

Acute Infections in Hospice

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Disclosures

- Dr. Muraida discloses his employment as
 - VistaCare Regional Medical Director
- VistaCare has provided commercial support for this activity
- Palliative medicine frequently involves the use of medications for “off-label” purposes. Such use may be discussed during this presentation.

Objectives

- List several types of acute infections that may be encountered in the hospice setting
- Describe how being on hospice may alter the management of such infections
- Discuss the management of urinary and respiratory infections

Treating Acute Infections

- In the non – hospice patient this decision can be fairly straightforward
- Paucity of direction in the hospice literature
- In hospice patients, many complex issues arise
- Will non - treatment change life –expectancy or cause suffering?

Acute Infections

- ◆ Urinary Tract Infection
- ◆ Respiratory Tract
- ◆ Mouth / Pharynx
- ◆ Skin / Subcutaneous
- ◆ Blood / Bacteremia

Urinary Tract

- ◆ Very common in elderly
- ◆ May be complicated by co-morbidities
- ◆ Asymptomatic bacteriuria
- ◆ Treatment regimens differ including duration of treatment
- ◆ Authors of non systematic literature often recommend longer treatment durations (7 – 14 days)

UTI

- Broader range of etiologies in the elderly
- More frequent occurrence of gram positive organisms
- One prospective study identified *E. coli* as the offending agent in 54.7%
- Indwelling catheter patients and males have lower rates of *E. coli* and increasing rates of *Pseudomonas* in comparison to females and non-catheterized patients

UTI – Duration of Tx

- Remains controversial in the uncomplicated UTI
- RCT using ciprofloxacin in either 3 day or 7 day courses showed that the 3 day course was not inferior to the 7 day course
- On the other hand...a study from Stanford recommends 7 days of a fluoroquinolone or if sulfa-sensitive, TMP-SMX for 7 days

Cochrane Review says..

- After reviewing 13 trials involving over 1300 elderly women and including single dose, as well as 3 - 7 day courses... No Difference!
- No significant difference between short or longer treatment regimens was noted
- Poor methodological quality limited the ability to determine optimal duration of therapy

Muraida says..

- Treatment duration = 3 days for an uncomplicated UTI
- This is intraluminal (bladder) vs. tissue infection
- Tissue infection: pyelonephritis, cystitis – 10 days
- Deep tissue: prostatitis : 3 weeks minimum

Community Acquired Pneumonia (CAP)

- ♦ Major cause of death in the world
- ♦ Major cause of death secondary to infectious diseases
- ♦ Mgt and Tx are very controversial
- ♦ ATS, BTS, CIDS, & IDSA all publish guidelines

CAP

- ♦ Acute infection of the lung parenchyma
- ♦ Acute infiltrate on a chest radiograph
- ♦ Auscultatory findings c/w pneumonia (such as altered breath sounds and/or localized rales)

Symptoms

- Fever or hypothermia
- Rigors or sweats
- New cough with or without sputum production or change in color of respiratory secretions in a patient with chronic cough
- Chest discomfort, or the onset of dyspnea
- Most patients also have nonspecific symptoms, such as fatigue, myalgias, abdominal pain, anorexia, and headache.

Epidemiology

- Sixth most common cause of death in the U.S.
- Overall rates of death due to pneumonia and influenza increased by 59%
- A greater proportion of persons aged 65 years may explain this, however, age-adjusted rates also increased by 22%, which suggests that other factors may have contributed to a changing epidemiology of pneumonia, including a greater proportion of the population with underlying medical conditions at increased risk of respiratory infection.

Epidemiology

- Annually, 2.3 million cases of CAP lead to 10 million physician visits, 500,000 hospitalizations, and 45,000 deaths in the United States persons per 100,000 population and 962 per 100,000 persons aged 65 years
- The average mortality for hospitalized pts is 14%
- Mortality estimated <1% for pts not hospitalized
- The incidence of CAP is heavily weighted toward the winter months.

Prognostication

- Understanding the prognosis has clinical relevance
- The ability to accurately predict medical outcomes in cases of CAP has a major impact on management.
- The decision to hospitalize a patient or to treat him or her as an outpatient is perhaps the single most important clinical decision.
- This has direct bearing on the location and intensity of laboratory evaluation, antibiotic therapy, and **costs**.
- The estimated total treatment cost for an episode of CAP managed in the hospital is \$7500 (US dollars) >20-fold higher than the cost of outpatient treatment.

