BACTERIAL PNEUMONIA

Pneumonia is a common medical problem. In the U.S., community-acquired pneumonia (CAP) is the sixth leading cause of death, and the number one cause of infectious death. It is estimated that two to four million cases occur each year, with 20% requiring hospitalization. The cost of pneumonia in direct patient care and lost wages is greater than $20 billion per year. Mortality rates vary 3-30%, with an overall mortality rate of 10%; more than 90% of these deaths occur among hospitalized patients. The elderly (>65) make up 80% of patients hospitalized for pneumonia, accounting for a disportionate number of pneumonia related deaths. Guidelines for the management of CAP have been published by the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA). These guidelines strive to streamline decision-making regarding patient care, including when to hospitalize, and to rationalize the use of antibiotics to minimize resistance and maximize effective treatment. Management suggestions that follow have been taken from these guidelines.

Pathogenesis:
Pneumonia develops from the inhalation of droplets small enough to reach the alveoli and aspiration of colonized secretions from the upper airways. Lung infections may also occur when there is direct inhalation of infectious agents, such as TB or influenza.

Pre-disposing factors:

Viral URI
COPD
institutionalization
mmunocompromise
dysphagia
cigarette smoking
debility
heart failure
age extremes
exposure to transmissible agents

Signs/Symptoms:
Typical S/S are cough, fever, productive sputum, pleuritic chest pain, usually developing over several days. PE may demonstrate tachypnea and signs of consolidation such as crackles.

Other S/S that may present: fatigue, headache, anorexia, nausea/vomiting, malaise, arthralgia, nasal flaring, hemoptysis, abdominal pain.

S/S vary widely. Symptoms are often blunted or absent in elderly in whom the presenting symptom is often confusion.

Diagnosis/Testing:
Diagnosis is usually made by clinical picture. Diagnostic tests to aid diagnosis include:

Chest x-ray: distinguish pneumonia from proximal respiratory tract processes, may aid in identifying those at risk for complications, serves as a baseline. CXR will often demonstrate an infiltrate, However, CXR may not demonstrate an abnormality in all patients, and is not is not useful in determining the causative agent. While CXR may be used to monitor progress, changes may initially worsen, and infiltrates may continue to be observed for an extended period after treatment and improvement of clinical status.

Sputum gram stain: Cost-effective test for aiding in determining empiric therapy. Reliable results depend on the quality of the specimen. Contamination with upper airway colonization is common. S. pneumoniae is the most frequent cause of CAP, however, other pathogens may be present, and a causative agent cannot be identified in up to 50% of cases.

Gram stain results suggesting a causative agent:
S. pneumoniae: gram positive diplococci
H. influenzae: pleomorphic gram negative coccobacilli
S. aureus: gram positive cocci in clumps
Klebsiella pneumoniae: gram negative encapsulated rods
E.coli: gram negative rods
Psuedomonaes aeruginosa: gram negative rods

Other agents such as Mycoplasma and Legionella will not show specific pathogens on gram stain. It is important for the provider to have knowledge of the common infectious agents in their communities.

Sputum culture and sensitivity: Provides a more useful tool for determining causative agents and effective treatment. Again, the quality of the specimen will affect results. In addition, the length of time involved in obtaining results, at least 48 hours, makes this test more appropriate for making decisions to change or augment empiric therapy.

CBC: Often shows leukocytosis with left shift. This finding is often absent in the elderly. Can also be used to monitor therapy.

Blood cultures: Not routinely ordered for outpatients, but can be useful for hospitalized patients. Relatively cost-effective, they can give information that predicts a more severe clinical course.

Other tests: In the hospitalized patient who has more severe and/or complicated disease the following tests may be considered:
Pulse oximetry/ABG
Thoracentesis
Bronchoscopy
Cytologic testing

Hospitalization:
The vast majority of CAP is treated successfully on an outpatient basis. Mildly ill patients who are treated early with appropriate empiric therapy generally show signs of improvement in 24-48 hours.

Patients considered for hospitalization include those who have chronic health problems, clinical evidence of severe infection, significant risk of complicated CAP, lack of response to outpatient therapy.

