Community Acquired Pneumonia: Synthesis of Current Diagnostic and Treatment Recommendations

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Key Points from Recent Policy Statements

- The first dose of antibiotics for patients admitted to the hospital for pneumonia should be given in the Emergency Department (ED) (4).
- Empiric treatment for MRSA is not indicated in most patients (4,51).
- The role of neuramidase inhibitors in influenza pneumonia and influenza with a concomitant bacterial pneumonia has not been sufficiently studied, but their use is recommended in patients who test positively for influenza (4).
- A "severity of illness" tool helps determine the patient's disposition, but should not replace physician judgment or clinical gestalt (4).
- Blood and sputum cultures have the most significant role in patients with severe pneumonia, a minimal role in outpatients, and a variable role in inpatients without severe disease (6).

Case Presentations

Case #1: A 20 year-old female presents to the ED with complaints of cough, fever, and myalgias. She has no significant past medical history and is not pregnant. She does not smoke or use alcohol or drugs. Her vital signs are normal with the exception of a temperature of 100.5°F. Her oxygen saturation is 100% on room air. She is well-appearing and has a normal physical examination. Her chest radiograph shows a small, focal right lower lobe infiltrate. You make the diagnosis of community acquired pneumonia (CAP). Is further testing required? What is the disposition?

Case #2: A 70 year-old female is brought to the ED from home by her family who report that she seems confused, lethargic, and no longer ambulatory. She has a past medical history of congestive heart failure (CHF), hypertension, and a stroke. She does not smoke or use alcohol or drugs. Her vital signs are significant for a respiratory rate of 32, a temperature of 102°F, blood pressure of 100/60, and pulse of 110 beats per minute. Her oxygen saturation is 90% on room air. She is obtunded. Her chest radiograph shows a large right middle lobe infiltrate. You make the diagnosis of CAP. Is further testing required? Which key interventions are indicated?

Case #3: A 60 year-old male comes to the ED with his wife. He complains of shortness of breath, productive cough, and "not feeling well." His past medical history is significant for a stroke with no obvious neurologic deficit, hepatitis C virus, and non-metastatic prostate cancer treated with radical prostatectomy 10 months ago. He does not and has not ever smoked or used alcohol or drugs. His vital signs show a respiratory rate of 22, a temperature of 102°F, a heart rate of 110 beats per minute, and a blood pressure of 135/85. He appears tired, but non-toxic. He coughs frequently during the history and physical exam. His examination is otherwise normal. His chest radiograph shows a small right middle lobe infiltrate. You make the diagnosis of CAP. Is further testing required? What is the disposition?

Introduction

Pneumonia is the number one cause of death from an infectious disease in the United States and the 7th leading cause of death overall when combined with influenza (1). Community acquired pneumonia costs $10 billion annually to treat. The majority of cost, approximately $8 billion, is spent on inpatient management (2). The high mortality and high cost of CAP has led multiple groups to develop diagnostic and management guidelines. The Center for Disease Control and Prevention (CDC), Infectious Disease Society of America (IDSA), American Thoracic Society (ATS), and British Thoracic Society (BTS) have all published practice guidelines regarding care of the patient with CAP.

The Joint Commission (JC, formerly the Joint Commission for the Accreditation of Hospitals or JC) has developed seven "Quality Measures" that are markers of hospital and physician performance (3). These "Quality Measures" have clouded the ED management of CAP due to their vague nature, their reliance on a superficial interpretation of the literature, and the negligence of physician clinical decision making. In addition, the guidelines focus on individual interventions, rather than a global improvement in the care of the patient with CAP. The alteration of a single element of care, such as changing the timing of antibiotics by a number of hours, has not been shown to decrease mortality. Unfortunately, the JC "Quality Measures" address isolated patient care events rather than global issues in the care of the patient. The IDSA/ATS joint committee comments that guidelines should address the comprehensive care of a patient as a measure of quality, rather than distract from the care of the patient with arbitrary markers of performance (4).

The number of guidelines, their frequent revision, increasing drug resistance in the community, and the proliferation of antibiotic choices makes it difficult for the physician to stay abreast of current trends in CAP. The objective of this article is to synthesize the current recommendations of the major organizations and the supporting literature on the diagnosis and treatment of CAP.

Diagnosis

Physicians suspect the diagnosis of pneumonia in patients with the appropriate clinical findings of fever, cough, and sputum production. Physical examination may reveal focal or diffuse adventitious lung sounds. However, the physical examination is less sensitive than radiography **(**5). The IDSA/ATS Guidelines state that "lung imaging is required in the routine evaluation of patients with suspected pneumonia" (4). Plain radiograph is the imaging study of choice. The BTS does not feel that imaging is required in the routine management of outpatients, but prioritizes a chest radiograph as mandatory in patients admitted to the hospital with CAP (6). The role of CT scan of the chest following a normal plain film of the chest has not been delineated (7). Physicians should utilize chest X-ray to diagnose pneumonia. In the setting of a normal chest X-ray, physicians should look for other etiologies of the patients symptoms. Routine use of chest CT to evaluate patients with cough and fever with a normal chest X-ray is not indicated.

