

THE SEASONAL CHALLENGE OF URGENT  
CARE CENTERS : PNEUMONIA- THE  
HIDDEN RISK OF INFLUENZA

**Presented By: Glenn Harnett, MD**  
**Board Certified Emergency Medicine**

# Learning Objectives

- ▣ Identify the common pathogens that cause Community Acquired Pneumonia (CAP)
- ▣ Recognize the signs and symptoms of CAP
- ▣ Recognize that *streptococcus pneumoniae* is the most common pathogen in CAP
- ▣ Identify the relationship between influenza and pneumonia – the most common pneumonia complication
- ▣ Identify patients most at risk for CAP
- ▣ Become familiar with the current Infectious Disease Society of America (IDSA) CAP treatment guidelines
- ▣ Understand the dangers of antibiotic resistance and how it applies to CAP
- ▣ Learn Current lab testing modalities in CAP

# What is CAP?

- ❑ Pneumonia is an acute alveolar lung infection that presents with infiltrates/consolidation upon chest imaging
- ❑ CAP is defined as pneumonia not acquired in a hospital, hospital environment, or a long-term care facility and includes pneumonia caused by bacterial, viral, and fungal organisms
- ❑ Community-acquired bacterial pneumonia (CABP) refers to CAP specifically caused by bacteria
- ❑ Ambulatory CAP (also known as walking pneumonia) is most common among young adults and is usually due to atypical CAP pathogens.

# CAP Pathogens

## Community acquired bacterial pneumonia (CAPB)

- New FDA designation created to better identify individuals most likely to have bacterial pneumonia, therefore benefit from antimicrobial therapy

### Typical CABP Pathogens

Streptococcus pneumoniae, Haemophilus influenza and Moraxella catarrhalis

- Account for 85% for all CABP
- Strep pneumo alone accounts for approx. 30-40% of CABP cases in US adults and 40-60% of patients > 65 years old

### Atypical CABP Pathogens

Mycoplasma pneumonia, Legionnaires disease and Chlamydia pneumonia

- Account for the majority of remaining cases of CABP
- Mycoplasma is epidemic in nature and is more common in younger patients

# Epidemiology

## Community acquired pneumonia

- 7-10 million cases/yr. with up to 1 million admissions
- 5-7% case fatality rate, higher in the elderly
- Costs of treating CAP exceeds \$17 billion/yr<sup>1</sup>.

## Pneumococcal bacteremia

- 12,000 cases/yr. in the US
- 20% case fatality rate, up to 60% among the elderly

1. Woolfrey KG. Pneumonia in adults: the practical emergency department perspective. Emerg Med Clin North Am. 2012; 30(2):249-70.

# Epidemiology

- ▣ In the United States, the annual incidence of CAP is approximately 5 million people with almost 75% of these cases being treated on an outpatient basis.
- ▣ Pneumonia is the second leading cause of hospitalization and is the 7th leading cause of death claiming more lives than breast or prostate cancer.<sup>2</sup>
- ▣ Pneumonia is the #1 cause of death due to infection.
- ▣ Pneumonia is responsible for approximately 3.2 million emergency department visits, 2.6 million hospitalizations, and 4.5 million ambulatory care visits.

2. Pfunter A, Wier LM, Stocks C. Most frequent conditions in U.S. hospitals, 2010. HCUP Statistical Brief #148. Accessed 15 July 2016.

# Presentation

- ▣ A sputum-producing cough is the most common presenting symptom and the color of the sputum may assist the clinician in determining the offending pathogen

| <b>Table 2. CAP pathogens identified by sputum color</b> |                     |
|----------------------------------------------------------|---------------------|
| <b>Pathogen</b>                                          | <b>Sputum color</b> |
| <i>Streptococcus pneumoniae</i>                          | Rust                |
| <i>Pseudomonas</i>                                       | Green               |
| <i>Haemophilus</i>                                       | Green               |
| Pneumococcal species                                     | Green               |
| Klebsiella species                                       | Red                 |
| Anaerobic species*                                       | Multicolored        |

\*Sputum is often foul smelling and bad tasting.

# Signs & Symptoms

- ▣ Incubation period typically 1-3 days
- ▣ Symptoms may include:
  - • Abrupt onset of fever and chills, or rigors
  - • Productive cough – mucopurulent, rusty sputum
  - • Dyspnea
  - • Tachypnea
  - • Hypoxia
  - • Tachycardia
  - • Malaise
  - • Weakness

**Table 3. Physical examination findings in CAP**

|                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Adventitious breath sounds (rales/crackles, rhonchi, wheezes)</li><li>• Decreased intensity of breath sounds</li><li>• Egophony</li><li>• Whispering pectoriloquy</li><li>• Dullness to percussion</li></ul> | <ul style="list-style-type: none"><li>• Tracheal deviation</li><li>• Lymphadenopathy</li><li>• Pleural friction rub</li><li>• Bradycardia<sup>a</sup></li><li>• Periodontal disease<sup>b</sup></li><li>• Bullous myringitis<sup>c</sup></li><li>• Cutaneous nodules<sup>d</sup></li><li>• Decreased gag reflex<sup>e</sup></li></ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

<sup>a</sup>May indicate *Legionella* etiology.

<sup>b</sup>May indicate an anaerobic and/or polymicrobial infection.

<sup>c</sup>May indicate a *Mycoplasma pneumonia* infection.

<sup>d</sup>May indicate a *Nocardia* infection.

<sup>e</sup>Suggests risk for aspiration pneumonia.

