Pneumonia

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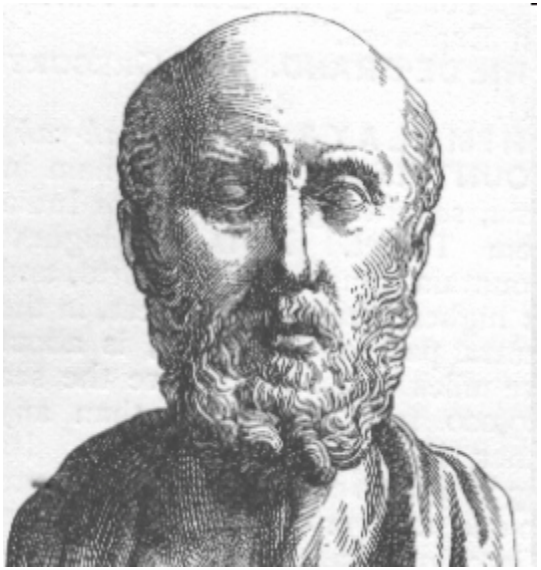
Terminology

- **Merriam Webster Dictionary**
  - **pneu·mo·nia** ***noun*** **\nu̇-mō-nyə, nyu̇-**
- **Origin of *PNEUMONIA***
  - New Latin, from Greek, from *pneumōn* lung, alteration of *pleumōn*
  - First Known Use: 1603

Historical Points

- Referred to pneumonia as a disease "named by the ancients."
- “If sweats come out about the neck and head, for such sweats are bad, as proceeding from the suffocation, rales, and the violence of the disease which is obtaining the upper hand”



Hippocrates Ancient Greek Physician known as the “Father of Medicine” (c. 460 BC – 370 BC)

Historical Points

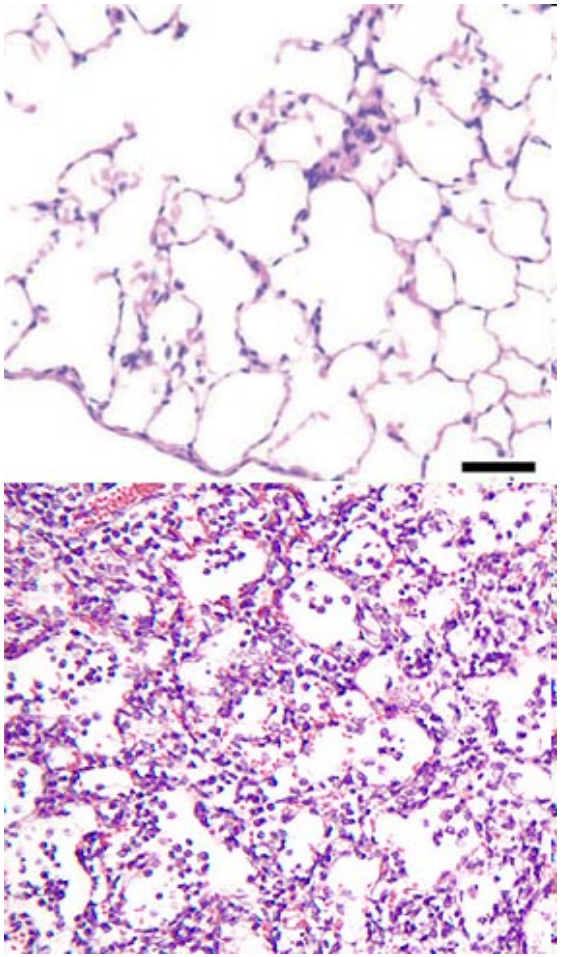
- “the most widespread and fatal of all acute diseases, pneumonia, is now Captain of the Men of Death.”

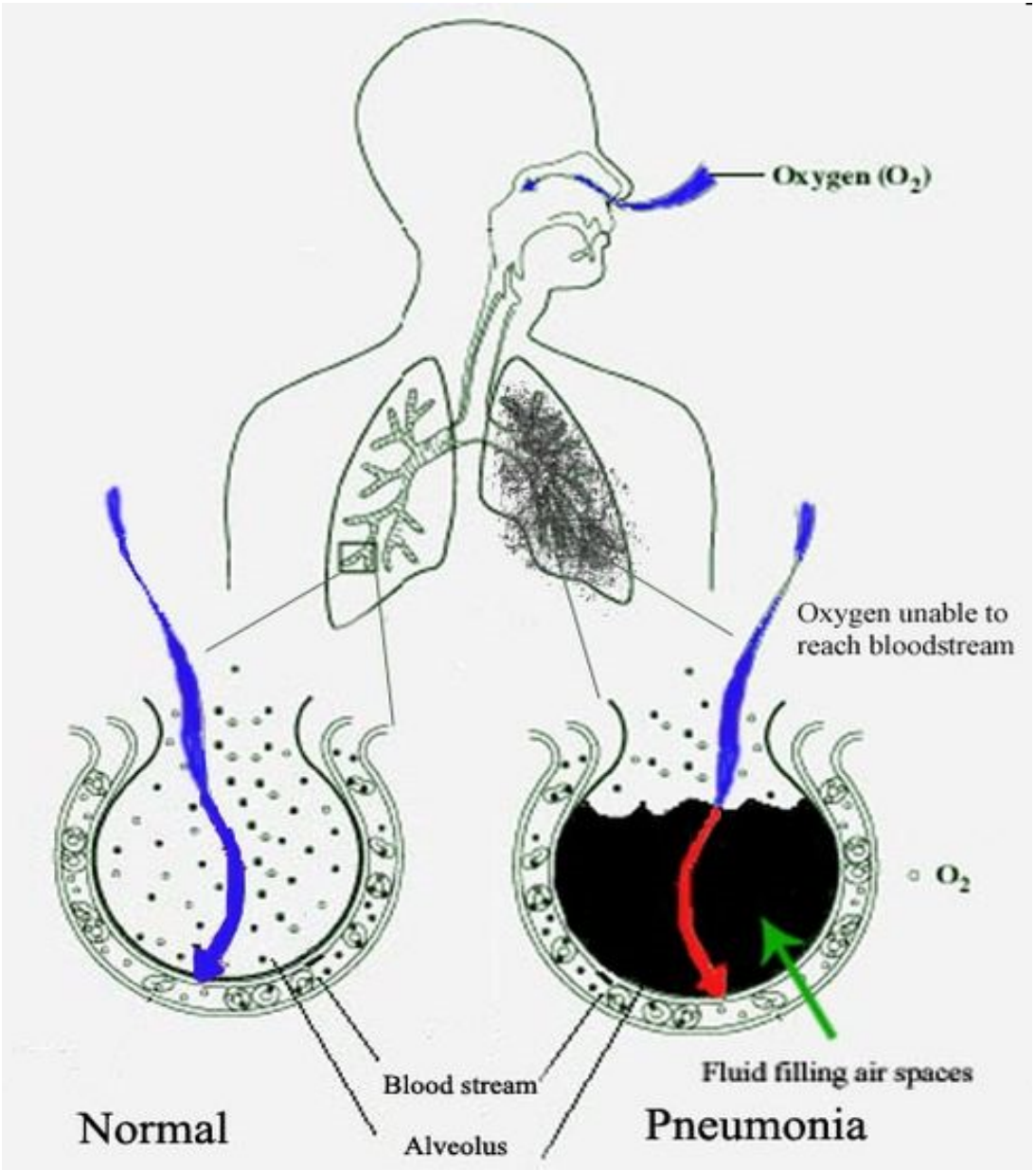
The Principles and Practice of Medicine; 4th ed. New York, Appleton, 1901