Microbiology

Improvements in organism detection have changed the understanding of the etiology of CAP. *Streptococcus pneumoniae* remains the most common etiologic agent among all patients with CAP. However, there is increased recognition of polymicrobial infections, including co-infection with viruses. Viruses are identified in up to 18% of patients admitted with CAP and in 9% of admitted CAP viruses are the only infectious agent identified (13). Influenza is the most commonly isolated virus in CAP. The new guidelines discuss the prediction of etiologic agents in CAP.

Drug-resistance is increasingly common in *Streptococcus pneumoniae* infections. Risk factors for drug resistant *S. pneumoniae* (DRSP) include: age less than 2 years of age or greater than 65 years, use of a ß-lactam antibiotic in the last 3 months, day care attendance, alcoholism, and immunosuppression (14-19). IDSA/ATS guidelines suggest that the most important risk factor for DRSP infection is recent treatment with an antibiotic (within the past 3 months), with resistance being specific to the class of antibiotic previously used (15-17,20). The IDSA/ATS guidelines report that community acquired MRSA is currently a rare occurrence, but is becoming significantly more frequent (4).

In patients who are candidates for outpatient therapy and in non-ICU inpatients, the organisms classically referred to as "atypical" and viruses are the next most common etiologic organisms. The atypical organisms include *Mycoplasma pneumoniae*, *Hemophilus Influenza*, *Chlamydia pneumoniae*), and *Legionella* species.

Among patients admitted to the ICU, the primary organisms of concern include *S. pneumoniae, Staphylococcus Aureus, Legionella* species*,* Gram negative bacilli, and *H. Influenza.* Additional organisms can be predicted based on unique patient risk factors. These are listed in Table 1.

The concept that presentation characteristics or radiographic appearance of CAP reliably identifies the causative organism is outdated and not supported by microbiologic testing. Most patients with CAP do not present with signs or symptoms that differentiate the causative organisms (8-10). Polymicrobial and viral infection are more common than previously suspected (10,11). One study, using polymerase chain reaction, found viruses to be co-existent in 36% of patients with CAP (12). Another study of inpatients, showed a significant number of patients with viral infections (13). Due to the common presence of multiple organisms and viral infections, the IDSA/ATS and BTS Guidelines recommend that the practitioner avoid making antibiotic choices on clinical presentation and radiographic appearance (4,6). Physicians should rely on epidemiologic risk factors and laboratory testing rather than radiologic appearance and clinical presentation to determine pathogens (Tables 1 and 2).

Table 1 – *Risk Factors That Modify Epidemiology*

Condition/Exposure	**Pathogens**
Alcoholism	Oral anaerobes, Gram negative pathogens – Klebsiella pneumoniae, Acinetobacter species, Tuberculosis
Travel/cruise ship/hotel	*Legionella*
Altered mental status/loss of airway reflexes	Oral anaerobes, Gram negative pathogens
HIV	Tuberculosis
AIDS	*Pneumocystis jiroveci, Cryptococcus, Histoplasma, Aspergillus, Pseudomonas*
Southwest US	*Coccidioides species,* Hantavirus
Structural lung disease	*Pseudomonas aeruginosa, Burkholderia cepacia, Staphylococcus aureus*
IV drug use	*Staphylococcus aureus (MRSA), Anaerobic bacteria, Tuberculosis*

Table 2 – *Etiology of CAP* (*Etiologic agent listed in order of frequency*).

Outpatient	**Inpatient**	**Inpatient ICU**
S. pneumoniae	*S. pneumoniae*	*S. pneumoniae*
M. pneumoniae	*M. pneumoniae*	*S. aureus*
H. Influenza	*C. pneumoniae*	*Legionella* species
C. pneumoniae	*H. Influenza*	Gram-negative bacillus
Viruses	*Legionella species*	*H. Influenza*
	Viruses	

Additional Testing

The advent of antigen detection and rapid point-of-care testing has increased the number of tests available to perform on patients with CAP. The routine application of all tests to all patients with CAP would not be cost-effective and would have little impact on patient care. The IDSA/ATS guidelines make specific recommendations for some of these tests, but in general support the use of additional testing in the scenario when the test is higher yield and when the results would change patient management (4). Similarly, the BTS recommends using additional testing as guided by severity of illness and epidemiological risk factors (6). The JC "Quality Measures" limit the recommendation of additional testing to blood cultures (3). The role of each of these tests is discussed below.

Blood cultures

The utility of blood cultures has been recognized to be low when applied to all patients with CAP. A minority of blood cultures yield microorganisms, with positive rates in the range of 5-20% (21- 28). Positive blood cultures have been shown to have little impact on the management of CAP (23,24). False positive cultures commonly complicate the treatment of CAP. False positive cultures have been shown to increase length of hospital stay and increase vancomycin utilization (21,30). Empiric antibiotic regimens are often not adjusted based on the results of blood cultures.

The low impact of blood cultures on treatment decisions may reflect the fact that *S. pneumoniae* is the organism most commonly isolated. Empiric antibiotic choice usually includes antibiotics effective against *S. pneumoniae*. However, studies show that antibiotic regimens are not narrowed based on blood culture results.

In patients with severe CAP (Table 4), the yield of blood cultures increases. Some studies site positive results as high as 30% in patients with severe disease (31,32). Because of the increased yield and the increased likelihood of less common organisms, the utility of blood cultures in patients with severe CAP is higher.