**Table 1. Risk factors for CAP**

- Lung disease (asthma, chronic obstructive pulmonary disease, cystic fibrosis, bronchiectasis)
- Diabetes
- Heart failure
- Chronic renal disease
- Chronic hepatic disease
- Sickle cell anemia
- Compromised immune system
- Decreased cough reflex or swallowing problems
- Influenza
- Smoking
- Alcohol abuse
- Homelessness
- Malnourished
- Recent cold or flu
- Chemical, pollutants or toxic fume exposure

## Table 4. Differential diagnosis in CAP

- Asthma
- Atelectasis
- Bronchiectasis
- Bronchiolitis
- Bronchitis
- Chronic obstructive pulmonary disease
- Foreign body aspiration

- Fungal pneumonia
- Lung abscess
- Pneumocystis jiroveci pneumonia
- Respiratory failure
- Viral pneumonia
- Neoplasm

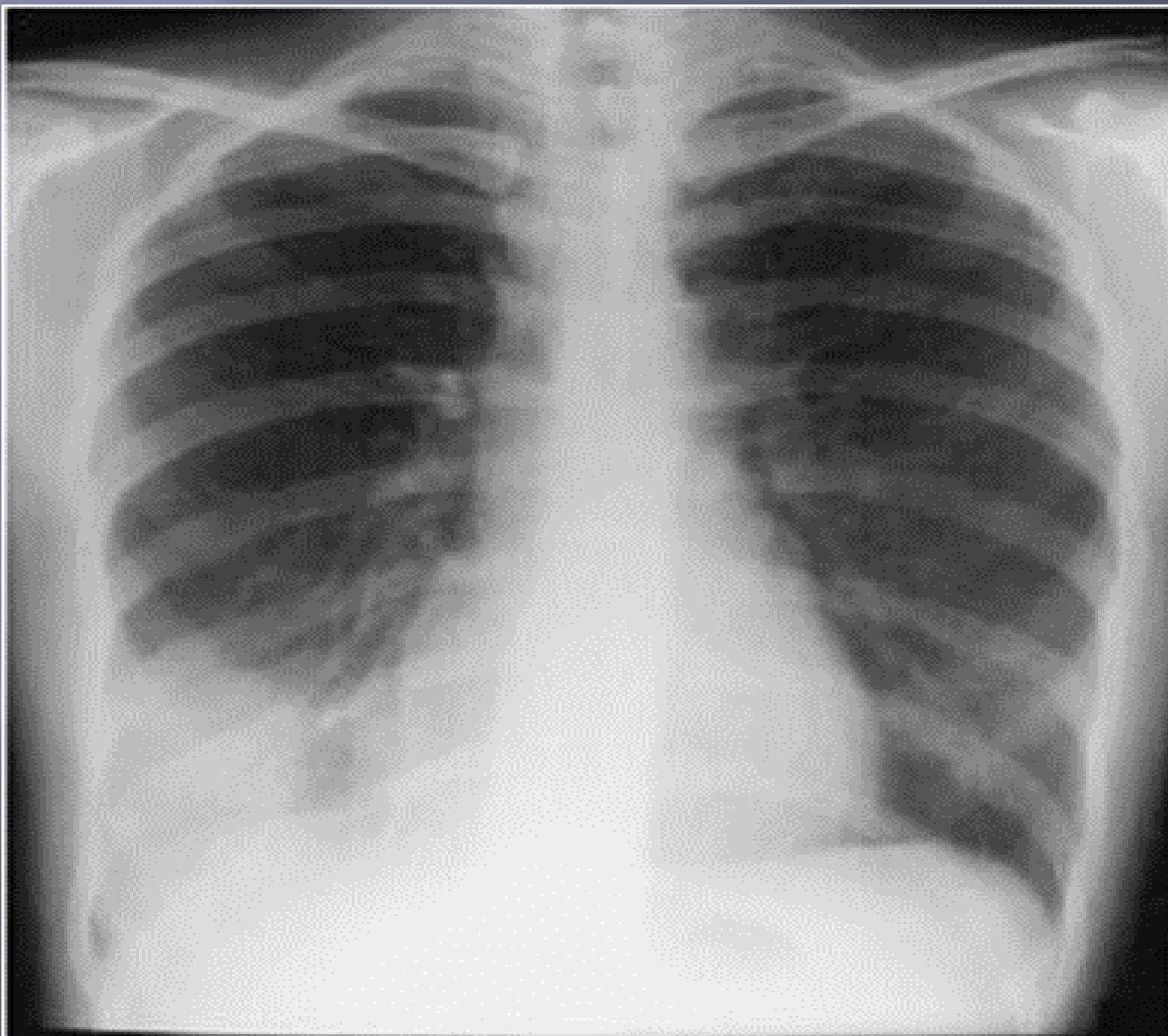
# 7 Deadly Causes of Chest Pain

- ▣ Many patients who present with pneumonia may also have chest pain. Although it may be pleuritic in nature – other deadly causes should also be considered:
  - ▣ 1. Tension pneumothorax (persistent cough)
  - ▣ 2. Pulmonary embolus (immobility)
  - ▣ 3. Myocardial infarction (metabolic and cardiopulmonary stress)
  - ▣ 4. Cardiac tamponade, pericardial effusion
  - ▣ 5. Aortic dissection/aneurysm (tachycardia, elevated BP)
  - ▣ 6. Ruptured esophagus (vomiting)
  - ▣ 7. Pneumonia

# Diagnostic Aids

- ▣ Chest radiography is indicated in all patients with suspected CAP to confirm the presence of an infiltrate and help exclude other diagnoses.
- ▣ Chest x-rays are considered the standard method for diagnosing the presence of pneumonia---the presence of an infiltrate confirms the diagnosis.
- ▣ Despite that, it must be noted that the accuracy of plain chest radiography for detecting pneumonia decreases depending on the setting of infection.
- ▣ CAP does not always appear on chest x-rays because the disease may be in its initial stages or involves a part of the lung that an x-ray does not see well.<sup>3</sup>
- ▣ It is wise to consider a repeat chest x-ray in 24 hours if there is a high clinical suspicion for CAP.

3. Hagaman, Jared T., Ralph J. Panos, Gregory W. Rouan, and Ralph T. Shipley. "Admission Chest Radiograph Lacks Sensitivity in the Diagnosis of Community-Acquired Pneumonia." *The American Journal of the Medical Sciences* 337.4 (2009): 236-40. Web.