Sir William Osler

What is Pneumonia?

- **Pneumonia** is an inflammatory condition of the lung
- characterized by inflammation of the parenchyma of the lung (alveoli)
- Abnormal alveolar filling with fluid causing Air space disease (consolidation and exudation)




Oxygen (O_2)
Oxygen unable to reach bloodstream
O_2
Fluid filling air spaces
Blood stream
Alveolus
Normal
Pneumonia

Pneumonia: Definitions

- Community-acquired pneumonia **(CAP)**
  Cough/fever/sputum production + infiltrate, related to community
- Healthcare-associated pneumonia **(HCAP)**
  Pneumonia that develops **within 48 hours** of admission in pts with:
  - Hospitalization in acute care hospital for ≥2 d in past 90 d
  - Residence in NH or LTC facility
  - Chronic dialysis within 30 days
  - Home IV therapy, home wound care in past 30 days
  - Family member with MDR pathogen
- Hospital-acquired pneumonia **(HAP)**
  Pneumonia ≥ 48 hours after admission
- Ventilator-associated pneumonia **(VAP)**
  pneumonia ≥ 48 hours after intubation

Epidemiology

- Unclear Few population-based statistics on the condition alone
- Pneumonia & influenza = 6th leading causes of death in the world
- Single most common cause of infection-related mortality
- Age-adjusted death rate = 22 per 100,000 per year
- Mortality rate: 1-5% out-Pt, 12% In-Pt, 40% ICU
- Death rates increase with comorbidity and age
- Affects race and sex equally

Pathogenesis

- Inhalation, aspiration and hematogenous spread are the 3 main mechanisms by which bacteria reaches the lungs
- **Primary inhalation**: when organisms bypass normal respiratory defense mechanisms or when the Pt inhales organisms that colonize the upper respiratory tract or respiratory support equipment

Pathogenesis

- **Aspiration**: occurs when the Pt aspirates colonized upper respiratory tract secretions
  - Stomach: reservoir of GNR that can ascend, colonizing the respiratory tract.
- **Hematogenous**: originate from a distant source and reach the lungs via the blood stream.

Pathogenesis

- Microaspiration from nasopharynx: *S. Pneumonia*
- Inhalation: TB, viruses, *Legionella*
- Aspiration: anaerobes
- Bloodborne: Staph endocarditis, septic emboli
- Direct extension: trauma