The IDSA/ATS guidelines support a graduated approach to blood cultures in patients with CAP. The societies state that a practitioner should not be faulted for obtaining blood cultures in any patient with CAP and emphasize that blood cultures are of the highest value in patients with severe CAP. Hospitalized patients with CAP who do not have severe disease warrant blood cultures in select cases; for example, blood cultures exhibit a higher yield when obtained from patients who are immune-compromised.

The various societies have differing recommendations concerning blood cultures on patients who are hospitalized with CAP, but agree that outpatients can be managed without them (4). All societies agree that blood cultures, when obtained, should be obtained prior to the administration of antibiotics, as long as antibiotic administration is not delayed (6). JC performance measures mandate blood cultures on all patients with CAP, prior to administration of antibiotics. The JC performance measures do not comment on patient severity of illness or disposition (3).

Currently, physicians must continue to obtain blood cultures on all hospitalized patients with CAP to meet the JC performance measures, although this is in conflict with current guidelines. Blood cultures are not necessary in outpatients. Cultures should be obtained prior to the administration of antibiotics when this does not delay the administration of antibiotics.

Sputum cultures

Sputum cultures also provide little useful information, with the majority of samples being inadequate, either due to the lack of phlegm or due to contamination from the oral flora (34-36). One study cites accurate results in only 14% of patients, without an improvement in yield with severity of illness. In this same study, the sputum Gram stain was found to correlate well with a dominant organism being found on sputum culture (11).

The IDSA/ATS and BTS recommend sputum Gram stain and culture only be utilized if a good sample can be obtained prior to antibiotic administration and expeditiously handled. In patients with increased severity of illness, both organizations note that the sputum studies are more likely to yield clinically relevant results (4,6). In mechanically ventilated patients from whom a sputum sample is obtained by aspiration or lavage, the results have higher yield. These results are more likely to be positive even subsequent to a dose of antibiotics (11, 37-42).

The IDSA/ATS guidelines support obtaining sputum Gram stain and culture in all patients with CAP who are intubated. The BTS more strongly recommends sputum studies with increasingly severity of illness (6). Sputum studies are not a JC "Quality Measure".

The decision to obtain sputum cultures can be deferred to the admitting physician. Antibiotic administration should not be delayed for sputum cultures.

Antigen testing

Urine can be tested for antigens to *Legionella pneumophila* (*L. pneumonphilia*) serogroup 1 (which accounts for 80-90% of all community-acquired Legionnaires disease) and *S. pneumoniae*. Urinary antigen tests rapidly produce results but have variable accuracy with sensitivities in the range of 50-80% and specificity of approximately 90%. Importantly, urinary antigen tests detect the antigens for several days after the administration of antibiotics. False positives have been documented in children with chronic respiratory disease and patients with previous episode of CAP within past 3 months. The yield from these tests, as with other microbiologic tests, improves with increasing severity of illness (43,44).

The IDSA/ATS guidelines support the use of the urine antigen tests in patients with severe CAP, especially in patients who are intubated (4). The BTS supports the use of the urinary antigen test for *L. pneumonphilia* in patients with severe CAP. The BTS interprets the current urine streptococcal antigen tests to be insufficiently sensitive and specific for use (6).

Because a single dose of antibiotic does not affect urinary antigen tests, the Emergency Physician can defer this decision to the admitting physician. Urinary antigen testing is not necessary in outpatient management of CAP.

Identification of influenza is considered a priority by the IDSA/ATS and the CDC (4,45). It is increasingly recognized as a primary etiologic agent and a co-infecting agent. The influenza rapid antigen detection is valued due to its ease of use and rapid results. The specificity approaches 100% (46,47). However, it is criticized for its lack of sensitivity (50-70%). Direct fluorescent antibody testing is more sensitive for influenza and may be the more reliable test. Testing for influenza during outbreaks is recommended by the CDC and the IDSA/ATS (4,45).

The rapid antigen test for influenza impacts treatment decisions in the ED. In the outpatient setting, a positive test may obviate the need further testing, such as a lumbar puncture, in an undifferentiated febrile illness. A positive test can also impact the decision to withhold antibiotics in a febrile patient with a normal chest X-ray who will be followed as an outpatient. For patients being admitted to the hospital, a positive test may prompt the physician to administer antiviral therapy. During influenza outbreaks, Emergency Physicians should utilize the rapid influenza test to differentiate febrile illness in outpatients. During outbreaks, all admitted patients with CAP should be tested for influenza. The CDC provides influenza surveillance results on its website (www.CDC.gov) to identify periods of influenza activity.

Polymerase Chain Reaction (PCR) testing

Currently, PCR testing of sputum in patients with CAP has insufficient reliability to be recommended (4,6,48). Currently, there is a lack of literature to support its routine use. To date, most PCR tests have not been rigorously tested in the clinical setting to allow an understanding of their applicability.

Adrenal Insufficiency

Increasing data supports the concept of relative adrenal insufficiency in critically ill patients (49-52). The IDSA/ATS guidelines assess the current literature discussing empiric steroids in severe CAP to "remain controversial" although they do recommend testing for adrenal insufficiency in patients with sepsis and CAP (4).