# Lab Testing

- ▣ Laboratory tests may include a serum chemistry panel and complete blood count (CBC) with differential.
- ▣ CBC results may reveal leukocytosis with a left shift in a bacterial infection, yet its' absence (particularly in elderly patients) should not cause the clinician to discount the possibility of a bacterial infection as leukopenia may be a clinical sign of impending sepsis.
- ▣ Hospital/ER testing may also include ABG, Blood and/or sputum cultures, and other tests to confirm the diagnosis or explore differential diagnoses

# Reasons to Consider Biomarkers in Pneumonia

1. Sometimes, the clinical signs of pneumonia can be elusive, especially in the elderly. The faster the diagnosis is reached, the earlier the treatment can begin. Biomarkers may prove to be useful in the diagnosis of Pneumonia
2. Biomarkers can be any biomolecule that is associated with a particular pathological or physiological state. Ideally, a biomarker should be one which cannot be detected or whose value is very low in the absence of inflammation but it should rise with increasing inflammatory processes and should decrease with resolving inflammation.
3. Clinicians and researchers are becoming more interested in the use of biomarkers since historically there has been no “gold standard” which is both sensitive and specific enough to help them reach the diagnosis and preferably the offending pathogen. Historically, only 30% of patients with radiologically confirmed CAP do not have the causative organism identified due to poor sensitivity and sensitivity of blood and sputum cultures
4. Procalcitonin has and is being studied as a potential biomarker for pneumonia and is already used quite extensively in Europe

# Strep Pneumo Urine Antigen Testing (UAT)

- ▣ According to the most recent IDSA guidelines: “Patients with CAP should be investigated for specific pathogens that would significantly alter standard management decisions, when the presence of such pathogens is suspected on the basis of clinical and epidemiologic clues”<sup>4</sup>
- ▣ Point-of-care *s. pneumoniae* urinary antigen testing can also be a useful adjunct in confirming the presence of pneumococcal CAP.
- ▣ This test is non invasive, relatively inexpensive, accurate, and results can be obtained within 15 minutes.
- ▣ Knowing the specific pathogen can optimize treatment by targeting therapy for that infection and help reduce the inappropriate use of antibiotics.

4. Mandell, L. A., Wunderink, R. G., Anzueto, A., Bartlett, J. G., Campbell, G. D., Dean, N. C., . . . Whitney, C. G. (2007). Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clinical Infectious Diseases*, 44(Supplement 2).

# Advantages of Strep Pneumo Urine Antigen Testing

- ▣ Rapidity (approx 15 minutes)
- ▣ Simplicity (non-invasive)
- ▣ Ability to detect pneumococcal pneumonia even after antibiotic therapy has been initiated
- ▣ Increases percentage of diagnosed patients by 25%
- ▣ Less than 50% of pneumococcal UAT positive patients can be diagnosed by conventional methods such as:
  - Blood cultures
  - Sputum culture

# Strep Pneumo UAT Indications

- ▣ The Infectious Disease Society of American (IDSA) has outlined clinical indications for Strep Pneumo UAT testing.
- ▣ Specifically, the IDSA recommends Strep Pneumo UAT testing for patients with the following clinical indications:<sup>5</sup>
  1. Outpatient antibiotic therapy failure
  2. Leukopenia
  3. Active alcohol abuse
  4. Severe liver disease
  5. Asplenia
  6. Pleural effusion
  7. Intensive care unit admission

**Table 5. Clinical indications for more extensive diagnostic testing**

| Indication                                 | Blood culture | Sputum culture | <i>Legionella</i> UAT | Pneumococcal UAT | Other          |
|--------------------------------------------|---------------|----------------|-----------------------|------------------|----------------|
| Intensive care unit admission              | X             | X              | X                     | X                | X <sup>a</sup> |
| Failure of outpatient antibiotic therapy   |               | X              | X                     | X                |                |
| Cavitary infiltrates                       | X             | X              |                       |                  | X <sup>b</sup> |
| Leukopenia                                 | X             |                |                       | X                |                |
| Active alcohol abuse                       | X             | X              | X                     | X                |                |
| Chronic severe liver disease               | X             |                |                       | X                |                |
| Severe obstructive/structural lung disease |               | X              |                       |                  |                |
| Asplenia (anatomic or functional)          | X             |                |                       | X                |                |
| Recent travel (within past 2 weeks)        |               |                | X                     |                  | X <sup>c</sup> |
| Positive <i>Legionella</i> UAT result      |               | X <sup>d</sup> | NA                    |                  |                |
| Positive pneumococcal UAT result           | X             | X              |                       | NA               |                |
| Pleural effusion                           | X             | X              | X                     | X                | X <sup>e</sup> |

NA=not applicable, UAT=urinary antigen test

<sup>a</sup> Endotracheal aspirate if intubated, possibly bronchoscopy or nonbronchoscopic bronchoalveolar lavage.

<sup>b</sup> Fungal and tuberculosis cultures.

<sup>c</sup> See Table 8 for details.

<sup>d</sup> Special media for *Legionella*.

<sup>e</sup> Thoracentesis and pleural fluid cultures.

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults Clinical Infectious Diseases. 2015; 44(Suppl 2). Used with permission.

# Strep UAT Sensitivity/Specificity

- ▣ Strep UAT sensitivity: 86%    Rare false negative results
- ▣ Strep UAT specificity: 94%    Rare false positive results
- ▣ Blood culture sensitivity: 10-30%    Many false negative results
- ▣ Sputum culture: poor sensitivity and specificity
  
- ▣ The higher the sensitivity, the less likelihood of false positive results
- ▣ The higher the specificity, the less likelihood of false negative results

# Strep Pneumo Targeted Therapy

Narrowing the antimicrobial spectrum to penicillin or amoxicillin

De-escalation: withdrawal of macrolides in patients empirically treated with beta-lactams and macrolide combination

Studies have suggested that a targeted therapy for pneumococcus is a valid strategy to treat patients with CABP<sup>6</sup>

# Center for Disease Dynamics, Economics, & Policy Study<sup>7</sup>

- ▣ What many people may not realize is that bacterial infections—acquired during or while recovering from the flu—can sometimes be the culprits of serious infection rather than the flu virus itself.
- ▣ The new CDDEP study, used the results from 27 different studies and found that the rate of bacterial co-infection in hospital inpatients was between 11 and 35 percent in most studies.
- ▣ The most common bacteria responsible for co-infection were *Streptococcus pneumoniae* (the main cause of community-acquired pneumonia) and *Staphylococcus aureus*

