Acute Pneumonia

DR FARZIN KHORVASH

PROFESSOR OF INFECTIOUS DISEASE DEPARTMENT

- **Pneumonia is the most common cause of infection-related death.**

- **Predominant pathogens of communityacquired pneumonia (CAP) in adults include Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, and Chlamydia pneumoniae.**

- **Legionella species, Staphylococcus aureus, and enteric gram-negative bacilli are less frequent causes that can produce more severe disease.**

- **Predominant pathogens of patients recently hospitalized or nursing home residents include S. aureus, aerobic gram-negative rods, including Pseudomonas aeruginosa, and mixed aerobic/anaerobic organisms.**

Diagnosis

- **CLINICAL EVALUATION**

History:

- **The history should attempt to define (1) symptoms consistent with the diagnosis of pneumonia, (2) the clinical setting in which the pneumonia takes place, (3) defects in host defense that could predispose to the development of pneumonia, and (4) possible exposures to specific pathogens.**

- **Respiratory symptoms are commonly encountered in primary care practices but are usually not associated with pneumonia.**

- **Therefore, a serious effort should be made to differentiate pneumonia from other clinical entities with which it may be confused.**

- **The predominant clinical findings of pneumonia related to the respiratory tract should be sought, including cough, sputum production, dyspnea, chest pain, and fever.**

- **It should also be recognized that nonrespiratory symptoms are commonly present, including fatigue, sweats, headache, nausea, and myalgia, and occasionally abdominal pain and diarrhea.**

- **With increasing age, both respiratory and nonrespiratory symptoms of pneumonia become less frequent.**

- **Unfortunately, symptoms at presentation elucidated by a careful history may not always be able to distinguish pneumonia from other respiratory problems.**

- **Specific etiologic agents** of pneumonia have been associated with **certain underlying diseases** and patient populations.
- Pneumonia due to *M. pneumoniae occurs more often in younger people*
- Gram-negative bacterial pneumonia tends to occur in older adults, especially those who are debilitated with comorbid diseases or are ill enough to require management in an intensive care unit (ICU).

- **Staphylococcal pneumonia** classically has been noted during epidemics **of influenza**.
- Pneumonia has been noted to occur with increased frequency in patients with a variety of **underlying disorders** such as congestive heart failure, diabetes, alcoholism, and COPD.
- in one series of 292 patients with pneumonia, only 18% were found to have no underlying disease.

- **Certain lifestyle factors have also been associated with an increased risk for pneumonia. These include cigarette smoking; alcohol use, especially in males; contact with children and pets; and living in a household with more than 10 people.**

- **Special note needs to be made of the relationship between pneumonia and patients with COPD. Although well-controlled studies are lacking, it does appear that patients with COPD have an increased incidence of pneumonia.**
- **Cystic fibrosis**
- **HIV**

- **Recently, it has been recognized that patients with outpatient contact with the health care system develop pneumonia with etiologic agents that may be seen in both CAP and nosocomial pneumonia.**
- **Important aspects of a patient's history that may suggest specific potential infectious agents include occupational, animal, and travel history**

- **Exposure to contaminated aerosols (e.g., air coolers, hospital water supply) : Legionnaires' disease**

- **Exposure to goat hair, raw wool, animal hides Anthrax**

- **ingestion of unpasteurized milk Brucellosis**

- **Exposure to water contaminated with animal Urine Leptospirosis**

- **Exposure to birds (parrots, budgerigars, cockatoos, pigeons, turkeys) Psittacosis**

Physical Examination

- **Most, but not all, patients with pneumonia look ill, sometimes acutely.**

- **They may be breathing with accessory muscles. Elderly patients may appear apathetic.**

- **Fever is reported to be present in 65% to 90% of patients with pneumonia.**

- **Fever patterns per se, however, are not useful for establishing a specific diagnosis.**

- **Oral temperature** assessment should **be avoided** to reduce error caused by rapid mouth breathing.

- **The pulse usually increases by 10 beats/min for every degree (centigrade) of temperature elevation. A pulse-temperature deficit (e.g., a relative bradycardia for the amount of fever) should suggest viral infection, mycoplasmal infection, chlamydial infection, tularemia, or infection with *Legionella*.**

- Cutaneous abscesses or "track marks" from **injection drug** use may signal a source of bacteremia with subsequent pneumonia via **hematogenous spread**.
- **Bullous myringitis** is an infrequent but significant finding in mycoplasmal pneumonia.
- The presence of **poor dentition** should suggest a mixed infection due to aspiration of anaerobes and aerobes that colonize the oropharynx. Although edentulous patients may develop anaerobic pneumonia as a result of aspiration, it is uncommon.