Risk Factors for Death in CAP

- Pre-penicillin era: studies of adults showed an increased risk with alcohol consumption, increasing age, leukopenia, bacteremia, and radiographic changes c/w infiltrate
- Recent independent associations with increased mortality have also been demonstrated for a variety of co-morbid illnesses, such as active malignancies, immunosuppression, neurological disease, congestive heart failure, coronary artery disease and diabetes mellitus
- Signs and symptoms independently associated with increased mortality consist of dyspnea, chills, altered mental status, hypothermia or hyperthermia, tachypnea, and hypotension

Lab Findings

- ♦ hyponatremia
- ♦ hyperglycemia
- ♦ azotemia
- ♦ hypoalbuminemia
- ♦ hypoxemia
- ♦ liver function test abnormalities
- ♦ pleural effusion
- ♦ Infections due to gram-negative bacilli or *S. aureus*, postobstructive pneumonia, and aspiration pneumonia are also independently associated with higher mortality

The Pneumonia PORT

- A methodologically sound clinical prediction rule that quantifies short-term mortality for patients with CAP
- Used as a guideline, this rule may help physicians make decisions about the initial location and intensity of treatment for patients with this illness

PORT

- Over 52,000 patient were studied in the derivation, and validation of this rule
- Stratification into 5 severity classes by means of a 2-step process.
- First, patients are classified into risk classes : I (the lowest severity level) if they are aged 50 years, have none of 5 important co morbid conditions (neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, or renal disease), and have normal or only mildly deranged vital signs and normal mental status.

PORT Step 2

- In step 2, all patients who are not assigned to risk class I on the basis of the initial history and physical examination findings alone are stratified into classes II to V, on the basis of points assigned for 3 demographic variables (age, sex, and nursing home residence), 5 co morbid conditions (listed above), 5 physical examination findings (altered mental status, tachypnea, tachycardia, systolic hypotension, hypothermia, or hyperthermia), and 7 laboratory or radiographic findings (acidemia, elevated blood urea nitrogen, hyponatremia, hyperglycemia, anemia, hypoxemia, or pleural effusion)
- Point assignments correspond with the following classes: 70 = class II; 71- 90 = class III; 91- 130 = class IV; and >130 = class V.

Pneumonia PORT

- Risk classes patients 1 and 2 generally are candidates for outpatient treatment
- Risk class 3 patients are potential candidates for outpatient treatment or brief inpatient observation
- Patients in classes IV and V should be hospitalized.
- Estimates from the Pneumonia PORT cohort study suggest that these recommendations would reduce the proportion of patients receiving traditional inpatient care by 31% and that there would be a brief observational inpatient stay for an additional 19%.

Pneumonia PORT Prediction Rule

- Identifies valid predictors for mortality and provides a rational foundation for the decision regarding hospitalization
- It is validated as a mortality prediction model and **not** as a method to triage patients with CAP.
- New studies are required to test the basic premise underlying the use of this rule in the initial site-of-treatment decision, so that patients classified as "low risk" and treated in the outpatient setting will have outcomes equivalent to or better than those of similar "low-risk" patients who are hospitalized.
- **This rule does not supercede physician judgment !**

Etiologic Agents

- *S. pneumonia* is the most common etiologic agent identified in virtually all studies of CAP and accounts for about two-thirds of all cases of bacteremic pneumonia cases
- Other pathogens *H. influenzae* (most strains of which are nontypeable), *Mycoplasma pneumoniae*, *C. pneumoniae*, *S. aureus*, *Streptococcus pyogenes*, *N. meningitidis*, *Moraxella catarrhalis*, *Klebsiella pneumoniae* and other gram-negative rods, *Legionella* species, influenza virus (depending on the season), respiratory syncytial virus, adenovirus, parainfluenza virus, and other microbes.

Seasonal Variations

- There are seasonal differences in incidence of many of the causes of CAP. Pneumonia due to *S. pneumoniae*, *H. influenzae*, and influenza occurs predominantly in winter months
- *C. pneumoniae* appears to cause pneumonia year-round.
- Although there is a summer prevalence of outbreaks of legionnaires' disease, sporadic cases occur with similar frequency during all seasons
- Some studies suggest that there is no seasonal variation in mycoplasma infection; however, other data suggest that its incidence is greatest during the fall and winter months

Differential Diagnosis

- The ddx of lower respiratory tract symptoms is quite extensive.
- Both upper and lower resp. tract infections and noninfectious causes
- Reactive airways disease, atelectasis, congestive heart failure, bronchiolitis obliterans with organizing pneumonia (BOOP), vasculitis, pulmonary embolism, and pulmonary malignancy