7. Klein, Eili Y., Bradley Monteforte, Alisha Gupta, Wendi Jiang, Larissa May, Yu-Hsiang Hsieh, and Andrea Dugas. "The Frequency of Influenza and Bacterial Coinfection: A Systematic Review and Meta-analysis." *Influenza Other Respi Viruses Influenza and Other Respiratory Viruses* (2016)

# Center for Disease Dynamics, Economics, & Policy study excerpted below<sup>7</sup>

- ▣ The symptoms of CAP overlap with influenza (think fever, cough, lethargy and so on). Despite the fact that antibiotics are completely useless against the flu virus alone, many doctors prescribe antibiotics just in case there is a bacterial co-infection.
- ▣ We may have to change the way we think about co-infection. Though it is important for doctors to diagnose and properly treat them, bacterial testing should be the norm, even if patients are started presumptively on antibiotics before lab test results are available.”<sup>1</sup>

7. Klein, Eili Y., Bradley Monteforte, Alisha Gupta, Wendi Jiang, Larissa May, Yu-Hsiang Hsieh, and Andrea Dugas. "The Frequency of Influenza and Bacterial Coinfection: A Systematic Review and Meta-analysis." *Influenza Other Respi Viruses Influenza and Other Respiratory Viruses* (2016)

# Legionella Considerations

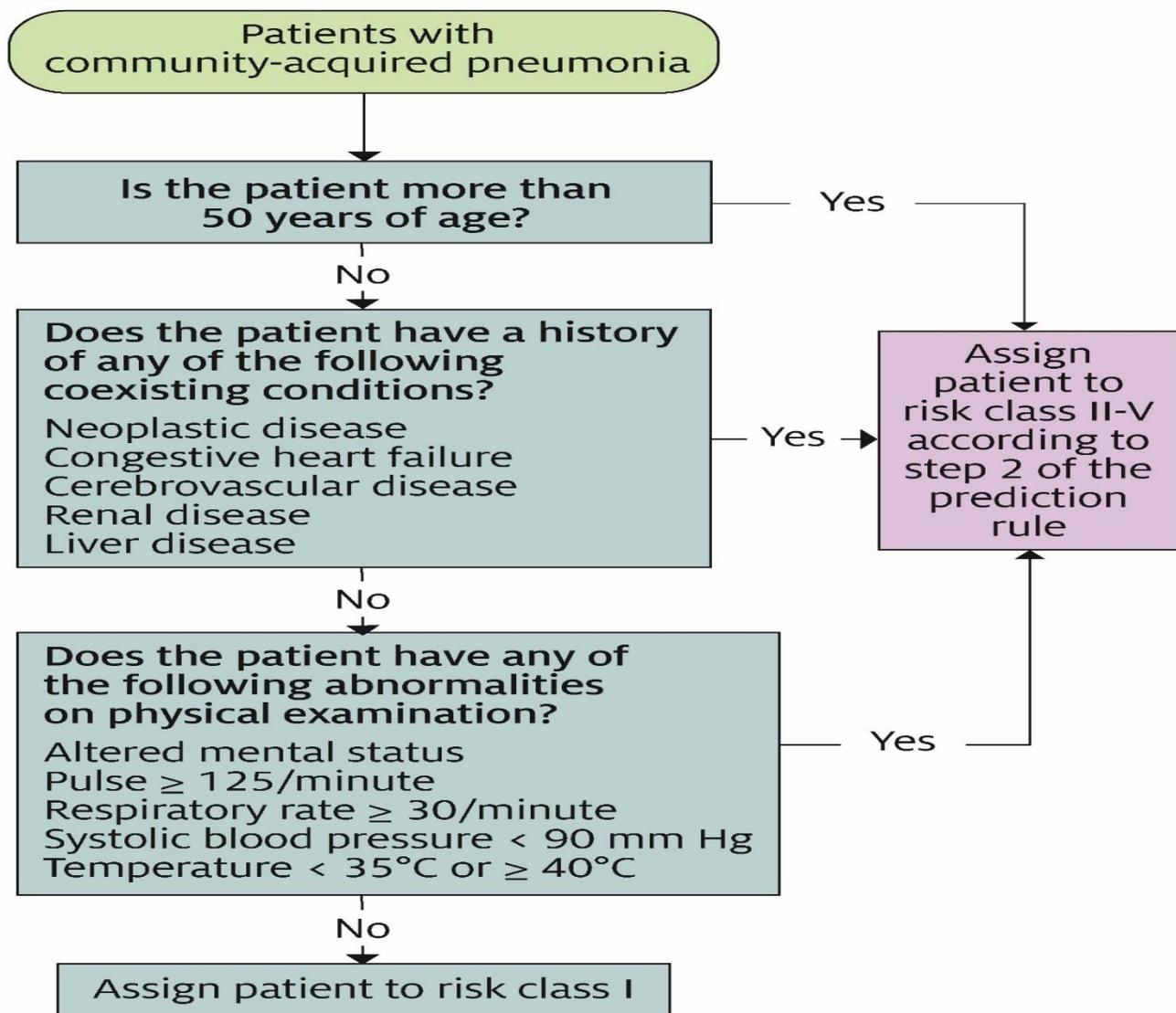
- ▣ The possibility of Legionella infection should also be considered when evaluating CAP, because delayed treatment significantly increases mortality.
- ▣ Clinical features of Legionnaires' disease are similar to other causes of CAP but often include gastrointestinal symptoms.
- ▣ Recent cruise travel or hotel stays should prompt consideration of legionella
- ▣ The only way to clearly identify if a patient's CAP is due to legionella is by ordering specific testing

# Legionella

- ▣ IDSA guidelines outline the following indications that warrant legionella testing include:
  - a. Patients who have failed outpatient antibiotic therapy for CAP
  - b. Patients with severe pneumonia, in particular those requiring intensive care
  - c. Immunocompromised patients with pneumonia
  - d. Patients with pneumonia in the setting of a Legionnaires' disease outbreak
  - e. Patients with a travel history within 2 weeks before the onset of illness

The preferred diagnostic tests for Legionnaires' disease are culture of lower respiratory secretions on selective media and the Legionella urinary antigen test. The urinary antigen test detects Legionella pneumophila serogroup 1, the most common cause of Legionnaires' disease.

**Table 6. Pneumonia Severity Index Scoring System**



Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997; 243-50. Used with permission.