- **Early in the disease process, definite signs of pulmonary involvement may be lacking or may be manifest only as fine rales.**

- **Chest examination may reveal these early signs of pneumonia even though the chest radiograph is normal.**

- **Evidence of consolidation (dullness on percussion, bronchial breath sounds, and E to A changes) is highly suggestive of bacterial infection but may be absent in two thirds of patients ill enough to be hospitalized and may be absent more often in patients treated as outpatients.**
- **Patients with mycoplasmal or viral infection may exhibit few abnormalities on physical examination despite the presence of impressive infiltrates on the chest radiograph.**

- The overall **usefulness of the history and physical examination** to detect the presence of pneumonia has been questioned.
- The probability of detecting pneumonia varies with the patient population, the prevalence of pneumonia in that population, the threshold values for defining a vital sign as abnormal, and the ability of the clinician to detect abnormal physical findings.

- **Rare findings such as egophony and asymmetrical chest movements have a high predictive value for pneumonia but occur so infrequently that they are of limited utility.**

Diagnostic Testing

- **Clinical features derived from a careful history and physical examination, and confirmed by radiographic imaging of the chest that shows a pulmonary infiltrate, suggest the presence of pneumonia.**

- **The role of microbiologic tests to identify the specific cause is an important, although controversial, element of care.**

- **Studies comparing empirical therapy with laboratoryguided pathogeFn-directed care have shown no differences in efficacy, although increased side effects were noted in the patients receiving empirical therapy**

- **Efforts to determine the specific cause of CAP are justified by the fact that they (1) may enable the clinician to narrow the antibiotic spectrum by using fewer agents, thereby decreasing exposure of the patient to potential side effects and potentially reducing the development of resistance; (2) may aid in the specific antibiotic choice for an individual patient depending on the specific epidemiology f infection and the specific resistance patterns of the locale; and (3) may identify pathogens not usually suspected and therefore not usually covered by empirical therapy.**

- **The combined use of the standard microbiologic testing in conjunction with nucleic amplification assays can now define the etiology of CAP in up to 89% of cases.**

Sputum Examination and Examination

of Other Respiratory Tract Samples

- **Microscopic examination and culture** of expectorated sputum remain the mainstays of the laboratory evaluation of pneumonia despite ongoing controversy concerning their sensitivity and specificity.

- Of patients admitted to the hospital with CAP, 40% to 60% will not be able to produce sputum. Of those that do, between 40% to 60% of samples may be judged to be inadequate for further study because of **oropharyngeal contamination.**

- **Many patients have received antibiotics before the studies are carried out, which drastically reduces the diagnostic yield.**

- **A variety of organisms cannot be detected by Gram stain, including *Legionella spp., Mycoplasma spp., and Chlamydia spp.***

- **However, in patients who produce sputum of adequate quality to be examined (minimal or no oropharyngeal contamination), and who have not received prior antibiotics, diagnostic yields of 80% for sputum Gram stain have been reported in the small fraction of patients with bacteremic *S. pneumoniae pneumonia.***

- Despite its pitfalls, the sputum Gram stain is noninvasive, can be performed no risk to the patient, and under the right circumstances may aid in the diagnosis and choice of empirical therapy in patients with CAP.
- **Examination of the sputum** should include observation of the color, amount, consistency, and odor of the specimen.

- **The morphologic and staining characteristics of any bacteria seen should be recorded and an estimate made of the predominant organisms When no bacterial predominance exists, this should be noted as well.**

- **In the appropriate clinical setting, a predominance of gram-positive, lancet-shaped diplococci should suggest pneumococcal infection.**

- **Because pneumococci may be part of the nasopharyngeal microbiota in 10% to 50% of healthy adults and often colonize the lower airways in patients with chronic bronchitis, identification of the organism does not mean that it is the cause of disease. However, it is our experience that the large number of pneumococci necessary to produce a positive Gram stain is unusual in carriers.**

- **Microscopic sputum examination can be helpful to identify organisms other than pneumococci.**
- **The finding of small gram-negative coccobacillary organisms on sputum Gram stain is characteristic of *H. influenzae***
- **However, the sensitivity of the sputum Gram stain for detecting *H. influenzae is usually less than that for S. pneumoniae***

- **Staphylococci appear as gram-positive cocci in tetrads and grapelike clusters**
- **Organisms of mixed morphology are characteristic of anaerobic infection.**

- **Sputum culture** as a means of diagnosing pneumonia is as controversial as the sputum Gram stain.

- Both *S. pneumoniae and H. influenzae are relatively fastidious and the* sensitivity of cultures decreases with the prior use of antibiotics or with delays in transport of specimens to the clinical microbiology laboratory.

- A lack of correlation between findings from sputum culture and findings from blood cultures and serologic studies has been observed.