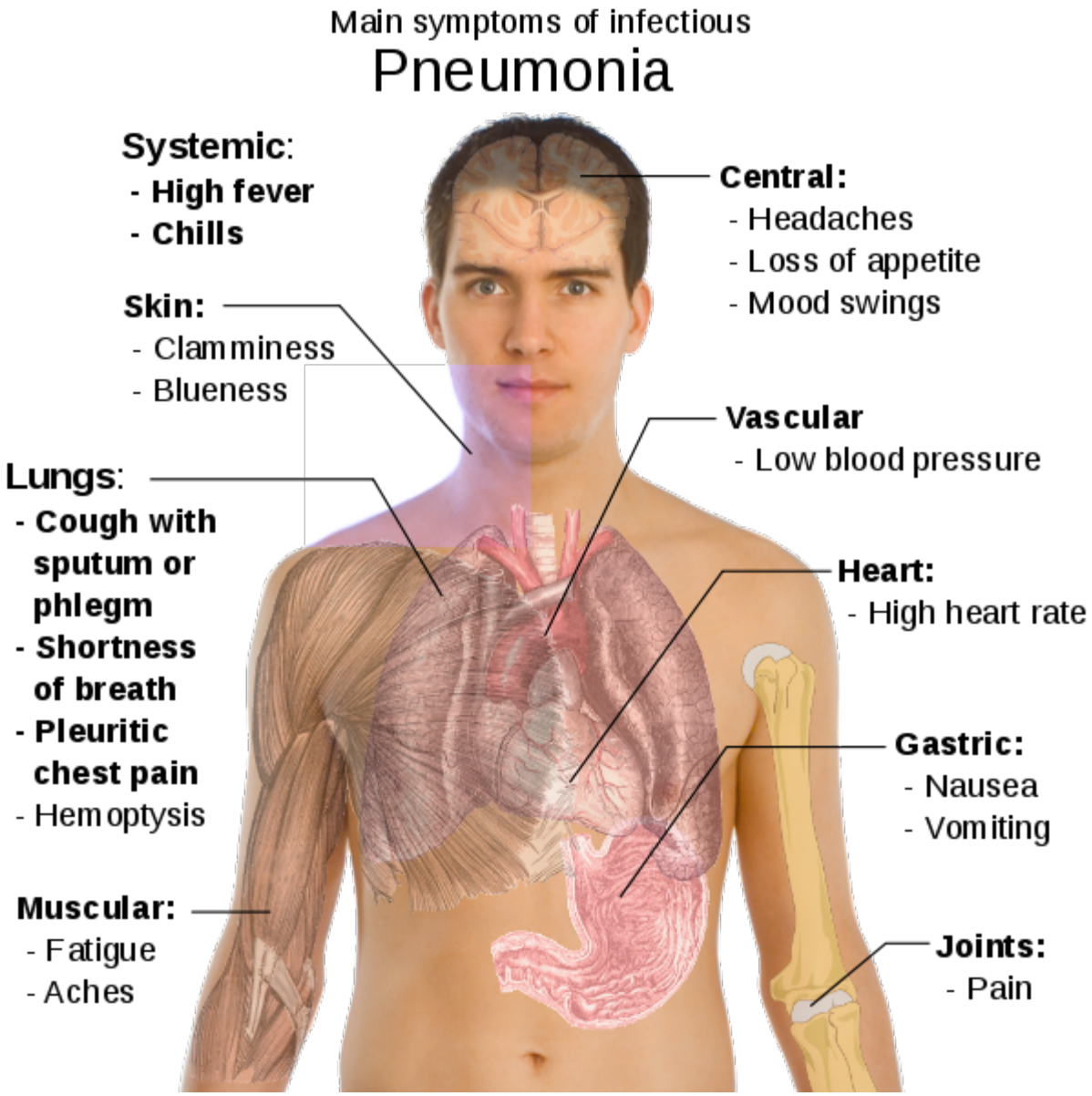
Pathogens

- CAP usually caused by a single organism
- Even with extensive diagnostic testing, most investigators cannot identify a specific etiology for CAP in ≥ 50% of patients.
- Caused by a variety of Bacteria, Viruses, Fungi
- *Streptococcus pneumoniae* is the most common pathogen 60-70% of the time

Pathogenic Organisms

Outpatient	*Strep pneumo* *Mycoplasma / Chlamydophila* *H. influenzae* Respiratory viruses
Inpatient, non-ICU	*Strep pneumo* *Mycoplasma / Chlamydophila* *H. influenzae* *Legionella* Respiratory viruses
ICU	*Strep pneumo* *Staph aureus*, *Legionella* Gram neg bacilli, *H. influenzae*

Don’t forget ABC and V/S including O_2 sats!



Clinical Signs	Positive LR	Negative LR
General appearance		
Cachexia	4.0	NS
Abnormal mental status	2.2	NS
Vital signs		
Temp >37.9 C	2.2	0.7
RR > 28/min	2.2	0.8
HR >100 bpm	1.6	0.7
Lung findings		
Percussion dullness	3.0	NS
Reduced breath sounds	2.3	0.8
Bronchial breath sounds	3.3	NS
Aegophony	4.1	NS
Crackles	2.0	0.8
Wheezes	NS	NS

NS= not significant. LR= Likelihood Ratio

From McGee S, *Evidence-based physical diagnosis*, 2nd edition. St Louis: Saunders, 2007.

Triaging Patients with Pneumonia

- Febrile respiratory illness (FRI) should be placed on droplet and contact precautions (Single room, use mask, gown and gloves)
- Upgrade to Airborne Infection Isolation (AII)- Negative pressure room with HEPA-Filter, with use of fit-tested respirator (e.g. N-95), in addition to contact precautions for:
  - Sick patients anticipating intubation
  - Aerosolizing procedures e.g. suctioning, nebulization

Investigations

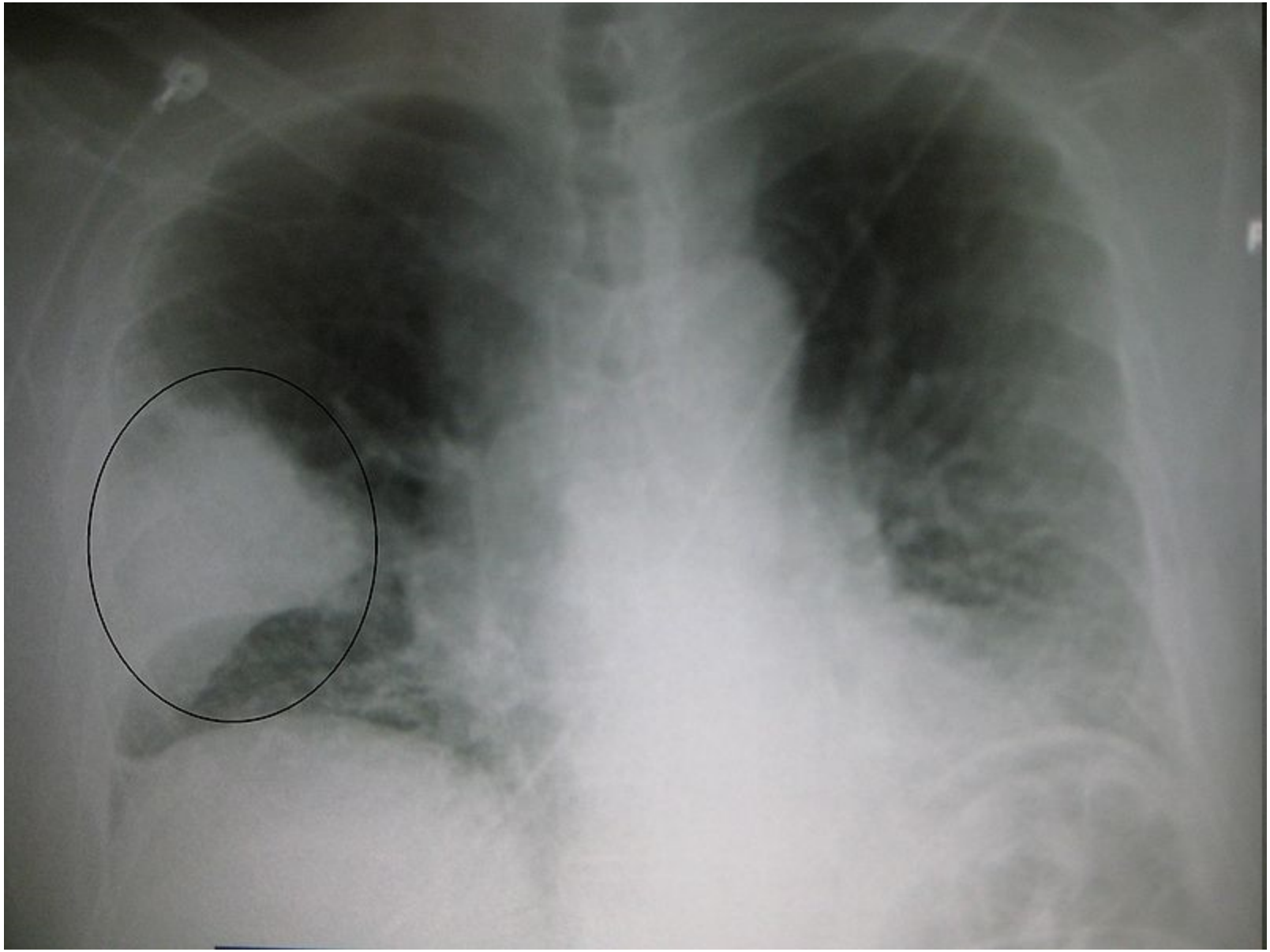
- **<u>CXR</u>**
- **CBC with diff**
- **Sputum gram stain, culture susceptibility**
- **Blood Culture**
- **NPA MERS-CoV, Influenza PCR**
- **ABG**
- **Urea / Electrolytes**
- Influenza rapid Ag test
- Respiratory viruses multiplex PCR
- Sputum AFB and TB culture
- Sputum fungal culture
- Special stain, eg. Silver stain, India Ink
- LFT
- CT chest
- Pleural fluid analysis
- Bronchoscopy
- Urine *Legionella* Ag
- Serology, eg Q fever