## Risk Stratification and Point of Care Decision Making<sup>8</sup>

8. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, Kapoor WN. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997 Jan 23;336(4):243-250.

**Table 7. Classifications of Pneumonia Risk**

| Characteristic                                              | Points Assigned*    |
|-------------------------------------------------------------|---------------------|
| <b>Demographic Factor</b>                                   |                     |
| Age                                                         |                     |
| Men                                                         | +Age (in years)     |
| Women                                                       | +Age (in years) –10 |
| Nursing home resident                                       | +10                 |
| <b>Coexisting Illnesses</b>                                 |                     |
| Neoplastic disease <sup>†</sup>                             | +30                 |
| Liver disease <sup>‡</sup>                                  | +20                 |
| Congestive heart failure <sup>§</sup>                       | +10                 |
| Cerebrovascular disease <sup>  </sup>                       | +10                 |
| Renal disease <sup>¶</sup>                                  | +10                 |
| <b>Physical Examination Findings</b>                        |                     |
| Altered mental status <sup>#</sup>                          | +20                 |
| Respiratory rate $\geq$ 30/min                              | +20                 |
| Systolic blood pressure < 90 mmHg                           | +20                 |
| Temperature < 35°C or $\geq$ 40°C                           | +15                 |
| Pulse $\geq$ 125/min                                        | +10                 |
| <b>Laboratory and Radiographic Findings</b>                 |                     |
| Arterial pH < 7.35                                          | +30                 |
| Blood urea nitrogen $\geq$ 30 mg/dL (11 mmol/L)             | +20                 |
| Sodium < 130 mmol/L                                         | +20                 |
| Glucose $\geq$ 250 mg/dL (14 mmol/L)                        | +10                 |
| Hematocrit < 30%                                            | +10                 |
| Partial pressure of arterial oxygen < 60 MmHg <sup>**</sup> | +10                 |
| Pleural effusion                                            | +10                 |

\*A total point score for a given patient is obtained by adding the patient's age in years (age minus 10 (–10), for females) and the points for each applicable patient characteristic. Points assigned to each predictor variable were based on coefficients obtained from the logistic regression model used in step 2 of the prediction rule.

<sup>†</sup>Any cancer, except basal or squamous cell cancer of the skin, that was either active at the time of presentation or diagnosed within 1 year of presentation.

<sup>‡</sup>A clinical or histologic diagnosis of cirrhosis or other form of chronic liver disease, such as chronic active hepatitis.

<sup>§</sup>Systolic or diastolic ventricular dysfunction documented by history and physical examination, as well as chest radiography, echocardiography, MUGA scanning, or left ventriculography.

<sup>||</sup>A clinical diagnosis of stroke, transient ischemic attack, or stroke documented by MRI or CT scan.

<sup>¶</sup>A history of chronic renal disease or abnormal blood urea nitrogen and creatinine values documented in the medical record.

<sup>#</sup>Disorientation (to person, place, or time, not known to be chronic), stupor, or coma.

<sup>\*\*</sup>In the pneumonia PORT cohort study, an oxygen saturation value < 90% on pulse oximetry or intubation before admission was also considered abnormal.