Treatment Guidelines

Empiric antibiotic choice is dependent on severity of illness and epidemiologic factors. Physicians should consider the patient's co-morbidities, local and regional antimicrobial resistance patterns of the pathogens causing CAP, local outbreaks of infectious agents, the patient's known exposures, risk factors for drug resistant organisms, and the patient's history of recent antibiotic use when choosing empiric antibiotics (Table 3). A JC "Quality Measure" is

the prescription of the most appropriate initial antibiotic (3). This recommendation allows for clinician judgment and recommendations of expert societies.

Table 3 – IDSA/ATS Empiric Antibiotic Choice in CAP (4)

	Outpatient, no antibiotics in past 3 months Previously healthy	**Outpatient, recent antibiotics or co morbidities**	**Inpatient**	**Inpatient, pseudomonas suspected**	**Inpatient ICU**
First line therapy	Macrolide or ß-lactam*	Respiratory fluoroquinolone^	Macrolide plus ß-lactam#	Anti-pseudomonal ß-lactam++ plus ciprofloxacin or levofloxacin (750mg)	Anti-pseudomonal ß- lactam++ plus ciprofloxacin or levofloxacin (750 mg)
Alternative	Doxycycline	Macrolide plus ß- lactam*	Respiratory fluoroquinolone	Anti-pseudomonal ß- lactam++ plus aminoglycoside plus azithromycin	Anti-pseudomonal ß- lactam++ plus aminoglycoside plus azithromycin
ß-lactam allergy	Avoid ß-lactam	Avoid ß-lactam	Respiratory fluoroquinolone	Aztreonam in place of ß-lactam	Aztreonam in place of ß-lactam

* Outpatient ß-lactam regimens: high dose amoxicillin 1 gram 3 times daily, high dose amoxicillin-clavulanate 2 grams 2 times daily, cefuroxime 500mg 2 times daily
# Inpatient ß-lactam options: cefuroxime, ceftriaxone, ampicillin-sulbactam
++ß-lactams with anti-pseudomonal activity: cefepime, imipenem, meropenem, and piperacillin-tazobactam
^ Respiratory fluoroquinolones – moxifloxacin, gemifloxacin, levofloxacin (750mg)

Outpatient

The IDSA/ATS and CDC recommend a macrolide as the first choice of antibiotic for outpatient treatment of healthy adults of CAP. Doxycycline is the alternative first line agent, when it is not contra-indicated (i.e. in pregnancy and children less than 8 years of age). The CDC also recognizes certain ß-lactams (high dose amoxicillin 1 gram 3 times daily, high dose amoxicillin-clavulanate 2 grams twice daily, cefuroxime 500mg twice daily) as effective first line treatment agents (4,53).

The BTS recommends high dose amoxicillin as a first line therapy for outpatient therapy in CAP. The alternative first line agent is erythromycin. Of note, the BTS reports that ß-lactamase producing organisms are rare in the British community (6). The IDSA/ATS and BTS guidelines recognize the increased gastrointestinal distress due to erythromycin, and support more well-tolerated macrolides in spite of increased cost (4,6).

Patients with co-morbidities such as chronic obstructive pulmonary disease, chronic heart, liver, or renal disease, diabetes mellitus, alcoholism, malignancy, AND immune-compromising conditions have increased risk of infection with a drug resistant organism and increased risk of infection with gram negative organism. In these patients who are candidates for outpatient treatment, a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin 750mg) is the recommended first line therapy according to the IDSA/ATS. Alternative options in these patients include combination therapy with a ß-lactam at high doses plus a macrolide or plus doxycycline (4).

In regions with >25% prevalence of high level (>16mg/ml) macrolide-resistant *S. pneumoniae* resistance, the IDSA/ATS guidelines recommend that combination therapy be used as first for all outpatients. The recommended

combination therapy is a ß-lactam plus a macrolide or plus doxycycline. The routine first line use of respiratory fluoroquinolones in these areas is still discouraged in an effort to prevent further resistance (4).

The IDSA/ATS committee is awaiting further safety studies before recommending in favor or against the newly released ketolide, telithromycin. Concerns regarding toxicity, in particular, hepatotoxicity have delayed any recommendations from the IDSA/ATS. The BTS and CDC do not comment on this family of antibiotics.

Inpatient

The first line therapy for inpatients who are not in the intensive care unit is a respiratory fluoroquinolone or combination therapy with a ß-lactam plus a macrolide. This regimen is expanded from the outpatient regimen in order to cover drug resistant organisms and gram negatives. Recommended ß-lactams include cefotaxime, cefuroxime, and ampicillin. Doxycycline is an alternative to the macrolide. In patients with a ß-lactam allergy, a respiratory fluoroquinolone as a single agent is an alternative agent. The IDSA/ATS committee and the CDC recommend the sparing use of respiratory fluoroquinolones to reduce the development of resistance (4,6).

The IDSA/ATS guidelines acknowledge that ertapenem can be utilized in patients in who have recently taken antibiotics or who have other risk factors for drug-resistant *S. pneumoniae*. Although if these patients with risk factors for multi-drug resistant pathogens in particular *Pseudomonas aeruginosa,* ertapenem would be a poor selection due to its lack of activity against this bad bug (4). Neither the IDSA/ATS, BTS, or CDC recommend vancomycin as a first line therapy against drug-resistant *S. pneumoniae* (4,6,53).