Clinical Diagnosis: CXR

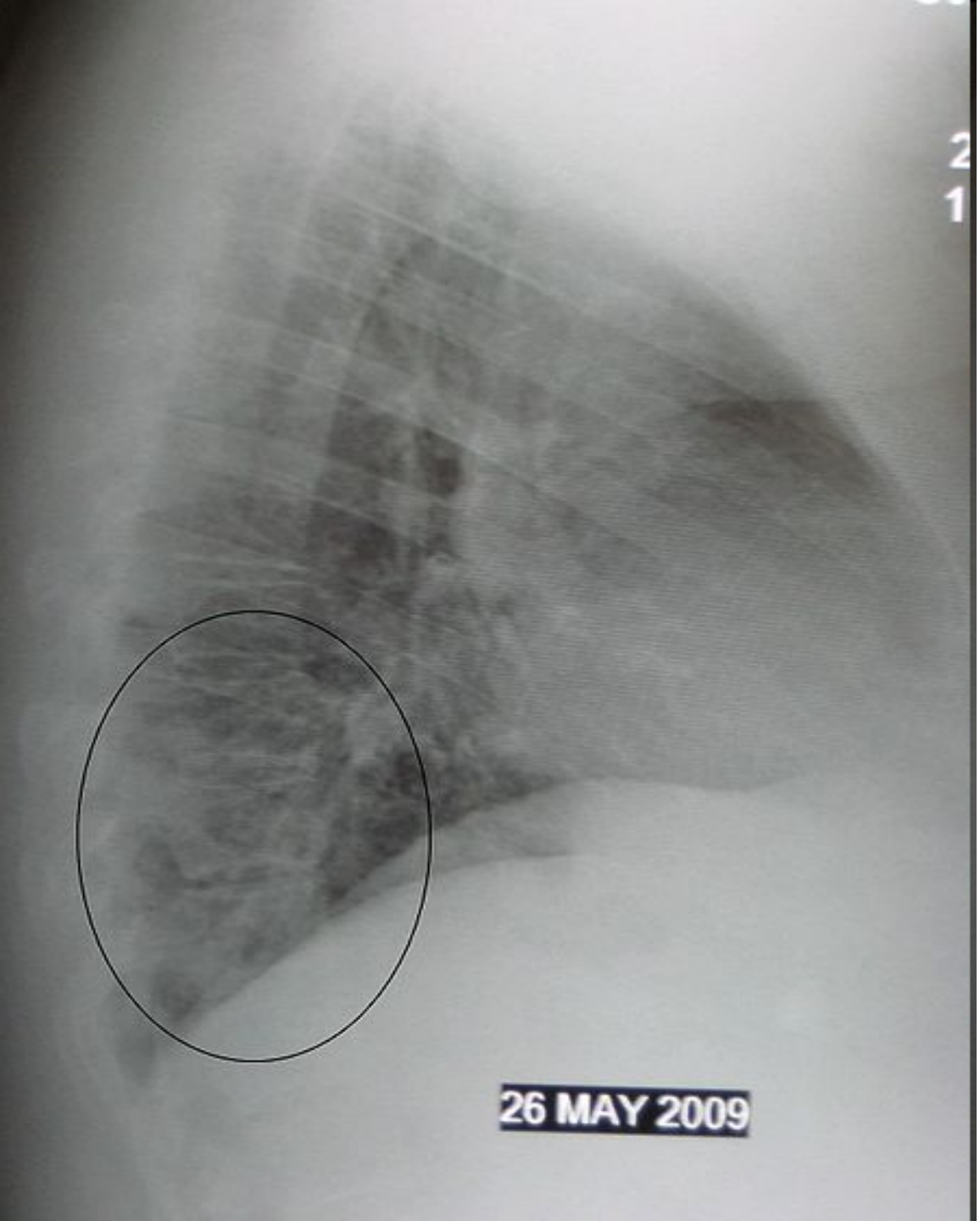
- Demonstrable infiltrate by CXR or other imaging technique
  - Establish Dx and presence of complications (pleural effusion, multilobar disease)
  - May not be possible in some outpatient settings
  - CXR: classically thought of as the gold standard