- **When culture of sputum is delayed, the isolation of pneumococci is less likely because of overgrowth by oropharyngeal microbiota. Rapid processing of samples is therefore another important factor leading to higher diagnostic yield.**

- **Antigen detection in respiratory secretions**

- *S. pneumoniae, Pneumocystis, Legionella pneumophila, and a variety of respiratory viruses.*

- **Detection of microbial nucleic acid in respiratory tract secretions, both nasopharyngeal and sputum, remains an area of ongoing study.**

Radiologic Examination

- **Chest radiography plays a critical role in the diagnosis of pneumonia, and for many it represents the gold standard of making a clinical diagnosis.**

- **Because overuse of antibiotics for therapy for upper respiratory tract infections has been documented and may contribute to the growing problem of antibiotic resistance, identifying patients who really should be receiving antibiotic therapy is clearly of importance.**

THERAPY

- **The first decision confronting the clinician is whether the patient presenting with respiratory symptoms in fact has pneumonia**

- **The next decisions are whether the patient is to be hospitalized and if so whether the patient needs admission to an ICU, both of which have consequences as to the level of treatment, the cost of care, and associated iatrogenesis.**

- **PORT score**, also known as the pneumonia severity index **(PSI).**
- **This system uses 20 clinical parameters in categories of age, presence of comorbidities, vital sign abnormalities, and laboratory and radiologic findings.**
- **Based on a point system, five prognostic groups (I to V) were defined.**
- **As a guideline for hospitalization, patients in groups I and II are usually treated as outpatients, patients in group III are in a "borderline" group, and patients in groups IV and V are admitted to either a routine ward or ICU.**

- **A limitation of the PSI system is its relative complexity**
- **CURB score**
- **CURB-65**
- **CRB-65**
- **new onset of confusion, urea level greater than 7 mmol/L, respiratory rate greater than 30 breaths/min, and systolic blood pressure less than 90 mm Hg or a diastolic blood pressure less than 60 mm Hg.**
- **The presence of two or more criteria suggested an increased mortality and defined severe pneumonia.**

- **The CURB-65 score, which was developed later, added age older than 65 years to the system with the presence of more than three parameters leading to prediction of increased mortality, and the CRB-65 modified this index to eliminate inclusion of blood urea determination, making the index free of laboratory testing and allowing for patient assessment completely at the bedside.**

- **However, it is critical to recognize that any severity assessment index serves only as a guideline, not as an absolute.**
- **Clinical judgment** **regarding presence of other** **comorbid conditions****, hypoxia, stability of the home situation, ability to take** **oral medications****, reliability in taking medication, likelihood of returning for** **follow-up****, and likelihood of calling for help when needed all play a role in deciding whether a patient can be treated at home or in a hospital.**

- **In addition, the IDSA/ATS guideline has recommended major and minor criteria to define patients who should be directly admitted to an ICU:**

- **The major criteria are either septic shock requiring vasopressor support or acute respiratory failure requiring invasive mechanical ventilation.**

- **The presence of <u>three</u> of the following minor criteria also were indicative of the need for ICU care: increased respiratory rate greater than or equal <u>to 30 breaths/min</u>, low Pao2/fraction of inspired oxygen ratio (<u>≤250), multilobar</u> infiltrates, <u>confusion/disorientation</u>, uremia (blood urea nitrogen <u>level ≥20</u> mg/dL), leukopenia (white blood cell count <u><4000</u> cells/mm3), thrombocytopenia (platelet count <u><100,000</u> cells/mm3), hypothermia (core temperature <u><36</u>° C [96.8° F]), <u>and hypotension requiring aggressive fluid resuscitation.</u>**

Antimicrobial Therapy

- **for most patients, a specific diagnosis cannot be established with certainty prior to the onset of therapy and an antibiotic regimen must be selected empirically.**

- **Pharmacokinetics and pharmacodynamics are important in defining appropriate antibiotic dosing.**

- **β-Lactam compounds are timedependent killers**; when a penicillin, cephalosporin, or carbapenem is being used, the active drug levels need to be above the minimal inhibitory concentration (MIC) of the organism being treated for 40% to 50% of the dosing interval for an optimal outcome.
- Parenteral administration of **aminoglycosides leads to low concentration in bronchial fluids**

- The **empirical antimicrobial** regimen selected to treat acute pneumonia is dependent on the clinical situation.

- For a patient who does not require hospitalization and for whom no clear distinction between **typical** (e.g., pneumococcal) and **atypical** (mycoplasmal, chlamydial) pneumonia can be made, both types of organisms should be covered.