Intensive Care Unit

Patients with a severity of illness that warrants ICU admission need broad spectrum empiric therapy. Consideration must be given to Gram negative organisms and drug-resistant organisms. The first line therapy for these patients is a combination of a ß-lactam plus either azithromycin or plus a respiratory fluoroquinolone. The preferred ß-lactams include cefotaxime, ceftriaxone or ampicillin/sulbactam. In patients with a ß-lactam allergy, aztreonam can be substituted for the ß-lactam and used in combination with the respiratory fluoroquinolone.

In patients with risk factors for *P. aeruginosa* or *Legionella* species, use triple therapy (see Table 1 - Risk Factors that modify epidemiology). A ß-lactam with anti-pseudomonal activity plus an aminoglycoside plus azithromycin or levofloxacin (750 mg) ensures adequate coverage of pseudomonas. ß-lactams with anti-pseudomonal activity include cefepime, imipenem, meropenem, and piperacillin-tazobactam (4).

Broadening empiric coverage

Admission to the ICU, recent travel, failed outpatient therapy, alcoholism, a pleural effusion, asplenia, and chronic severe liver disease are indications to broaden empiric coverage. In these patients, epidemiologic risk factors must guide the clinician. Risk factors for methicillin-resistant *S. Aureus* (MRSA) include end stage renal disease, injecting drug use, recent influenza and recent antibiotic use. MRSA is often identified early in the course of treatment by the presence of Gram positive cocci on sputum Gram stain. If MRSA is suspected, the IDSA/ATS guidelines recommend the empiric addition of vancomycin or linezolid.

Risk factors for Pseudomonal infection include severe COPD, frequent steroid or antibiotic use, and structural lung disease. The risk factor for other gram-negative bacteria is active alcoholism. The major pathogens are *Klebsiella pneumoniae* and Acinetobacter species. These Gram negative infections warrant double coverage**.** The first line recommended therapy is an anti-pseudomonal ß-lactam plus ciprofloxacin or plus levofloxacin (750 mg). An alternative therapy is an anti-pseudomonal ß-lactam plus an aminoglycoside and azithromycin.

Community-acquired Methicillin-resistant *Staphylococcus aureus* Pneumonia

The past decade has seen the emergence of community-acquired MRSA (CA-MRSA). CA-MRSA primarily causes skin infection and is responsible for more than half of the skin infections seen in EDs across the country (54). There have also been reports of CA-MRSA causing more severe disease, such as myositis, necrotizing fasciitis, sepsis and pneumonia (55-57).

Rare reports of severe CAP caused by CA-MRSA are increasing. Patients include previously healthy adults and children. The morbidity and mortality are high. CA-MRSA pneumonia has been associated with an antecedent influenza-like illness. Patients present with severe necrotizing CAP, including multilobar disease and cavitary lesions. Blood and sputum cultures produce high yields. Risk factors include prior CA-MRSA infection or colonization, severe CAP, multilobar disease, history of injection drug use, and possibly close contact with a person infected or colonized with CA-MRSA. CA-MRSA can cause a lung abscess which may appear as a cavitary lesion on chest radiograph.

Patients with severe CAP should be treated empirically for the pathogens of CAP as well as CA-MRSA with the addition of either vancomycin or linezolid.

Healthcare-Associated Pneumonia

Healthcare-associated pneumonia (HCAP) is increasingly being recognized in patients presenting to the emergency departments across the United States, and it poses a challenge to Emergency Physicians. The patient population at risk for HCAP is thought to be enormous, estimated to be almost 80 million in the United States, including the elderly, and potentially younger patients suffering with wounds and/or trauma who require hospitalization.

Identifying patients with HCAP is vital because the management and treatment strategies are different for such patients. Patients with HCAP are not only at risk for pneumonia caused by the pathogens of CAP, but additional pathogens more commonly associated with the nosocomial pneumonias.

The 2005 ATS guidelines include recommendations for the management HCAP. HCAP is defined as any patient with pneumonia who has any one of the following: hospitalization for $\geq$ 2 days within the past 90 days, residence in a nursing home or long-term care facility, receipt of intravenous antibiotics, chemotherapy or wound care within the past 30 days, or attendance in a hospital or hemodialysis clinic. This definition, unfortunately, is not precise. It is not known what duration or extent of exposure represents risk for HCAP. There is also debate regarding whether or not health-care workers who develop pneumonia are at risk for HCAP. More investigation is required to better identify who is at risk for HCAP (59).

The newly designated HCAP is not nosocomial pneumonia. The new subcategory of community acquired pneumonia describes patients who are dwelling in the community and have contracted pneumonia following exposure to a health care setting. These patients present to the ED with signs and symptoms of pneumonia. Due to exposure to the health-care setting these patients develop infections with nosocomial pathogens, in particular multi-drug resistant pathogens, as well as community acquired pathogens. The additional pathogens of concern in patient with HCAP include aerobic Gram-negative bacilli (*P. aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli*), and multi-drug resistant pathogens such as *Acinetobacter* and MRSA Patients with HCAP are at risk for more infection with more virulent organisms.