CXR

- ◆ Chest radiography is considered sensitive and, occasionally, is useful for determining the etiologic diagnosis, the prognosis, and alternative diagnoses or associated conditions.
- ◆ Treating patients for CAP on the basis of presenting manifestations, without radiographic confirmation has been discouraged by the ID Society.
- ◆ The cost of a cxr and potential dangers of antimicrobial abuse in terms of side effects and resistance

Hospitalized CAP Patients

- ◆ Structural lung disease: antipseudomonal agents (piperacillin, piperacillin-tazobactam, carbapenem, or cefepime) plus a fluoroquinolone (including high-dose ciprofloxacin)
- ◆ Lactam allergy : fluoroquinolone ± clindamycin
- ◆ Suspected aspiration: fluoroquinolone with or without clindamycin, metronidazole, or a -lactam / -lactamase inhibitor

Outpatient CAP Abxs

- Generally preferred: doxycycline, a macrolide, or a fluoroquinolone for 7 to 10 days depending on comorbidities
- The most likely pathogens in this setting include *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*

Outpatient CAP Patients

- Antibiotic selection should be influenced by regional antibiotic susceptibility patterns for *S. pneumoniae* and the presence of other risk factors for drug-resistant *S. pneumoniae*. In Albuquerque, hospitals have seen fluoroquinolone - resistant pneumococcus
- For older patients or those with underlying disease, a fluoroquinolone may be a preferred choice; some authorities prefer to reserve fluoroquinolones for such patients along with hospitalized patients

Recommended Abx for Pneumococcus

- amoxicillin (500 mg thrice daily)
- cefuroxime axetil (500 mg twice daily)
- cefpodoxime (200 mg twice daily)
- cefprozil (500 mg twice daily)
- azithromycin, clarithromycin, erythromycin, or a quinolone (Avelox) or doxycycline in ordinarily prescribed dosages.

Pneumococcus

- Amoxicillin is preferred to penicillin because of more reliable absorption, longer half-life, and slightly more favorable MICs.
- While surveillance studies indicate increasing resistance to macrolides, few reports of clinical failure in patients without risk factors for infection with drug-resistant *S. pneumoniae* exist
- With increasing use, however, there is concern about reduced efficacy of macrolides.

Hospitalized Patients

- Susceptible or intermediately resistant to penicillin Pneumococcal organisms respond to treatment with penicillin (2 million units every 4 h), ampicillin (1 g every 6 h), cefotaxime (1 g every 8 h), or ceftriaxone (1 g every 24 h).
- Pneumonia due to penicillin- or cephalosporin-resistant organisms probably requires higher doses of these drugs.
- A CDC study found mortality associated with treated pneumococcal pneumonia to be increased 3-fold when the condition was due to penicillin-resistant pneumococci and 7-fold when due to ceftriaxone-resistant pneumococci, even after adjusting for severity of underlying illness and previous hospitalization, both of which increase the likelihood that resistant pneumococci will be present. This study, however, did not determine the nature of the treatment in each case. It seems likely that, ultimately, penicillin or ceftriaxone may not reliably cure infection caused by strains of *S. pneumoniae* for which penicillin MICs are 4g/mL and ceftriaxone MICs are 8 g/mL.

Tx Recommendations

- Cefotaxime (1 g every 6-8 h) or Ceftriaxone (1 g every 12-24 h)
- Many patients have received 1 - 2 g of ampicillin (with or without sulbactam) every 6 h, with a good response.
- Although vancomycin is nearly certain to provide antibiotic coverage, there is a strong impetus not to use this drug until it is proven to be needed because of fear of the emergence of resistant organisms.
- Vancomycin or a fluoroquinolone should be used for initial treatment of pneumococcal pneumonia in critically ill patients who are allergic to -lactam antibiotics.

Aspiration Pneumonia

- Aspiration pneumonia is broadly defined as the pulmonary sequelae of abnormal entry of material from the stomach or upper respiratory tract into the lower airways. The term generally applies to large-volume aspiration.

Aspiration Pneumonia

- Most studies show that aspiration is suspected in 5% -10% of patients hospitalized with CAP
- In general, the diagnosis should be suspected when patients have a condition that predisposes them to aspiration (usually compromised consciousness or dysphagia) and radiographic evidence of involvement of a dependent pulmonary segment (lower lobes are dependent in the upright position; the superior segments of the lower lobes and posterior segments of the upper lobes are dependent in the recumbent position).