Risk factors for CAP death include:

Age >65	neoplastic disease	CAD/CHF
Neurologic disease	renal disease	liver disease
altered mental status	pulse >125	SBP<90mmHg
Temp <35C(95F) >40C(104F)	multilobar infiltrates	Sao2 <90%

identified high-risk pathogen (eg. S.aureus, gram negative)

Antibiotic Therapy:
Due to the difficulties that occur in attempting to identify a specific pathogen, antibiotic therapy is chosen empirically. ATS guidelines for empiric therapy were formulated for immunocompetent patients; it is necessary to consider a patient's clinical status and risk factors when determining appropriate empiric therapy.

<u>Younger, immunocompetent patients</u>: most common pathogens are S.pneumoniae, M.pneumoniae, C.pneumoniae, and respiratory viruses. The ATS recommends Erythromycin as a cost-effective treatment for most of the causative agents except H.influenzae. The newer macrolides, Azithromycin and Clarithromycin are active against this agent. While a more expensive treatment option, these drugs offer greater convenience with less frequent dosing and greater tolerability, which can significantly impact compliance. Azithromycin offers qd dosing for five days. Clarithromycin is generally used bid for 10-14 days. Erythromycin requires qid dosing for 10-14 days. Macrolides bind to the 50S subunit of bacterial ribosomes, blocking protein synthesis; dependent upon concentration they may be bactericidal or bacteriostatic, Tetracycline can be used as an alternative for patients allergic or intolerant to macrolides; response must be carefully monitored due to increasing resistance of S. pneumoniae to tetracycline.

The IDSA recommends macrolides, doxycycline and flouroquinolones for empiric therapy due to the activity each has against common pathogens and many atypical agents. Concerns have been raised in the literature regarding the use of flouroquinolones for empiric treatment of pneumonia due to concerns about spreading antibiotic resistance. It is often suggested that these drugs be reserved for situations where other empiric treatment options cannot be used.

Older (>60 yr) outpatients with underlying disease: most common pathogens are: S.pneumoniae, H.influenzae, respiratory viruses, anaerobic gram negative bacilli, S.aureus. ATS recommends a second-generation cephalosporin such as cefuroxime empirically. Cefuroxime inhibits cell wall synthesis, promoting osmotic instability; it is generally bactericidal. Dosing is bid for 10-14 days. Trimethoprim-sulfamethoxazole may also be used. Pneumococcal resistance may be endemic in some areas. A beta-lactam/beta-lactamase inhibitor such as amoxicillin-potassium clavulanate may also be considered. If legionella is known to be present this should be combined with a macrolide.

Hospitalized patients: in addition to S.pneumoniae and H.influenzae, more virulent agents must be considered. These agents include: S.aureus, Legionella species, P.aeruginosa and other aerobic gram-negative bacilli, and anaerobes. IV antibiotic therapy is initiated with a second or third generation cephalosporin active against S.pneumoniae and anaerobes (such as cefuroxime, ceftriaxone, cefotaxime) or a beta-lactam/beta-lactamase inhibitor. If P. aerugenosa is suspected only a cepalosporin active against this pathogen should be used. If Legionella is suspected a macrolide should be added to the therapy regimen. If Legionella is confirmed Rifampin should be added to the macrolide.

Critically ill patients will require multiple IV antibiotics including a macrolide plus a third-generation cephalorsporin plus an aminoglycoside. Anti-psuedomonal, and/or anti-Legionella agents may also be considered.

Monitoring therapy:
Fever, respiratory rate, and cough should show improvement within 72 hours of initiating antibiotic therapy. If a suitable specimen has been obtained and a specific pathogen has been identified, therapy can be adjusted as indicated . Hospitalized patients who are responding appropriately to IV therapy may be changed to oral agents, usually about the third hospital day. Most infections can be treated with 7-10 days of antibiotic therapy, but some infections may require up to 14 days of treatment. Immunocopromised patients may require 21 days of treatment.