- Risks for the presence of drugresistant *S. pneumoniae should be assessed.*

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- ***Use of previous antibiotics,*** especially a β-lactam, macrolide, or fluoroquinolone in the prior 3 to 6 months,
- as well as residence in a long-term care facility are predictive of the presence of resistance to β-lactams, macrolides, and fluoroquinolones

- Where risk for drug-resistant *S. pneumoniae* infection is low, **oral β-lactam** agents (high-dose amoxicillin, amoxicillin-clavulanate, cefuroxime axetil), **azalides/macrolides** (azithromycin, clarithromycin, or erythromycin), or respiratory tract quinolones (levofloxacin, gemifloxacin, moxifloxacin) are all adequate choices.
- **Doxycycline and trimethoprim-sulfamethoxazole** may be used, but there is concern for an increasing incidence of **resistance** to both of these agents in strains of pneumococci.

- **Increased resistance to the azalide/macrolide agents *is also becoming a problem in S. pneumoniae, and therapeutic failures have been noted.***
- **For patients with an increased risk for poor outcome because of age or underlying disease, or when the risk for infection with resistant pneumococci exists owing to prior antibiotic use, the respiratory tract quinolones are the agents most likely to be effective. They currently are active against more than 99% of strains of *S. pneumoniae, including* penicillin-resistant strains, and they have the added benefit of activity against atypical agents.**

- **Although increasing resistance is a potential problem with an increased use of quinolones, it has not yet emerged as a significant problem. A β-lactam plus a macrolide is a comparable regimen.**

- **Regardless of the initial choice of antibiotic, once an organism is isolated, coverage should be narrowed down, if possible, on the basis of susceptibility test results.**
- **Patients who are ill enough to require hospitalization should be treated with parenteral agents that cover the likely pathogens.**

- **Our choice for most individuals would be a β-lactam (ceftriaxone or cefotaxime) plus azithromycin**

- **except in patients at high risk for cardiovascular disease when a respiratory fluoroquinolone seems preferable.**

- Although these regimens represent the basic course of therapy, specific clinical circumstances may warrant variation.

- For example, *S. aureus pneumonia including community-associated MRSA should be* considered during an influenza outbreak even though *S. pneumoniae* is still the major etiologic agent. Linezolid and vancomycin are the best-studied agents for treatment of MRSA pneumonia, and clindamycin has also appeared effective in children.

- **When gram-negative bacilli are suspected, infection with _P. aeruginosa should be a concern and_ therapy with an antipseudomonal β-lactam compound (e.g., cefepime, ceftazidime, piperacillin-tazobactam, imipenem, or meropenem) is a reasonable choice.**

- **Outpatient**

Previously Healthy

- **No recent antibiotic therapy: Macrolidea or doxycycline (100 mg 2 times/day)**

- **Recent antibiotic therapy: A respiratory fluoroquinolonec alone, an advanced macrolided plus oral β-lactam**

Comorbidities (COPD, Diabetes, Renal Failure or Congestive Heart Failure, or Malignancy)

- **No recent antibiotic therapy:** An advanced macrolide plus oral β-lactam or a respiratory fluoroquinolone

- **Recent antibiotic therapy:** A respiratory fluoroquinolone alone or an advanced macrolide plus a β-lactam

- **Suspected aspiration with infection:** Amoxicillin-clavulanate or clindamycin (600 mg IV q8h or 300 mg PO q6h)

- **Influenza with bacterial superinfection :** Vancomycin, linezolid, or other coverage for MRSA, including community-acquired MRSA

- **Inpatient**

Medical Ward

- **<u>No recent antibiotic therapy:</u> A respiratory fluoroquinolone alone or an advanced macrolide plus an intravenous β-lactamg**

- **<u>Recent antibiotic therapy :</u>An advanced macrolide plus an intravenous β-lactam, or a respiratory fluoroquinolone alone (regimen selected will depend on nature of recent antibiotic therapy)**

Intensive Care Unit (ICU)

- ***Pseudomonas infection is not a concern :*** *A β-lactamg plus either an advanced macrolide or a respiratory fluoroquinolone*

- ***Pseudomonas infection is not a concern but*** patient has a β-lactam allergy: A respiratory fluoroquinolone, with or without clindamycin

- ***Pseudomonas infection is a concern : (cystic*** fibrosis, impaired host defenses)Either (1) an antipseudomonal β-lactami plus ciprofloxacin (400 mg IV q8h or 750 mg PO q12h), or (2) an antipseudomonal agent plus an aminoglycosidej plus a respiratory fluoroquinolone or a macrolide

- ***Pseudomonas infection is a concern but the*** patient has a β-lactam allergy: Aztreonam (2 g IV q8h) plus aminoglycoside

Health Care–Associated Pneumonia

Either (1) an antipseudomonal β-lactam plus ciprofloxacin or levofloxacin or

(2) an antipseudomonal agent plus an

aminoglycoside plus a respiratory fluoroquinolone or

a macrolide plus vancomycin or linezolid (for MRSA coverage)