Aspiration Pneumonia

- Aspiration pneumonia is the presumed cause of nearly all cases of anaerobic pulmonary infection, and microaerophiles and anaerobes from the mouth flora are the anticipated pathogens in bacterial infections associated with aspiration.
- **Anaerobic Bacterial Infections**
- The frequency of infection that involves anaerobes among patients with CAP is not known, because the methods required to obtain uncontaminated specimens that are valid for anaerobic culture are rarely used.

Aspiration

- Clindamycin to be superior to iv penicillin
- Metronidazole alone as antimicrobial therapy is associated with a high failure rate, presumably because of the role played by facultative and microaerophilic streptococci. Coupling metronidazole with a quinolone provides good coverage.
- Amoxicillin-clavulanate also appears to be effective.
- Other anti-anaerobic antibiotics include imipenem, meropenem, metronidazole, chloramphenicol, and any combination of a -lactam / -lactamase inhibitor.

Treatment of Aspiration

- Moxifloxacin, gatifloxacin, and trovafloxacin also have good in vitro activity against most anaerobes.
- Macrolides, cephalosporins, and doxycycline have variable activity.
- TMP-SMZ and aminoglycosides are not active against most anaerobes.
- The IDSA panel recommends clindamycin, a β -lactam / β -lactamase inhibitor, imipenem, and meropenem as preferred drugs for treating pulmonary infections

Other Pathogens

- ***C. pneumoniae* Pneumonia** 5-15 % of CAP with low mortality
- Commonly affect elderly with significant comorbidities
- Sore throat, hoarseness, and headache are important nonpneumonic symptoms
- For therapy, a macrolide, doxycycline, or a fluoroquinolone for 7-10 days

Other Pathogens : *M. pneumoniae* Pneumonia

- Commonly seen in young adults.
- Small percentage of cases of CAP requiring hospitalization
- Most common presentation is tracheobronchitis; 3% of patients who are acutely infected with *Mycoplasma* have pneumonia on cxr.
- Common symptoms with pneumonia include a prodromal period with fever, chills, headache, and sore throat, followed by a dry cough often most severe at night and may persist for 3-4 weeks.
- A history of contact with a person with a similar condition, characterized by a long incubation period should alert suspicion of Mycoplasma.
- Extrapulmonary manifestations may include cold hemagglutination and hemolytic anemia; nausea; vomiting; and, rarely, myocarditis, skin rash, and, diverse neurological syndromes.

Mycoplasma Pneumonia

- Cold agglutinin titers 1 : 64 support this diagnosis, and the cold agglutinin response correlates with the severity of pulmonary symptoms
- The test lacks both sensitivity and specificity. It is suggested that a single CF antibody titer 1 : 64, combined with a cold agglutinin titer 1 : 64, supports this diagnosis
- The antibody response usually develops at 7-10 days after the onset of symptoms and shows peak levels at 3 weeks.
- Changes on chest radiography are nonspecific. Most common is a unilateral infiltrate, but one-third of patients have bilateral changes.
- The IDSA panel concluded that no available diagnostic test reliably and rapidly detects *M. pneumoniae*. Thus, therapy must usually be empirical

Abx for Mycoplasma

- The panel recommends treatment with tetracycline or a macrolide for most cases; an alternative is a fluoroquinolone.
- Treatment should be given for 2 to 3 weeks to reduce the risk of relapse. The role of antibiotic therapy for extrapulmonary manifestations is not established.

Viral

- Most cases of upper respiratory tract infection and AB are of viral origin, do not require antimicrobial therapy, and are the source of great antibiotic abuse
- By contrast, antimicrobial therapy is usually indicated for pneumonia, and a chest radiography is usually necessary to establish the diagnosis of pneumonia. Physical examination to detect rales or bronchial breath sounds is neither sensitive nor specific for detecting pneumonia

Influenza

- Influenza is clearly the most common serious viral airway infection of adults in terms of morbidity and mortality.
- Seasonal epidemics in the U.S. can be associated with 20,000 deaths either directly with this infection or its complications, primarily bacterial superinfections.
- "Spanish flu," which in 1918 was responsible for >20 million deaths worldwide,
- "Asian influenza (1957),
- Hong Kong influenza (1968
- The great majority of deaths occur in patients who are aged >65 years and / or residents of chronic care facilities
- The most common cause of bacterial superinfection is *S. pneumoniae*

Influenza

- Rapid identification tests are available and can lead to an etiologic diagnosis in 15-20 min with a sensitivity of 70%-90%. A diagnosis can often be made with comparable sensitivity on the basis of typical symptoms in nonvaccinated patients during an influenza epidemic.
- Amantadine or rimantadine appears to reduce the duration and severity of symptoms in patients with influenza A, but these drugs have no activity against influenza B
- Zanamivir and oseltamivir are active against influenza A and B viruses.
- The relative efficacy of these neuraminidase inhibitors versus that of amantadine and rimantadine for treating or preventing influenza A is unknown
- Clinical trials to date show that all 4 drugs reduce the duration of fever by 1-1.5 days when given within 48 h of the onset of symptoms.