If patients fail to respond to empiric treatment, or the clinical condition worsens it is necessary to determine if the correct diagnosis has been made, or if host, drug or pathogen issues need to be addressed. Incorrect diagnosis could include failure to consider or recognize such problems as CHF, embolus, neoplasm, drug reactions. Host issues could include superinfection, obstruction. Pathogen issues could include unusual or resistant organisms. Drug issues include choosing the wrong drug, wrong dose/route, noncompliance.

Successful cost-effective treatment of CAP depends upon careful clinical assessment of patients presenting with suspected CAP, diagnostic testing appropriate to patient status and risk factors, and empiric therapy based on clinical factors and community epidemiology.

CASE PRESENTATION

cc "I still have that cough."

HPI: Sandra White is a 65 yo woman who presents with moderate respiratory distress after 3 days of outpatient treatment with oral erythromycin for suspected bronchitis. She presents with mild dehydration, cough productive purulent sputum, and a persistent low-grade fever.

PMH: Asthma since childhood, chronic bronchitis (last occurrence 1 month prior, treated with several days of amoxicillin), Type II DM (treated with oral hypoglycemics for last 5 years).

FH: lives with her daughter; pre-school grandchild has recent history of URI.

SH: smokes 1ppd, does not drink alcohol, active in community with social and senior groups.

Meds:
Alupent MDI 2 puffs TID
Theo-dur 300 mg PO BID
Micronase 5 mg po QD
No significant OTC use
Known to be compliant with medication regimen

Allergies: NKDA

ROS: noncontributory

PE:
general: mildly disoriented and confused

VS: 100/70 38.1-100-40. wt=60kg.

HEENT: dry mucous membranes

Lungs: fine rales and rhonchi bilaterally, mild pleuritic chest pain, decreased bronchial breath sounds.

Remainder of PE: noncontributory

Labs:
WBC 14,000, bands 15%, BUN 34, Cr 1.8, FBS 140, theophylline level 18.

ABG: pH 7.42, pO2 90, pCO2 50

CXR: RLL infiltrate

Sputum gram stain: many WBCs, few gram-positive cocci, numerous gram-negative coccibacilli

Sputum & Blood cultures pending

1. Problem identification:

a. What information (signs, symptoms, laboratory values) indicates the presence of pneumonia in this patient?

Ms. White presents with a persistent cough, purulent sputum production, low-grade fever, pleuritic chest pain. She is a regular smoker with a history of chronic lung disease and diabetes, and experienced a recent episode of respiratory infection of unknown cause and inadequate antibiotic treatment. She has had recent exposure to a URI through her grandchild, and possible exposure to infectious agents through social activities. PE demonstrates confusion, tachycardia, tachypnea, ?hypotension (baseline is unknown), adventitious lung sounds. Labs indicate leukocytosis with left shift, dehydration, hypoxia. CXR demonstrates an infiltrate. Sputum gram stain shows numerous gram-negative coccibacilli indicative of H.influenzae.

b. What medical problems may be considered risk factors for pneumonia in this patient?

Ms White's risk factors per ATS guidelines include: age, comorbities (diabetes, chronic lung disease), respiratory rate >30/min, altered mental status.

c. Could any of the patient's current problems be caused by present drug therapy?

Ms. White experienced a recent episode of presumed bronchitis that was treated for "several days" with amoxicillin. It has not been established that Ms. White experienced an infection that required antibiotic therapy. Many URIs are caused by viral agents that are not susceptible to antibiotics. Antibiotic therapy may have been warranted in Ms. White's case. Although it is not known if amoxicillin was the appropriate antibiotic of choice, it is appropriate for use in bronchitis in areas where the prevalence of beta-lactamase and H.influenzae are low. As we now know that Ms. White is demonstrating H.influenzae in her sputum, this antibiotic was probably not the best choice for her bronchitis. Ii is not known if

gram stain was done at that time. In addition, to the wrong drug choice, had this been the appropriate drug, the time frame for use - "several days" - would probably have been inadequate.
In addition, ATS recommends a second-generation cephalosporin such as cefuroxime empirically. Erythromycin is not effective in treating H.influenzae, which is a particular concern in smokers.

d. What additional information may be needed to completely assess this patient?