Infiltrate Patterns

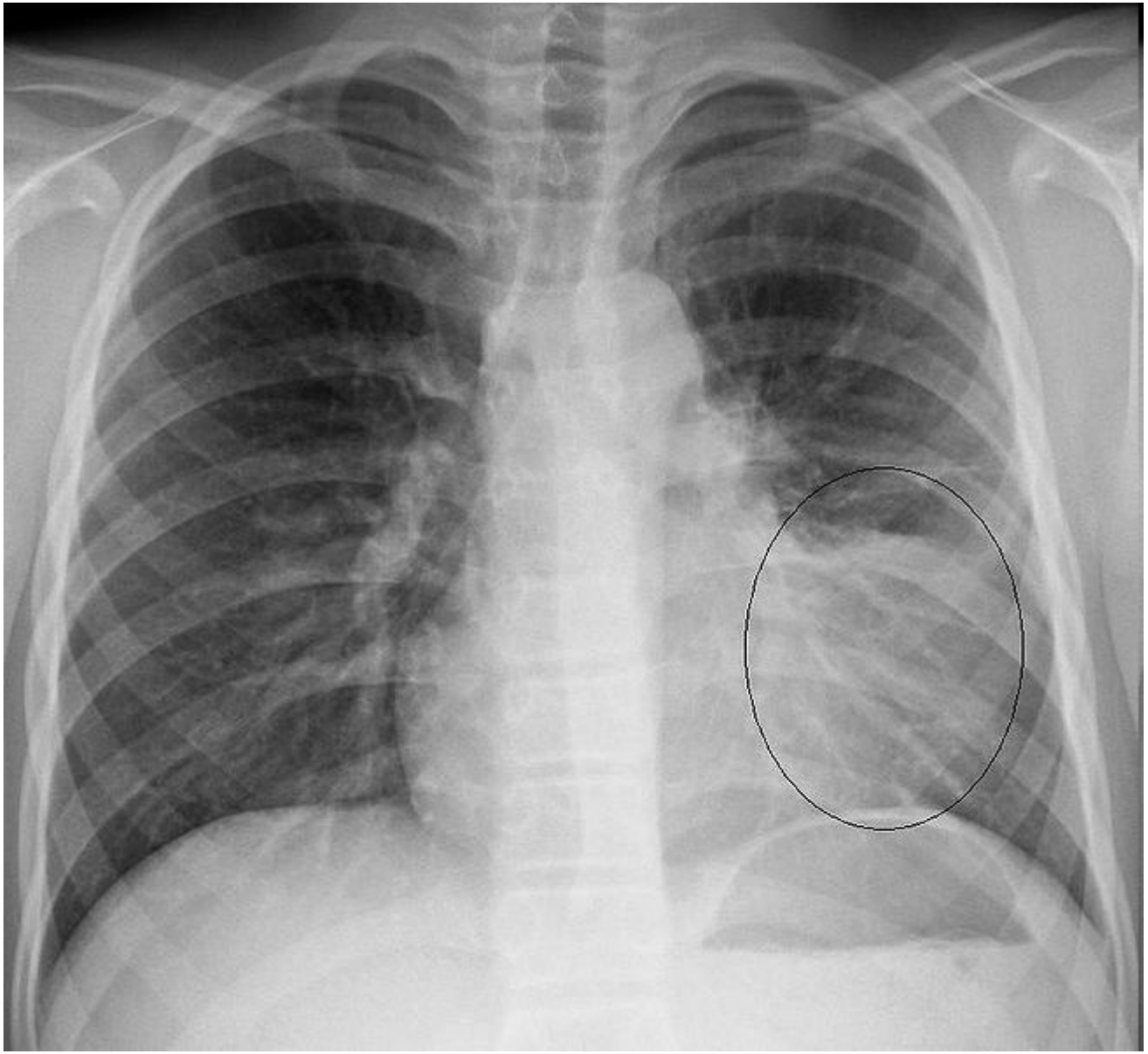
Pattern	Possible Diagnosis
Lobar	S. pneumo, Kleb, H. flu, GN
Patchy	Atypicals, viral, Legionella
Interstitial	Viral, PCP, Legionella
Cavitary	Anaerobes, Kleb, TB, S. aureus, fungi
Large effusion	Staph, anaerobes, Kleb