The emergency department management of patients suspected of having HCAP differs in the use of microbiological cultures, antibiotic selection, and disposition. All patients suspected of having HCAP should have blood and sputum cultures obtained regardless of the severity of illness. This recommendation is different than that for patients with CAP where cultures are obtained only for those with severe disease, or co-morbid illnesses. This aggressive approach to microbiological testing is important in an effort to identify the causative pathogen and narrow the extensive empiric antibiotic regimen as rapidly and as safely as possible.

Patients with HCAP initially require very broad-spectrum empiric therapy. Mortality is significantly greater in patients hospitalized with HCAP when compared to those hospitalized with CAP, approximately 20% vs. 10% respectively (58). Additionally, failure to administer appropriate and adequate antimicrobial therapy promptly has been associated with increased mortality in patients with HCAP.

Recommended antibiotic therapy for patients suspected of having HCAP includes a combination of three antibiotic classes: an antipseudomonal ß-lactam (ceftazidime, cefepime, piperacillin/tazobactam, imipenem or meropenem) plus an antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or aminoglycoside (gentamicin or tobramycin) plus an agent active against MRSA (vancomycin or linezolid).

The current guidelines do not specifically address the topic of disposition from the emergency department of patients suspected of having HCAP. Generally, patients will require admission for intravenous antibiotics, however, clinical judgment and individual patient circumstances must be strongly considered. In the event of outpatient

management, blood and sputum cultures should be obtained and prompt follow-up should be arranged. Oral antibiotic regiments should reflect as closely as possible the current recommendations (67).

Influenza

Influenza is increasingly recognized as a co-existing infection in patients with CAP. Both the CDC and the IDSA/ATS guidelines recommend the use of neuraminidase inhibitors (oseltamivir or zanamivir) in patients with CAP and co-existing influenza A (4,51). The literature regarding the role of antiviral medications in the setting of CAP is weak. The empiric use of anti-viral medications in CAP is not indicated. The M2 inhibitors (amantadine and rimantadine) currently have no role in the treatment of influenza A and B or CAP.

Timing of Antibiotics

The JC "Quality Measure" of administering antibiotics within 4 hours of hospital arrival for patients with CAP has drawn much attention to the timing of antibiotics (3,59). The measure is based upon 2 studies of mortality and time to initiation of antibiotics (21,60). The "Quality Measure" as it currently reads is not supported by these studies. The studies looked at inpatients, predominantly over age 65 years. The "Quality Measure" does not limit its application by age or patient disposition. The studies both showed increased mortality in patients who received antibiotics within 0-2 hours of presentation to the hospital.

Neither of these studies investigated the causal relationship between early antibiotics and increased survival. Interpreting the administration of antibiotics between 2 and 4 hours after hospital arrival to be the cause of increased survival is an over-simplified and flawed interpretation of the data. Survival and medication administration decisions are complex, multi-factorial events that may be related causally, but certainly are not as simplistic as the JC "Quality Measure" implies.

CAP and all infectious diseases are progressive processes, with variable, often unpredictable clinical courses. Timing of patient presentation is a highly variable event, with some patients presenting within hours of the development of symptoms, others waiting until the onset of altered mental status and sepsis, and most patients presenting at arbitrary clinical points in between these 2 extremes. The timing of patient presentation to the hospital is an arbitrary measure with no relevance as a measure of clinical course.

The current JC "Quality Measure" of administering antibiotics within 4 hours of patient arrival has little basis in sound medicine, likely will contribute to over-utilization of antibiotics, represents a gross mis-interpretation of research, increases the cost of care for patients who will be managed as outpatients, and inappropriately expedites the care of patients who may be less ill when compared to others waiting to be seen. The JC mandate is not supported by the literature or the expert societies.

The IDSA/ATS supports the idea of early antibiotics in severely ill patients, including patients in whom CAP is suspected. It recommends that patients who require admission to the hospital receive the first dose of antibiotic in the ED, with the administration of antibiotics timed closely with the determination that bacterial CAP is the likely diagnosis (4).

The IDSA/ATS does not comment on the timing of antibiotics for outpatients with CAP. The BTS does not comment on timing of antibiotics in the ED for patients with CAP (6).

Emergency Physicians should administer empiric antibiotics early in the evaluation of patients with sepsis, including sepsis caused by pneumonia. For patients admitted to the hospital with pneumonia, the first dose of antibiotics should be administered in the ED. The best timing of the first dose of antibiotics in patients treated as outpatients is not defined.

Duration of treatment

The duration of antibiotic therapy in CAP is only relevant to the outpatient for ED physicians. The IDSA/ATS guidelines recommend that patients are treated for a minimum of 5 days. The patients should be afebrile for 48-72 hours prior to discontinuation of therapy (4). An informed discussion with outpatients is the best approach to this situation. If a patient is able to have follow-up with a primary care provider within 3-5 days, the physician can consider prescribing a limited course of antibiotics, deferring to the primary care physician to extend the course, as

needed. If a patient anticipates follow-up to occur after 5 days, a longer course of antibiotics can be prescribed or the patient can be instructed to return to the ED if they have not been afebrile for 48 hours or do not feel significantly clinically improved at the end of a 5 day course.

