheral neuropathy
• Seizures
Hematologic
• Transient neutropenia = 8%

PREVENTION
HOSPITAL ACQUIRED PNEUMONIA

Prophylaxis:
• Staff hand washing
• Adequate nutritional support
• Early removal of nasal & oral tubes
• Proton pump inhibitors, histamine 2 selective receptor blockers, antacids, or pernicious anemia →
  ◦ Loss of the protective gastric acid coating → gastrolesophageal colonization by oropharyngeal organisms →
    • Hospital acquired pneumonia risk via aspiration
    • Stress erosion/ ulceration mediated organism translocation risk → bacteremia
    … all being ↓ risk w/ the use of Sucralfate, which typically does not ↑ gastric pH
• Selective digestive decontamination
  ◦ Moderate to severe illness–induced loss of the protective fibronectin coating of the oropharynx →
  ◦ Oropharyngeal colonization by the organisms typically responsible for hospital acquired pneumonia

MUCOSAL COATING MEDICATIONS

<table>
<thead>
<tr>
<th>Generic (Trade)</th>
<th>M ♀ Dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucralfate (Carafate)</td>
<td>Ø P</td>
<td>2g PO q12hours (1 hour prior to meals &amp;/or qhs)</td>
</tr>
</tbody>
</table>

• Do not administer concomitantly w/ other acid suppressing medications, as ↑ gastric pH →
  ◦ Efficacy, as this medication requires an acidic environment
Mechanism:
• An aluminum hydroxide complex of sucrose that:
  ◦ Forms a protective coating over the inflammatory/ ulcerated area
  ◦ ↑ Gastric mucosal prostaglandin synthesis →
    − ↑ Epithelial cell proliferation
  ◦ ↑ Mucosal blood flow → ↑ bicarbonate delivery to the mucosa
  ◦ ↑ Mucus & bicarbonate secretion from gastric mucosal cells
  ◦ Binds to bile salts
... & does not ↑ gastric pH

Side effects:
Gastrointestinal
• Constipation

Genitourinary
• Aluminum toxicity, in the presence of renal failure

Hematologic
• Aluminum binding to intestinal phosphate →
  ◦ ↓ Intestinal phosphate absorption which may →
    − Hypophosphatemia, being rare

Interactions
• Binds to certain medications in the intestine →
  ◦ ↓ Absorption, such as:
    − Digoxin
    − Fluoroquinolone & tetracycline antibiotics
    − Phenytoin
    − Theophylline
    − Warfarin
... which should be administered ≥ 2 hours prior to Sucralfate

SELECTIVE DIGESTIVE DECONTAMINATION

<table>
<thead>
<tr>
<th>Location</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx</td>
<td>A methylcellulose paste† containing</td>
</tr>
<tr>
<td></td>
<td>• 2% Amphotericin</td>
</tr>
<tr>
<td></td>
<td>• 2% Polymyxin E</td>
</tr>
<tr>
<td></td>
<td>• 2% Tobramycin</td>
</tr>
<tr>
<td></td>
<td>... applied to the buccal mucosa &amp; tongue via a gloved finger q6hours</td>
</tr>
<tr>
<td>Distal gastrointestinal tract</td>
<td>A solution containing</td>
</tr>
<tr>
<td></td>
<td>• 500 mg Amphotericin</td>
</tr>
<tr>
<td></td>
<td>• 100 mg Polymyxin E</td>
</tr>
<tr>
<td></td>
<td>• 80 mg Tobramycin</td>
</tr>
<tr>
<td></td>
<td>... administered via nasogastric tube q6 hours</td>
</tr>
</tbody>
</table>

† The hospital pharmacy will make the paste

Mechanism:
• Eradication of Pseudomonas aeruginosa, as well as most gastrointestinal fungi & enterobacteriaceae @ 1 week
• The normal gastrointestinal bacterial flora, composed mostly of anaerobes, is relatively unaffected
...→ treatment & prevention of gastrointestinal colonization by the organisms typically responsible for hospital acquired:
• Pneumonia
• Urinary tract infections
• Bacteremia/ fungemia via mucocutaneous routes:
  ◦ Cutaneous lesion
  ◦ Gastrointestinal translocation
  ◦ Intravascular catheter

Side effects:
• The antimicrobials used are nonabsorbable, & thus do not cause systemic toxicity
VENTILATOR ASSOCIATED PNEUMONIA—1%/ 24 hours

Pathophysiology:
• Due to pericuff microaspiration of:
  ◦ Esophagogastric mucus
  ◦ Saliva
  ◦ Tube feedings

Outcomes:
• 30% mortality

Additional prophylaxis:
• Avoidance of gastric distention
• Routine orotracheal suctioning w/ continuous subglottic suctioning
• Semirecumbent positioning of the patient

PRE-EXPOSURE PROPHYLAXIS

INFLUENZA VACCINE

Indications:
• All persons ≥6 months old without a contraindication, as the vaccine is not FDA approved for children age <6 months
• Pregnancy
  ◦ Pregnancy is associated w/ ↑ influenza severity & complication risk. There is also an association between influenza infection during the 2nd & 3rd trimesters & the subsequent development of schizophrenia in the child

Dose for ages ≥9 years:
• 0.5mL IM injection qyear
  ◦ Best given within 2 months prior to the winter influenza season
    - Northern hemisphere: December to March
    - Southern Hemisphere: April to September
    - Tropics: All year

Mechanism:
• Inactivated virus (whole or fractionated) or surface antigens, w/ the strains (2 influenza A & 1 influenza B) being determined annually by the U.S. Public Health Service
  ◦ Protective antibody levels @ 2 weeks after administration

Outcomes:
• 75% efficacious for ages 6 months - 60 years, being ↓@ age >60 years

Contraindications:
• Hypersensitivity syndrome to eggs, as the vaccine is prepared from virus grown in chick embryos

Side effects:
General
• Fever
• Malaise
• Myalgia
  … from 6 hours – 2 days post–vaccination

Mucocutaneous
• Mild local inflammation ± soreness – 30%

Other
• Hypersensitivity reaction – rare
• Whether the vaccine causes Guillain–Barre syndrome is controversial

STREPTOCOCCUS PNEUMONEAE VACCINE

Indications:
• Age ≥50 years
• Children of all ages, w/ those age <2 years requiring the conjugate heptavalent pneumococcal vaccine (Prevnar), w/ doses & timing varying by age
• Chronic disease, including alcoholism
• Close residential contact
  ◦ Chronic care facilities
    – Board & care housing
    – Nursing home care housing
  ◦ Homeless shelters
  ◦ Military personnel
  ◦ Jails
• Prior Streptococcal pneumoneae infection
• Asplenia
  ◦ Anatomic
  ◦ Functional
  … being best if administered prior to asplenia, w/ repeat q6 years
• 2 weeks prior to immunosuppressive treatment
  ◦ Chemotherapy
  ◦ Immunomodulating medications

Dose
  • 0.5mL SC/ IM X 1, w/ a booster @ 5 years

Mechanism:
  • Bacterial capsular polysaccharides of 23 serotypes (Pneumovax), accounting for >90% of invasive disease (bacteremia, meningitis, pneumonia)

Side effects:
  • Mucocutaneous
    • Mild local inflammation ± soreness

Outcomes:
  • 70% efficacious for 10 years
    ◦ ↓ For immunosuppressed or age <2 years

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Indications:
• Asplenia
  ◦ Anatomic
  ◦ Functional
  … being best if administered prior to asplenia

Dose
  • 0.5mL IM X 1

Mechanism:
  • Bacterial capsular polysaccharide conjugated to protein

Contraindications:
  • Pregnancy