Antibiotic resistance patterns, and infections endemic to the area would aid in determining possible infectious agents. Knowledge of the causative agent for previously experienced bronchitis has been discussed.

e. When evidence indicates that a patient is not responding to or is deteriorating on empiric therapy, what possible factors should be considered?

If patients fail to respond to empiric treatment, or the clinical condition worsens it is necessary to determine if the correct diagnosis has been made, or if host, drug or pathogen issues need to be addressed. Incorrect diagnosis could include failure to consider or recognize such problems as CHF, embolus, neoplasm, drug reactions. Host issues could include superinfection, obstruction. Pathogen issues could include unusual or resistant organisms. Drug issues include choosing the wrong drug, wrong dose/route, noncompliance.

2. Desired Outcome

a. What are the goals of pharmacotherapy in this patient with chronic bronchitis complicated by pneumonia?

Pharmacologic treatment should be directed at eradicating the infective agents without causing superinfection or antibiotic resistance, and returns this patient to her baseline. Antibiotic treatment should take into account her risk factors for complications. Treatment should be as cost-effective as possible without compromising outcome goals, or patient safety and comfort.

CLINCIAL COURSE

The patient was admitted to the hospital for IV hydration and antibiotic therapy. Erythromycin was continued at a dose of 500 mg IV q 6 hr and piperacillin/tazobactam 3.375 gm IV Q 8 hr was added. Aminonophyllin was adjusted to a rate of 30 mg/hr. Respiratory therapy was consulted for nebulizer treatments.

3. Therapeutic Alternatives

a. Describe your assessment of these interventions.

As previously discussed, erythromycin is a cost-effective empiric treatment for most of the CAP causative agents except H.influenzae, and probably is not necessary for this patient. She shows some gram positive cocci. In addition, IV erythromycin is locally irritating, and requires slow, careful infusion. The ATS recommends a second- or third-generation cephalorsporin or a beta-lactam/beta-lactamase inhibitor for treatment of patients hospitalized with CAP. Ms. White is, therefore, being treated properly with piperacillin/tazobactam IV. The recommended dosing for piperacillin/tazobactam, however, is Q 6 hr. Ms. White may not be receiving enough antibiotic coverage to adequately meet treatment goals. Unless the pending cultures show an atypical organism this is probably the only antibiotic necessary.

4. Optimal Plan

a. Outline a specific antimicrobial regimen for this patient.

Discontinue erythromycin.
Increase piperacillin/tazobactam IV to every 6 hrs
When patient is clinically stable and it is determined that resolution is occurring, discontinue piperacillin/tazobactam and initiate Amoxcillin/clavulanate 500 mg PO Q 12 hr.

5. Assessment Parameters

a. What clinical and laboratory parameters are necessary to assess the resolution of pneumonia and success or failure of antimicrobial therapy?

Monitoring should include general assessment, VS, CBC, ?CXR. If therapy is effective it is expected that about Ms. White would be alert and oriented x3, afebrile, VS WNL for this patient, WBC <10,000 & bands <4%, or showing a return to normal ranges. CXRs may not show resolution of infiltrates for a long period following pneumonia, and may worsen before resolution begins; repeat CXR may be considered if response to therapy is not seen within a reasonable period. Lack or response to therapy may also warrant testing for more atypical pneumonia-causing agents such as mycoplasma or Legionella.

6. Patient Counseling

a. What important information concerning therapy should be provided to this patient?

Since full resolution of this pneumonia depends on adequate antibiotic therapy this patient will likely be discharged with an oral antibiotic. It is important for her to understand the necessity for taking the complete course of antibiotic even with improving health. Side effects and dosing information should be clearly presented. It should be determined before the patient leaves if she has any questions or concerns about taking the medication.

In order to prevent pneumonia from recurring Ms. White should be presented with information concerning influenza and pneumovax vaccines. As smoking places her at greater risk for further health problems, it should be determined if she is aware of these problems, is interested in smoking cessation, and what assistance is available to her to accomplish this. Information on avoiding agents that cause respiratory illness should also be prevented, including information on the importance of frequent hand washing.

Although Ms. White has been taking her other medications for a long period of time, these medications should be reviewed with her to ensure that her knowledge is current and complete.