Ventilatory support

Endotracheal intubation

Patients with severe hypoxemia (PaO_2/FiO_2 ratio < 150), bilateral alveolar infiltrates (due to pneumonia or acute respiratory distress syndrome) and respiratory distress, or altered mental status require immediate intubation for ventilatory support. These patients can not be anticipated to improve in the short term. The IDSA/ATS committee supports the use of low-tidal volume ventilation in these patients to prevent additional lung trauma. The guideline is 6 cc/kg of ideal body weight (4). This goal allows for permissive hypercapnia. As with all medical management, these guidelines must be used in conjunction with sound clinical judgment. Volumes may require adjustment to achieve adequate oxygenation.

Non-invasive ventilatory support

The IDSA/ATS guidelines recommend a trial of non-invasive ventilatory support for patients with hypoxia or respiratory distress who do not require immediate intubation (4). The guidelines do not distinguish between continuous or biphasic positive airway pressure modalities. The guidelines recommend intubation if there is failure to improve oxygenation or decrease hypercarbia after 1-2 hours of non-invasive ventilatory support.

Disposition

In determining disposition, objective measures of severity of illness should be used. These measures should complement but not replace the clinical judgment of the physician. Measures of clinical severity can not replace clinical gestalt, “ill appearance,” or social factors that can affect patient outcome.

Pulse oximetry

One of the simplest objective measures of severity of illness is pulse oximetry. It is a JC “Quality Measure.” (3) Pulse oximetry is considered mandatory in all patients who are suspected to have CAP by IDSA/ATS and BTS (4,6).

Severity of illness scales

The BTS and IDSA/ATS guidelines support the use of a severity of illness scale as an objective measure of prognosis and risk of mortality. Severity of illness measurements contribute to disposition decisions and choice of empiric antibiotics. Objective measures of severity of illness minimize unnecessary admissions and the subsequent morbidity of inpatient care. A severity of illness measure promotes ICU admission in patients who might not clinically be recognized as warranting intensive care. The objective measures should never override physician clinical judgment. The scales comprise only one aspect of physician decision making.

The IDSA/ATS guidelines support the use of the Pneumonia Severity Index (PSI) or the CURB-65 criteria as measures of severity of illness (The PSI may be found in the EMedHome.com PDF Database Section). The committee prefers the CURB-65 criteria due to the ease of use (4). The PSI involves 20 different criteria with a more complex scoring system, complicating its use in the busy ED setting. The BTS developed the CURB-65 criteria and supports its use (6).

CURB-65 is a measure of five factors: confusion, defined as any new mental status change, BUN > 20 mg/dL, respiratory rate $\geq$30 breaths/minute, blood pressure $\leq$90 systolic or $\leq$60 diastolic, and age 65 years or greater. Each criterion, when present is 1 point. Patients with 0 points have a 0.7% 30 day mortality. Patients with 1 point have 2.1% 30 day mortality.

Patients with scores of 0 and 1 are candidates for outpatient treatment at the physician's discretion. Patients with 2 points have a 9.2% 30 day mortality. It is recommended patients with scores of 2 points be admitted to the hospital in a non-ICU setting. Patients with scores of 3, 4, and 5 have 14.5%, 40%, and 57% 30 day mortality. The BTS recommends that patients with scores of ≥3 get admitted to the ICU (61). If laboratories are not clinically indicated, the urea level can be foregone (62).

The IDSA/ATS guidelines state some clear indications for admission of patients in spite of low PSI or CURB-65 scales. These indications include the inability to take oral medications, concomitant exacerbation of chronic illness, unmeasured complications of pneumonia, multiple risks present (yet each below the threshold for increasing the score, intravenous drug abuse, uncontrolled psychiatric illness, poor social system, and low functional status.

The IDSA/ATS committee supports the use of a scale to identify severe pneumonia that requires ICU admission. Previous studies have identified a significant portion of patients who are transferred to the ICU after initial admission to the ward (64). The most common reason for transfer to an ICU is respiratory failure. The goal of applying objective criteria is to anticipate patients at risk for respiratory failure and place them in the ICU with expectant management.

The IDSA/ATS has criteria for defining severe CAP (Table 4). There are minor criteria and major criteria. The joint committee recommends admission to the ICU for patients with 2 major criteria or 3 or more minor criteria. These criteria are the only criteria that have been validated for as markers for ICU admission (63). Although recommendations are made for ICU admission based on CURB-65 and PSI scores, these scales have not been studied for this predictive capacity.

All scoring systems have flaws. In particular, the PSI and CURB-65 do not account for the dynamic nature of patients with CAP. Patients may significantly improve or worsen in the ED, as an outpatient, or while hospitalized. For these reasons, clinician re-evaluation and clinical gestalt must always outweigh a static score. The IDSA/ATS guidelines clearly recognize that patients with low scores may require admission, even ICU admission. Some patients with higher scores may still be candidates for outpatient care (Table 4).