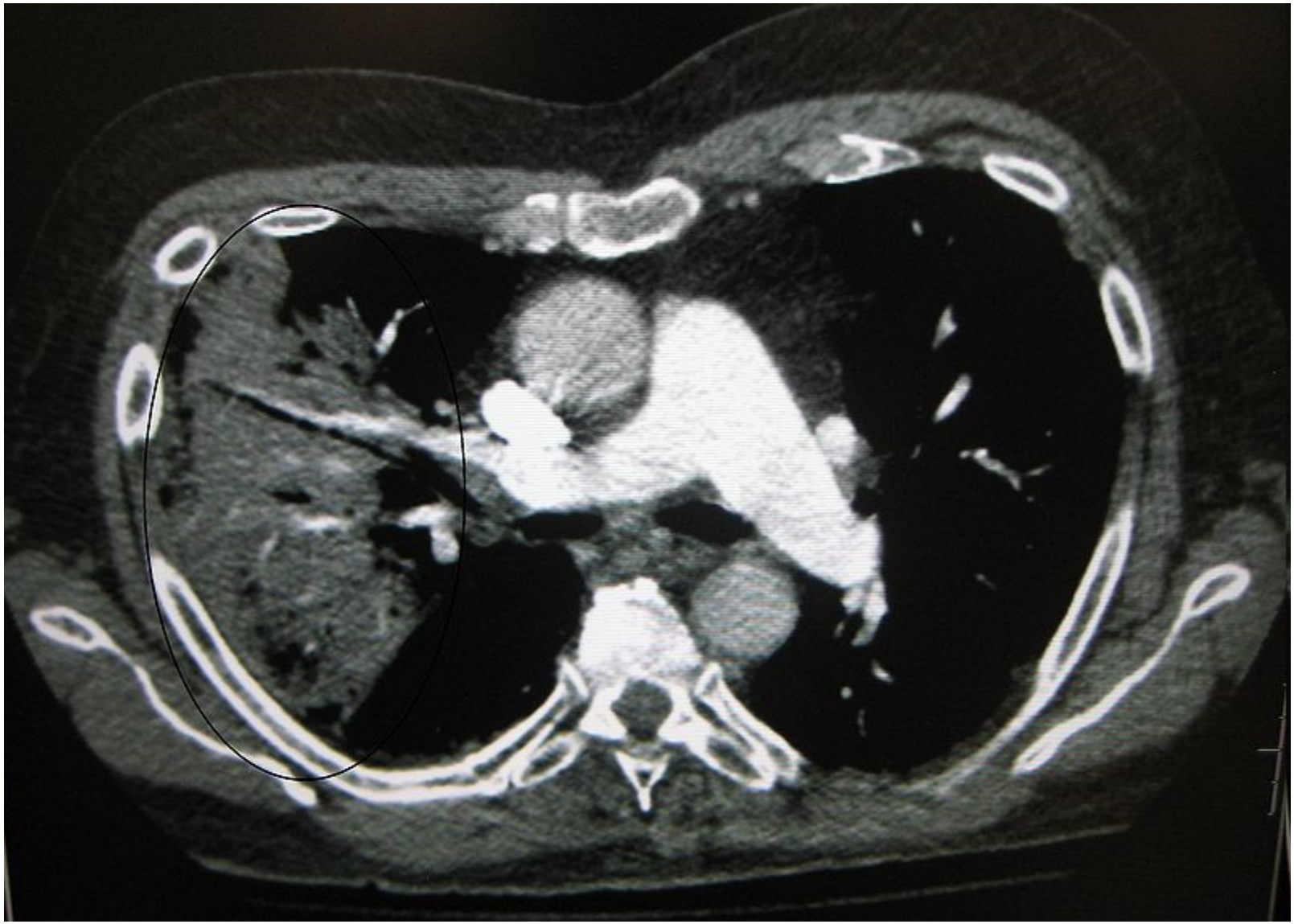
A chest X-ray showing a very prominent wedge shaped pneumonia in the right lung



Lat CXR: RLL pneumonia



PA CXR: pneumonia of the lingula



Empiric outpt Management in Previously Healthy Pt

- Organisms: *S. pneumoniae, Mycoplasma pneumoniae*, viral, *Chlamydophila pneumoniae, H.influenzae*
- Recommended abx:
  - Advanced generation macrolide (azithromycin or clarithromycin); or doxycycline
- If abx within past 3 months:
  - Respiratory quinolone (moxifloxacin, levofloxacin), OR
  - Advanced macrolide + amoxicillin, OR
  - Advanced macrolide + amoxicillin-clavulanate

IDSA/ATS Guidelines 2007

Empiric outpt Management in Pt with comorbidities

- Comorbidities: cardiopulmonary dz or immunocompromised state
- Organisms: *S. pneumoniae*, viral, *H. ifluenzae*, aerobic GN rods, *S.aureus*
- Recommended Abx:
  - Respiratory quinolone, OR advanced macrolide
- Recent Abx:
  - Respiratory quinolone OR
  - Advanced macrolide + beta-lactam

IDSA/ATS Guidelines 2007

Empiric Inpt Management-Medical Ward

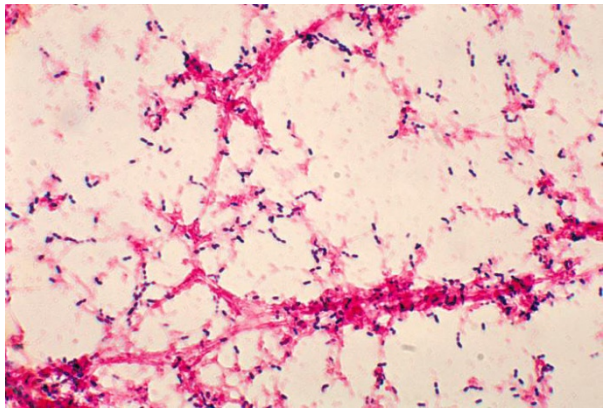
- Organisms: all of the above plus polymicrobial infections (+/- anaerobes), Legionella
- Recommended Parenteral Abx:
  - Respiratory fluoroquinolone, OR
  - Advanced macrolide plus a beta-lactam
- Recent Abx:
  - As above. Regimen selected will depend on nature of recent antibiotic therapy.

IDSA/ATS Guidelines 2007

Complications of Pneumonia

- Bacteremia
- Respiratory and circulatory failure
- Pleural effusion (Parapneumonic effusion), empyema, and abscess
  - Pleural fluid always needs analysis in setting of pneumonia (do a thoracocentisis)
  - Always needs drainage: Chest tube, surgical

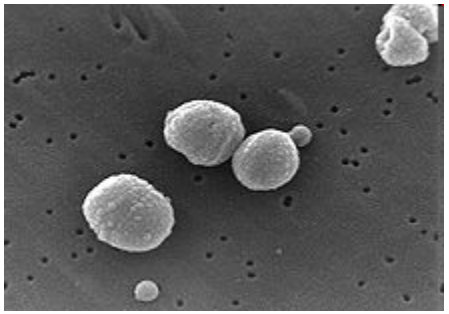
Streptococcus pneumonia



- Most common cause of CAP
- Gram positive diplococci
- “Typical” symptoms (e.g. malaise, shaking chills, fever, rusty sputum, pleuritic chest pain, cough)
- Lobar infiltrate on CXR
- 25% bacteremic