Influenza Prevention

- Annual administration of vaccine has shown an efficacy of >60% for preventing transmission in 10 of the last 11 influenza seasons.
- Efficacy for prevention is reduced in elderly residents of chronic care facilities, but effectiveness in preventing mortality is often reported to be 70% 80% in this population
- Dependant, to some extent, on the match between the epidemic strain and the constituents of the vaccine
- Vaccination of health care providers in CCF may be as important, or more important, than vaccination of the patients
- Report hospital-based health care workers showed an 88% rate of vaccine efficacy and reduced absence for respiratory illness.
- These data emphasize the importance of vaccine strategies that target the populations at greatest risk, including persons aged 65 years, patients with cardiopulmonary disease, and residents of nursing homes and their care providers.

Acute Bronchitis

- Very common but very misunderstood.
- 42% of all primary diagnoses assigned for patients with cough (compared with 5% for pneumonia)
- Similar presentations require that CXR be used to distinguish AB from pneumonia in order to optimize therapy.
- There is no clear consensus on the definition of AB and because of the high rate of spontaneous resolution no antibiotic is recommended
- Cough is an expected part of uncomplicated viral respiratory infection and not necessarily indicative of bacterial infection. This should help avoid unnecessary antimicrobial use
- Auscultatory findings are nonspecific and are often normal, but variable findings, such as localized rales, wheezing, and prolonged expiratory phase, may be noted, especially in patients with reactive airway disease.

AB vs. Pneumonia

- The absence of any vital sign abnormality or any abnormalities on chest auscultation substantially reduces the likelihood of pneumonia
- The syndrome of AB is most often associated with respiratory viruses for which antibacterial therapy is unwarranted
- The most common viruses identified have been the common cold viruses, rhinovirus and coronavirus; others include influenza virus, adenovirus, parainfluenza virus, and RSV. A small proportion of cases are of nonviral etiology.
- There is little evidence that *S. pneumoniae* or *H. influenzae* has an important role in the etiology of AB in adults with community-acquired infections in the absence of chronic obstructive lung disease, airway violation (e.g., tracheostomy), immunosuppression (e.g., AIDS), or serious associated disease, such as cystic fibrosis

Acute Bronchitis

- The use of antibiotics for AB is not recommended.
- Some studies have demonstrated bronchodilators (e.g., albuterol) to be more effective than antibiotics for the relief of symptoms
- Despite information that antibiotics are generally not indicated for AB, studies indicate that primary care providers use them in the majority of cases
- This overuse of antibiotics increases the pressure that leads to antimicrobial resistance
- A recent study found that patients' satisfaction did not depend on receipt of an antibiotic prescription, as long as physicians explained the rationale for management
- Another study showed that antibiotic abuse in cases of AB was reduced when both physicians and patients were warned of the consequences of this practice.

CAP Antibiotic Choices (by organism)

- ◆ Preferred :
 - ◆ A macrolide : erythromycin, clarithromycin, or azithromycin; clarithromycin or azithromycin is preferred if *H. influenzae* is suspected.
 - ◆ Doxycycline, or a fluoroquinolone : levofloxacin, moxifloxacin, gatifloxacin, or another fluoroquinolone with enhanced activity against *S. pneumoniae*.
- ◆ Alternative Abx :
 - ◆ Amoxicillin-clavulanate and some second-generation cephalosporins (cefuroxime, cefpodoxime, and cefprozil) are appropriate for infections ascribed to *S. pneumoniae* or *H. influenzae*. These agents are not active against atypical agents.
 - ◆ Some authorities prefer macrolides or doxycycline for patients aged <50 years who have no comorbidities and fluoroquinolones for patients who are aged >50 years or have comorbidities.

Summary

- ◆ Avoid the temptation to treat CAP on the basis of presenting manifestations, without radiographic confirmation. This approach should be discouraged, given the cost and potential dangers of antimicrobial abuse in terms of side effects and resistance.
- ◆ Duration of therapy as an outpatient varies from 7 –10 days.
- ◆ In the LTC setting, in the acute setting in order to get immediate blood levels of abx, parenteral route may be used. However, the quinolones if immediately available, will yield similar blood levels.