## PORT Scoring System<sup>8</sup>

Total Score <70 = Risk Class II

Total Score 71-90 = Risk Class III

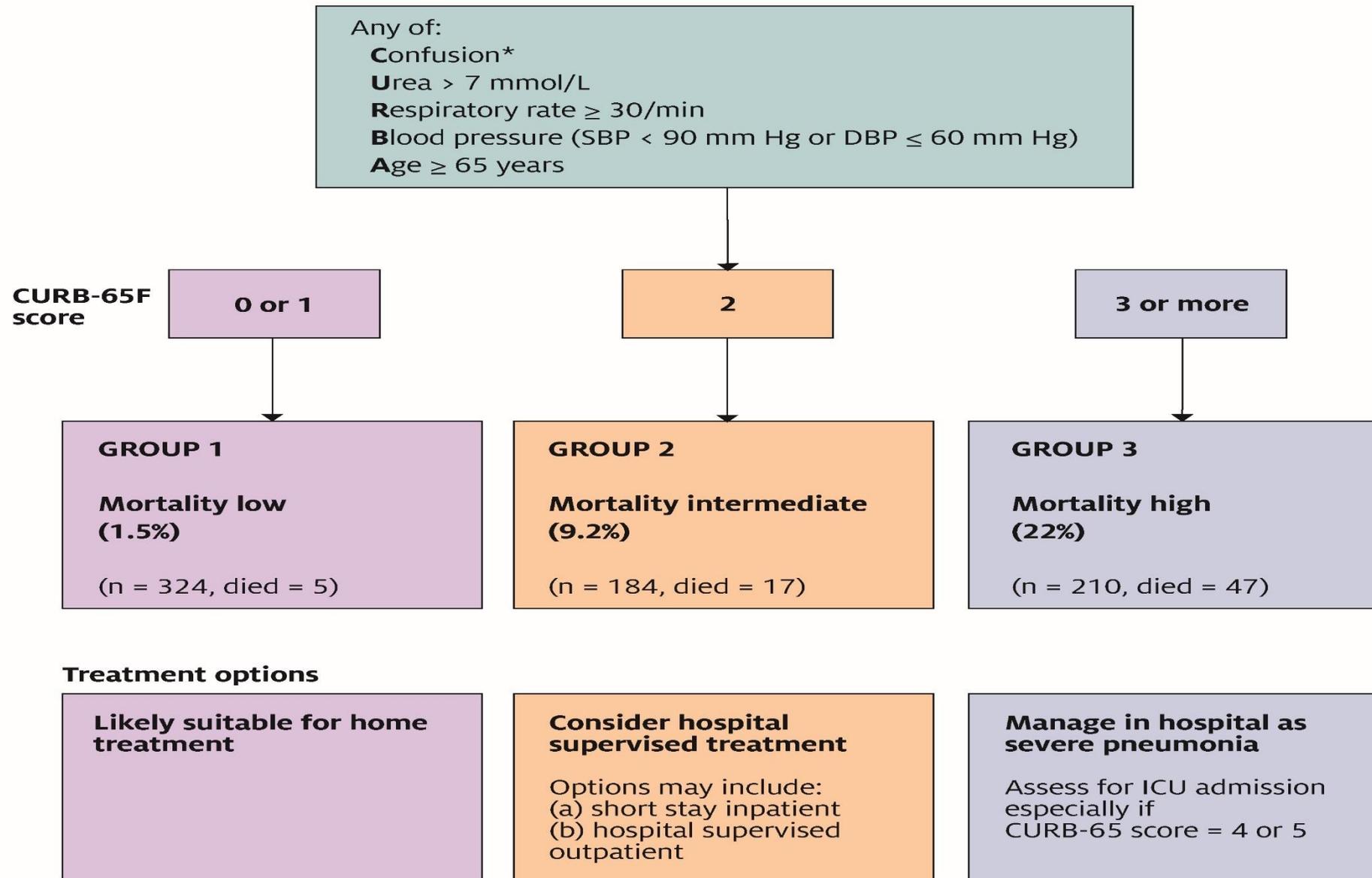
Total Score 91-130 = Risk Class IV

Total Score >130 = Risk Class V

PORT and CURB 65 scores used to determine the point of care for treatment – home vs hospital vs ICU

8. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, Kapoor WN. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997 Jan 23;336(4):243–250.

**Table 8. The CURB-65 Scale**



\* defined as a Mental Test Score of 8 or less, or new disorientation in person, place or time

Lim WS. Defining community acquired pneumonia severity on presentation to hospital: an international deviation and validation study. *Thorax*. 2003; 377-82. Used with permission.

# CAP Treatment

Summary\* of 2007 IDSA/ATS (Infectious Disease Society of America/American Thoracic Society) guidelines for outpatient treatment of community-acquired pneumonia:

| Conditions                                                                                                                                                                                                                                                  | Recommended treatment                                                                                             | Further detail                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Previously healthy <i>and</i> no risk factors for DRSP                                                                                                                                                                                                      | Macrolide (preferred) or doxycycline                                                                              | Macrolides: azithromycin, clarithromycin, or erythromycin                                                                                    |
| Co-morbidities, <i>including</i> :<br>1. Chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions; or use of immunosuppressing drugs<br>2. Use of antibiotics in previous 3 months | Either respiratory fluoroquinolone or $\beta$ -lactam <i>plus</i> macrolide (or doxycycline instead of macrolide) | Fluoroquinolones: moxifloxacin, gemifloxacin, or levofloxacin<br>Preferred $\beta$ -lactam: high-dose amoxicillin or amoxicillin-clavulanate |
| Region with >25% infection rate with macrolide-resistant <i>S. pneumonia</i>                                                                                                                                                                                | Consider the non-macrolide alternatives for above                                                                 |                                                                                                                                              |

\*\*\*IMPORTANT\*\*\*: In regions with a high rate (>25%) of infection with high-level macrolide-resistant *S. pneumoniae*, consider the use of alternatives including those without comorbidities.

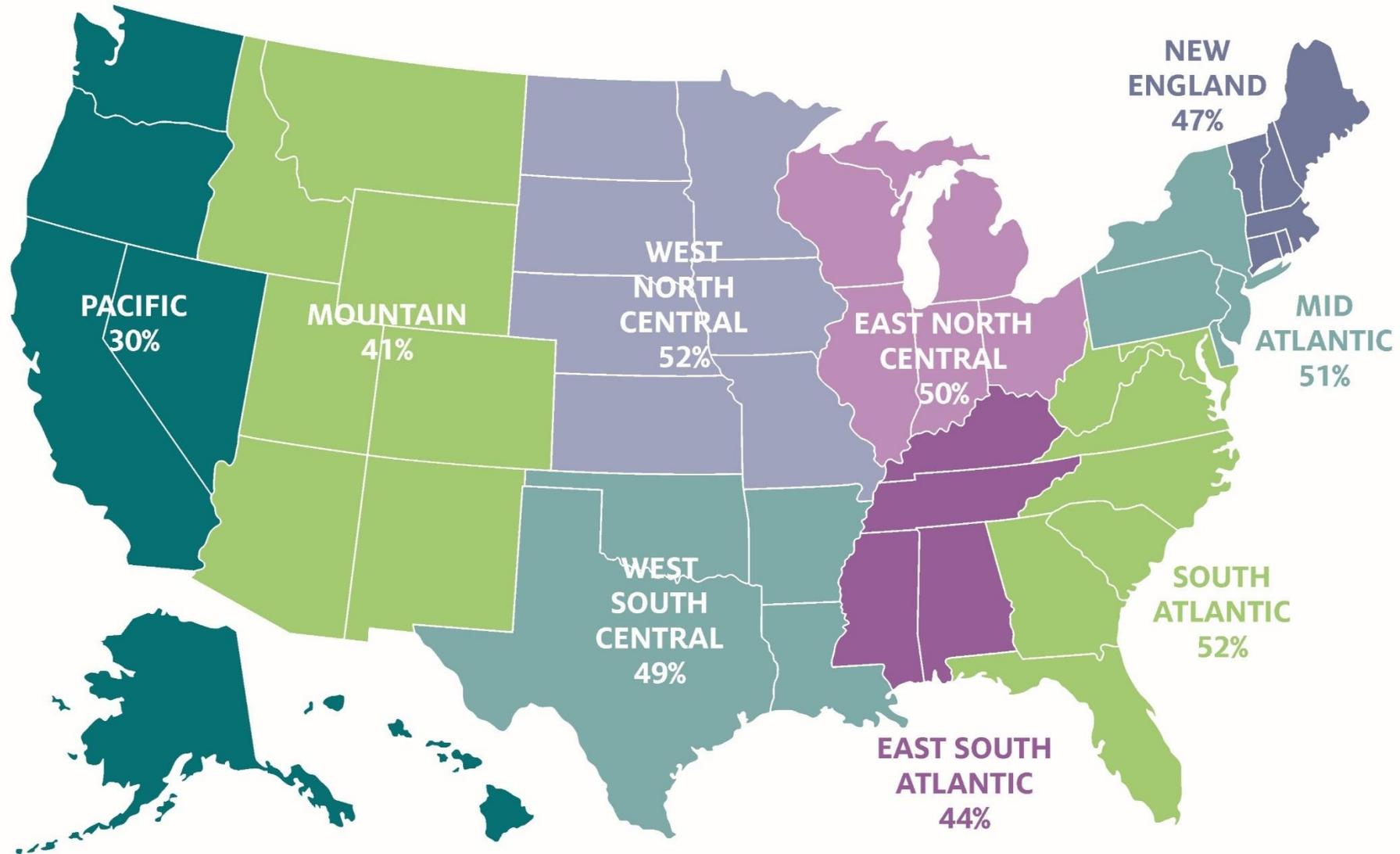
# CAP Treatment

- ▣ Along with local resistance rates, it is important that antibiotic selection decision making includes taking into account the patient's risk factors for possible infection with DRSP, which are listed below:

**Table 9. Risk factors for possible DRSP infection**

- |                                                                                                                                                                                                    |                                                                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Recent antibiotic use (within 3 months)</li><li>• Age &gt; 65 years</li><li>• Immunosuppressive illness</li><li>• Multiple medical comorbidities</li></ul> | <ul style="list-style-type: none"><li>• Exposure to a child attending a daycare center</li><li>• Alcohol abuse</li><li>• Asthma/COPD</li><li>• Diabetes mellitus</li></ul> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Figure 1. *S. Pneumoniae* Macrolide resistance map



Compiled from: [http://www.cddep.org/projects/resistance\\_map/macrolide\\_resistant\\_Streptococcus\\_pneumoniae](http://www.cddep.org/projects/resistance_map/macrolide_resistant_Streptococcus_pneumoniae)

# Important CAP Treatment Considerations

- ▣ With Strep Pneumo macrolide resistance rates >25% in all regions of the country, if the IDSA recommendations are correctly followed then current macrolides like azithromycin should not be used as monotherapy for CAP
- ▣ There are greater than 50,000,000 azithromycin prescriptions annually in the US (YES, that is 50 Million) many for CAP monotherapy
- ▣ IDSA guidelines call for CAP monotherapy to include either doxycycline or the fluoroquinolone class.
- ▣ In July of 2011<sup>9</sup> the FDA issued new warnings on the fluoroquinolone class in regard to disabling side effects involving tendons, muscles, joints, nerves, and the central nervous systems and declared that the risk of these side effects outweigh the benefits for patients with acute bacterial sinusitis, acute exacerbation of chronic bronchitis, and uncomplicated urinary tract infections.<sup>9</sup>

9.

# CAP Treatment

- ▣ Response to antibiotic therapy should be evaluated within 48-72 hours of treatment initiation.
- ▣ However, antibiotics should not be changed within the first 72 hours unless marked clinical deterioration occurs or the causative pathogen is identified.
- ▣ Chest x-rays usually clear within four weeks in patients < 50 years old, yet resolution may be delayed for 12 weeks or longer in older individuals.
- ▣ Patients of any age who remain symptomatic should undergo follow-up imaging.

# Strep Pneumo & Influenza

- ❑ CABP together with influenza remains the 7<sup>th</sup> leading cause of death in the US
- ❑ *S. pneumoniae* is the leading cause of pneumonia in those co-diagnosed with influenza and leads to higher morbidity and mortality.
- ❑ A common misperception is that influenza alone has a high mortality rate--- which may be due to public health campaigns that use alarming influenza yearly death counts presumably with the noble goal of encouraging people to get their yearly influenza vaccination.
- ❑ Complications are what cause the majority of morbidity and mortality in influenza and pneumonia is the leading significant complication of influenza.

## Table 10. *S. pneumonia* patients with higher morbidity and mortality with co-diagnosis of influenza

- Adults > 65 years of age
- Pregnant or post-partum (within 2 weeks after delivery) women
- Persons  $\leq$  19 years of age receiving long-term aspirin therapy
- American Indians and Alaska Natives
- Morbidly obese (i.e., body mass index  $\geq$  40)
- Residents of nursing homes and other chronic care facilities
- Immunosuppressed persons
- Chronic pulmonary (including asthma) disease
- Renal, hepatic, and/or hematological (including sickle cell) disease
- Cardiovascular (except hypertension) disease
- Metabolic disorders (including diabetes mellitus)
- Neurologic and neurodevelopment conditions (including disorders for the brain, spinal cord, peripheral nerve and muscle, epilepsy, stroke, intellectual disability [e.g., mental retardation])
- Moderate to severe development delay, muscular dystrophy, or spinal cord injury

# Strep Pneumo & Influenza

- ▣ Having influenza is a predisposing factor for acquiring Strep pneumo, esp. in older adults – some consider running a flu test and Strep pneumo UAT together during the typical respiratory season. It is common practice in patients hospitalized with influenza
- ▣ Influenza contributes to respiratory epithelial cell destruction and death.
- ▣ Propagation of the virus in the respiratory tract impairs clearance of bacteria and allows for increased bacterial adherence and invasion.<sup>10</sup>

10. Plotkowski MC, Puchelle E, Beck G, Jacquot J, Hannoun C. Adherence of type I streptococcus pneumoniae to tracheal epithelium of mice infected with influenza A/PR8 virus. Am Rev Respir Dis. 1986;134(5):1040-1044

# Strep Pneumo and Influenza- A “Can’t Miss” Combination

- ▣ Historical review of the 1918-19 influenza pandemic suggests that the majority of deaths were not a direct effect of the influenza virus---they were from bacterial co-infection causing pneumonia.<sup>11</sup>
- ▣ This remains true today and, for this reason, urgent care physicians treating patients with influenza need to have a high clinical suspicion for pneumonia.
- ▣ It is a co-infection that we cannot afford to miss.
- ▣ Between 1979-2009 there were an average of 66,000 deaths per year attributable to co-infection with influenza and pneumonia.
- ▣ Other complications may include bacteremia, sepsis, empyema, pericarditis, respiratory failure, and death.
- ▣ Bacterial co-infection is more common in the elderly, the very young, pregnant women, patients with preexisting conditions, and morbidly obese patients.