Risk factors for *S.pneumonia*

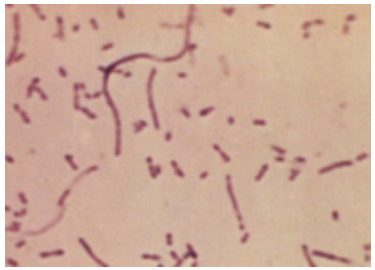
- **Splenectomy** (Asplenia)
- Sickle cell disease, hematologic diseases
- Smoking
- Bronchial Asthma and COPD
- HIV
- ETOH



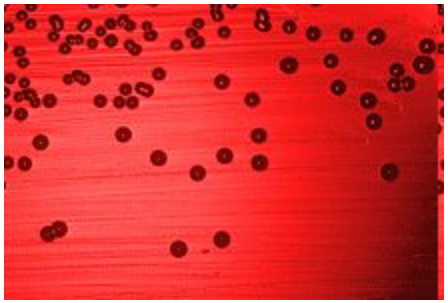
S. Pneumonia Prevention

- **Pneumococcal conjugate vaccine (PCV)** is a vaccine used to protect infants and young children
  - 13 serotypes of *Streptococcus*
- **Pneumococcal polysaccharide vaccine** (PPSV)
  - 23 serotypes of *Streptococcus*
- For both children and adults in special risk categories:
  - Serious pulmonary problems, eg. Asthma, COPD
  - Serious cardiac conditions, eg., CHF
  - Severe Renal problems
  - Long term liver disease
  - DM requiring medication
  - Immunosuppression due to disease (e.g. HIV or SLE) or treatment (e.g. chemotherapy or radio therapy, long-term steroid use
  - Asplenia

Haemophilus influenzae



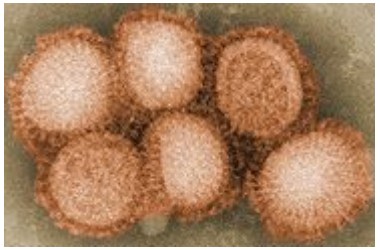
- Nonmotile, Gram negative rod
- Secondary infection on top of Viral disease, immunosuppression, splecnectomy patients
- Encapsulated type b (Hib)
  - The capsule allows them to resist phagocytosis and complement-mediated lysis in the nonimmune host
- Hib conjugate vaccine



Specific Treatment

- Guided by susceptibility testing when available
- *S. pneumonia:*
  - β-lactams Cephalosporins, eg Ceftriaxone, Penicillin G
  - Macrolides eg.Azithromycin
  - Fluoroquinolone (FQ) eg.levofloxacin
  - Highly Penicillin Resistant: Vancomycin
- *H. influenzae:*
  - Ceftriaxone, Amoxocillin/Clavulinic Acid (Augmentin), FQ, TMP-SMX

CAP: Influenza

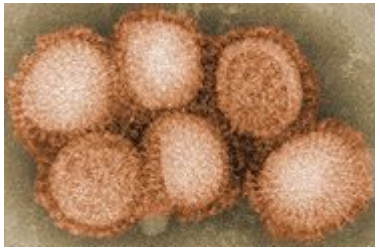


- More common cause in children
  - RSV, influenza, parainfluenza
- Influenza most important viral cause in adults, especially during winter months
- Preventable with annual vaccination

- Inhale small aerosolized particles from coughing, sneezing→1-4 day incubation→ 'uncomplicated influenza' (**fever, myalgia, malaise, rhinitis**)→Pneumonia

- Adults ≥ 65 account for 63% of annual influenza-associated hospitalizations and 85% of influenza-related deaths

CAP: Influenza



- First worlwide pandemic of H1N1 Influenza A (2009-2010)
- Ongoing epidemic in Saudi Arabia
- H1N1 risk factors
  - **pregnant, obesity, cardipulmonary disease, chronic renal disease, chronic liver disease**
- CXR findings often subtle, to full blown ARDS
- Respiratory (or Droplet) isolation for suspected or documented influenza (Wear mask and gloves)
- NP swab for, Rapid Ag test Influ A,B. H1N1 PCR RNA
- Current Seasonal Influenza Vaccine prevents disease (given every season**)**
- Bacterial pnemonia *(S. pneumo, S. aureus)* may follow viral pneumonia

Influenza: Therapy

Neuraminidase inhibitors	**Oseltamivir / Tamiflu**	75mg po bid	**Influenza A, B**
	Zanamivir / Relenza	10mg (2 inhalations) BID	
Adamantanes	**Amantadine / Symmetrel**	100mg po bid	**Influenza A**
	Rimantadine / Flumadine	100mg po qd	

- H1N1 resistant to Adamantanes
- Neuraminidase inhibitors:
  - 70-90% effective for prophylaxis
  - Give within 48h of symptom onset to reduce duration/severity of illness, and viral shedding
  - Osteltamivir dose in severe disease 150mg bid

CAP: MERS-CoV

- New novel Corona Virus first described in September 2012 in Saudi Arabia
- Titled Middle East Respiratory Syndrome Corona Virus (MERS-CoV)
- Causes severe disease, with high mortality rate reaching 40%
- Clinically indistinguishable from any other FRI
- 1643 laboratory-confirmed cases with 702 deaths (in KSA alone)
- Mostly related to hospital outbreaks
  - Early recognition and immediate placement on airborne and contact isolation vital in controlling spread of disease
- Camels well established as reservoirs of virus

CAP: Atypicals

- *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae, Legionella; Coxiella burnetii* (Q fever)*, Francisella tularensis* (tularemia)*, Chlamydia psittaci* (psittacosis)
- Approximately 15% of all CAP
- 'Atypical': not detectable on gram stain; won't grow on standard media
- Unlike bacterial CAP, often extrapulmonary manifestations:
  - Mycoplasma: otitis, nonexudative pharyngitis, watery diarrhea, erythema multiforme, increased cold agglutinin titre
  - Chlamydophila: laryngitis
- Most don't have a bacterial cell wall→ Don't respond to β-lactams
- Therapy: macrolides, tetracyclines, quinolones (intracellular penetration, interfere with bacterial protein synthesis)