Table 4. Criteria for severe community-acquired pneumonia (Adapted from IDSA/ATS Guidelines)

Minor criteria (a):
Respiratory rate (b) ≥30 breaths/min
PaO2/FiO2 ratio (b) ≤250
Multilobar infiltrates
Confusion/disorientation
Uremia (BUN level, ≥20 mg/dL)
Leukopenia (c) (WBC count ≤ 4000 cells/mm3)
Thrombocytopenia (platelet count≤100,000 cells/mm3)
Hypothermia (core temperature ≤36°C)
Hypotension requiring aggressive fluid resuscitation

Major criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors

- (a) Other criteria to consider include hypoglycemia (in nondiabetic patients), acute alcoholism/alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.
- (b) A need for noninvasive ventilation can substitute for a respiratory rate >30 breaths/min or a PaO2/FiO2 ratio >250.
- (c) As a result of infection alone.

Counseling

Vaccination

Pneumococcal and influenza vaccination status should be assessed at the time of diagnosis of CAP. This will help the physician with the determination of the likely etiology of CAP. The IDSA/ATS guidelines recommend administration of these vaccines to patients in whom it is indicated at discharge from inpatient hospitalization or at the first follow-up visit. This recommendation prevents immunization during times of acute illness and relieves society of the increased cost of providing immunizations through the ED (4). The CDC also recommends vaccination at discharge from inpatient care. (65) A JC "Quality Measure" is the assessment of pneumococcal and influenza vaccination status and percent of patients vaccinated.

Emergency Physicians should document the pneumococcal and influenza vaccination status of patients with CAP.

Smoking cessation

Smoking cessation is a goal for all smokers (66). The IDSA/ATS guidelines recommend smoking cessation as a goal during hospitalization (4). A JC "Quality Measure" is the provision of smoking cessation advice or counseling (3). In outpatient therapy, the ED physician is apparently mandated to mention smoking cessation prior to discharge. In inpatients, it is reasonable to defer this discussion to the admitting physician who has more of an opportunity to develop a therapeutic rapport with the patient, is able to conduct this intervention over a series of visits, and may approach the subject when the patient when the patient feels less acutely ill.

Case Summaries

Case #1: Is further testing required? What is the disposition? This healthy 20 year-old requires no further testing. Her CURB-65 score is 0. She is well-appearing to the physician. An assessment of oxygenation has been performed and is normal. She has no co-morbidities. The patient relates to you that she is able to purchase her antibiotics and has a stable social situation. She has a primary care doctor.

You may discuss with her the role of influenza vaccine on preventing future acute respiratory illness even within the current influenza season. She does not meet any criteria for the pneumococcal vaccine. She does not need smoking cessation counseling. You discharge her with a 5 day course of azithromycin and recommend that she her primary physician within 3-5 days. You provide Emergency Department warnings in case on an unexpected clinical course.

Case #2: Is further testing required? What is the disposition? This 70 year-old female has a CURB-65 score of 3 prior to obtaining her laboratories. She is ill-appearing and hypoxic. On arrival, it is apparent that this patient will benefit from an ICU admission, regardless of the need for emergent intubation. This patient's clinical course is expected to be prolonged with significant risk for worsening. Laboratories and an ABG will help define her number of major criteria for severe CAP and her true CURB-65 score. However, her disposition is clear before these results are obtained. The PaO_2/FiO_2 ratio may help the physician with the decision to intubate this patient. However, the patient's altered mental status precludes a trial of non-invasive ventilation. Her CHF complicates fluid resuscitation. Early intubation in this patient would be wise.

On the patient's arrival to the hospital, the physician should recognize the need for early antibiotics even if the source of infection is unclear. Blood and urine cultures should be obtained prior to antibiotics, if possible. Antibiotics should not be withheld if there is a delay in obtaining cultures. Once the diagnosis of pneumonia is made, the physician may broaden the coverage to include gram negative species and any additional pathogens that are suspected based on the patient's risk factors. Once intubated, an aspirated sputum culture should be sent for Gram stain and culture. Urine antigen testing for Legionella and *Streptococcus pneumoniae* are indicated in this patient due to her severity of illness. If the case occurs during influenza outbreak, the patient should be tested for influenza. The patient is a candidate for evaluation for relative adrenal insufficiency. The choice to give empiric steroids remains controversial.

Case #3: This patient's CORD-65 score is 0 prior to obtaining a blood urea nitrogen level. Even with an elevated blood urea nitrogen level (BUN), the patient's maximum CURB-65 score would be 1. Using the IDSA/ATS severity of illness criteria, the patient would only meet criteria for severe CAP if he has thrombocytopenia, uremia $\geq$20 mg/dL, and leucopenia, which is unlikely. However, the patient has had a stroke and he appears "tired".

In this setting further testing and disposition are at the discretion of the physician. No scale or test can replace the instinct of a good physician. In the setting of an influenza outbreak, a test for influenza is wise. After discussion of social support and outpatient care, if the physician and patient choose outpatient management, it should be with a plan for early re-evaluation and a low threshold to return to the ED. The choice to offer vaccinations in the ED involves an informed discussion with the patient.

If the physician and patient choose inpatient management, the decision to obtain blood cultures and sputum cultures are at the discretion of the physician. The patient does not meet criteria for urine antigen testing or testing for adrenal insufficiency. Vaccination status can be addressed at the time of discharge. The patient should receive a first dose of antibiotics in the ED.

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