Q fever

- *Coxiella burnetti*
- Exposure to farm animals or parturient cats
- Epidemic in Middle east, recent large outbreaks in Iraq, and Occupied territories (Israel)
- Acute Pneumonia, severe headache, hepatitis
- Diagnosis: complement fixation, new NAAT
- Chronic: endocarditis, FUO, granuloma in liver
- Treatment: Doxycycline, Rifampin, hydroxychloroquine

Psittacosis

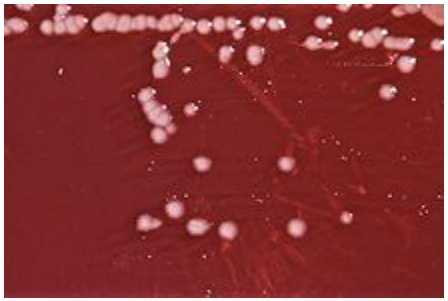
- *Chlamydophila psittaci*
- Exposure to birds
- Bird owners, pet shop employees, vets
- 1st: Tetracycline
- Alt: Macrolide

Tularemia

- *Francisella tularensis*
- Rabbits, squirrels, rodents
- Landscapers, Hunters
- Treat: streptomycin

Who is at risk for Pseudomonal Pneumonia?

- Immunocompromised pts (HIV, solid organ or bone marrow transplant, neutropenic, chronic oral steroids)
- Alcoholics
- Frequent prior antibiotic use
- Recent hospital admission
- **Structural lung abnormalities**
  - Cystic fibrosis, bronchiectasis, *severe* COPD
  - Prophylaxis with tobramycin nebs
- Rare in previously healthy pts



**Gram stain/sputum culture (if good quality) is usually adequate to exclude need for empiric coverage

*** Treatment: **Ceftazidime**, cefepime, pip/tazo, amikacin, tobramycin, aztreonam, ciprofloxacin, carbapenems, Polymixin B

Who is at risk for *Acinetobacter* Pneumonia?

- **CAP**
  - Alcoholics
  - Smoking
  - Chronic lung disease
  - DM
  - Residence in tropical developing country
- **HAP**
  - **Admission to burns unit or ICU**
  - **Mechanical ventilation**
  - Length of hospital stay
  - Surgey
  - Wounds
  - Previous infection (independent of previous Abx use)
  - Fecal colonization with *Acinetobacter*
  - Treatment with broad spectrum antibiotics
  - Indwelling central intravenous or urinary catheters
  - Parenteral nutrition
- Treatment: Polymixin B (colistin), tigecycline

Who is at risk for which pathogens?

- Pnemonia in nursing home/long term care facility residents similar to pneumonia in hospitalized pts:
  - *Pseudomonas*, *Acinetobacter,* MRSA
- Chronic hemodialysis:
  - Increased risk of MRSA (not *Pseudomonas* or *Acinetobacter*)
- COPD:
  - Increased risk for *Pseudomonas* (not MRSA)

Remember these associations:

- **Asplenia:** *Strep pneumo, H. influ.*
- **Alcoholism**: *Strep pneumo*, oral anaerobes, *K. pneumo., Acinetobacter*, MTB
- **COPD/smoking***: H. influenzae, Pseudomonas, Legionella, Strep pneumo, Moraxella catarrhalis, Chlamydophila pneumoniae*
- **Aspiration**: *Klebsiella, E. Coli*, oral anaerobes
- **HIV**: *S. pneumo, H. influ, P. aeruginosa,* MTB, PCP*, Crypto, Histo, Aspergillus*, atypical mycobacteria
- **Recent hotel, cruise ship**: *Legionella*
- **Structural lung disease (bronchiectasis**): *Pseudomonas aerogenosa, Burkholderia cepacia, Staph. aureus*

Pneumonia: Outpatient or Inpatient?

- **CURB-65**
  - 5 indicators of increased mortality: confusion, BUN >7, RR >30, SBP <90 or DBP <60, age $\geq$65
  - Mortality: 2 factors→9%, 3 factors→15%, 5 factors→57%
  - Score 0-1→outpt. Score 2→inpt. Score $\geq$3→ICU.
- **Pneumonia Severity Index (PSI)**
  - 20 variables including underlying diseases; stratifies pts into 5 classes based on mortality risk
- No RCTs comparing CURB-65 and PSI

Pneumonia: Medical floor or ICU?

- 1 major or 3 minor criteria= severe CAP→ICU
- **Major criteria:**
  - Invasive ventilation, septic shock on pressors
- **Minor criteria:**
  - RR>30; multilobar infiltrates; confusion; BUN >20; WBC <4,000; Platelets <100,000; Temp <36, hypotension requiring aggressive fluids, PaO2/FiO2 <250.
- No prospective validation of these criteria

CAP Inpatient therapy

- **General medical floor:**
  - Respiratory quinolone OR
  - IV β-lactam PLUS macrolide (IV or PO)
    - β-lactams: cefotaxime, ceftriaxone, ampicillin; ertapenem
    - May substitute doxycycline for macrolide
- **ICU:**
  - β-lactam (ceftriaxone, cefotaxime, Amox-clav) **PLUS EITHER** quinolone **OR** azithro
  - PCN-allergic: respiratory quinolone **PLUS** aztreonam
- **Pseudomonal coverage** :
  - Antipneumococcal, antipseudomonal β-lactam (pip-tazo, cefepime, imip, mero) **PLUS EITHER** (cipro or levo) **OR** (aminoglycoside AND Azithro) **OR** (aminoglycoside AND respiratory quinolone)
- CA-MRSA coverage: Vancomycin or Linezolid

CAP Inpatient Therapy: Pearls

- Give 1st dose Antibiotics in ER (no specified time frame)
- Switch from IV to oral when pts are hemodynamically stable and clinically improving
- Discharge from hospital:
  - As soon as clinically stable, off oxygen therapy, no active medical problems
- Duration of therapy is usually 10-14 days:
  - Treat for a minimum of 5 days
  - Before stopping therapy: afebrile for 48-72 hours, hemodynamically stable, RR <24, O2 sat >90%, normal mental status
  - Treat longer if initial therapy wasn't active against identified pathogen; or if complications (lung abscess, empyema)

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