11. Morens DM, Taubenberger JK, Fauci AS. Predominant Role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. *J Infect Dis.* 2008; 198(7): 962-970

# Pneumococcal Vaccination

- ▣ Most pneumococci are encapsulated with complex capsular polysaccharides. These polysaccharides are antigenic and form the basis for classifying pneumococci by serotypes.
- ▣ There were 92 serotypes documented as of 2011. In recent years these polysaccharides have been used to develop effective pneumococcal vaccines.
- ▣ Pneumococci are common asymptomatic inhabitants of the nasopharynx and 20-60% of school aged children are colonized
- ▣ 5-10% of adults are colonized and up to 50-60% of service personnel
- ▣ High carriage rates in children can contribute to high false positive rates of Strep Pneumo UAT testing in that population

# Pneumococcal Vaccines

- ▣ Between 2004 and 2040, as the population is expected to increase by 38%, pneumococcal pneumonia hospitalizations rates will likely double as population growth is fastest in older age groups who experience the highest rates of pneumococcal disease.<sup>12</sup>
- ▣ This is despite current efforts to increase pneumococcal Vax rates.
- ▣ Current recommendation to give both PPSV23 and PCV13 (PREVNAR 13). Adherence to a two-vaccine regimen is likely to be poorer than adherence to a one-vaccine regimen
- ▣ In addition, only 63% of adults > 65 years old and < 25% of adults in other high risk groups are properly vaccinated.

12. Wroe PC, Finkelstein JA, Ray GT, et al. Aging population and future burden of pneumococcal pneumonia in the United States. *J Infect Dis.* 2012; 205(10):1589-92.

# Why Should Providers Consider Strep UAT along with Influenza?

- ▣ Cost to treat one hospitalized pneumonia patient in US = \$15,000
- ▣ Average cost Strep Pneumo UAT <\$20 per test
- ▣ If one CAP hospitalization was prevented by early detection of pneumonia and timely antibiotic therapy its cost benefit would be equal to the cost of approx 750 Strep UAT's
- ▣ could save approx. \$1,000,000 in healthcare costs
- ▣ This could benefit all sides of our health care system and is one of the reasons I believe Point of Care lab testing will continue to gain traction in the U.S and globally
- ▣ “The right diagnosis at the right time, the right drug for the right bug”

# Why Should Providers Consider Strep UAT along with Influenza?

- ▣ Vast potential for decreased morbidity and mortality for patients
- ▣ Better diagnostic capability can save lives and money
- ▣ How??? Not all cases of pneumonia will be immediately evident on initial clinical impression or initial x-ray<sup>12</sup>
- ▣ Patients with comorbid conditions are at increased risk
- ▣ Influenza particularly increases risk of pneumonia. Flu symptoms may mask the provider's suspicion of possible pneumonia.
- ▣ An accurate, simple, fast, cheap, non-invasive test.

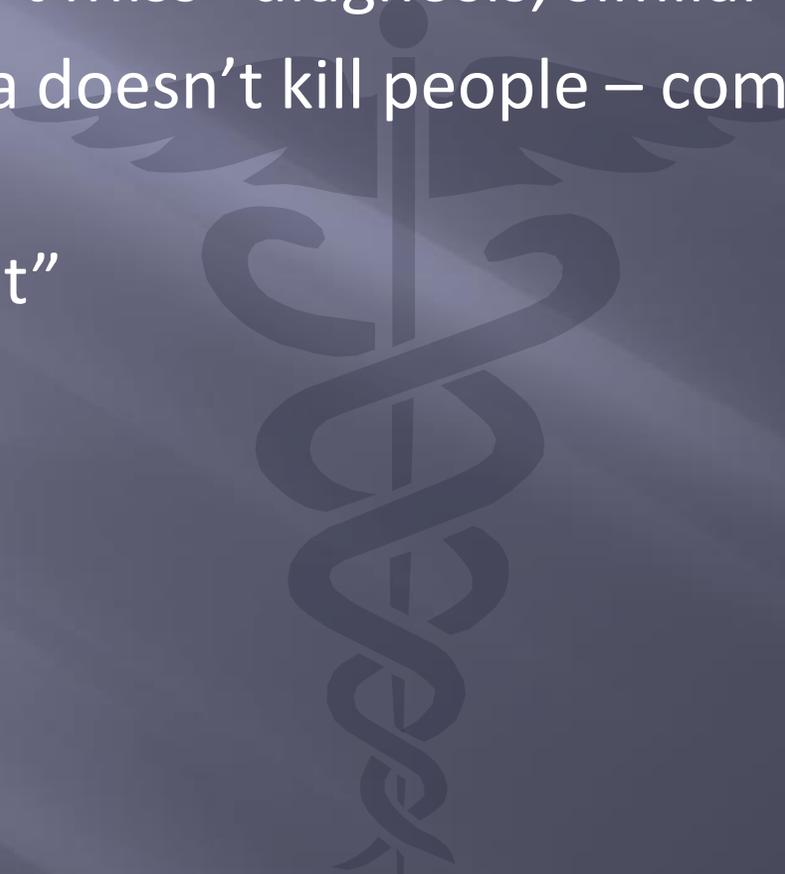
12. Basi, Sanraj K., Thomas J. Marrie, Jane Q. Huang, and Sumit R. Majumdar. "Patients Admitted to Hospital with Suspected Pneumonia and Normal Chest Radiographs: Epidemiology, Microbiology, and Outcomes." *The American Journal of Medicine* 117.5 (2004): 305-11.

# Challenges to Adoption of Strep UAT

- ▣ This is not a test you would run on every patient with an Upper Respiratory Infection or Influenza
- ▣ The value is in those patients most at risk – 65 and older and those with comorbid conditions. Many patients tested will be on Medicare
- ▣ Understand the potential pitfalls of missing even one undetected case of Strep Pneumo
- ▣ Patient follow up in Urgent Care more difficult than PCP. How many cases of pneumonia may you have missed?

# Some Things are “Can’t Miss”

- ▣ Pneumonia is a “Can’t Miss” diagnosis, similar to an MI
- ▣ Remember, Influenza doesn’t kill people – complications such as pneumonia do
- ▣ The “Merlot Moment”



# Antimicrobial Resistance

- ▣ Misuse and overuse of antibiotics is primary cause
- ▣ Per CDC, the threat level of DRSP is characterized as serious

Over 1 million drug resistant infections per year <sup>1</sup>

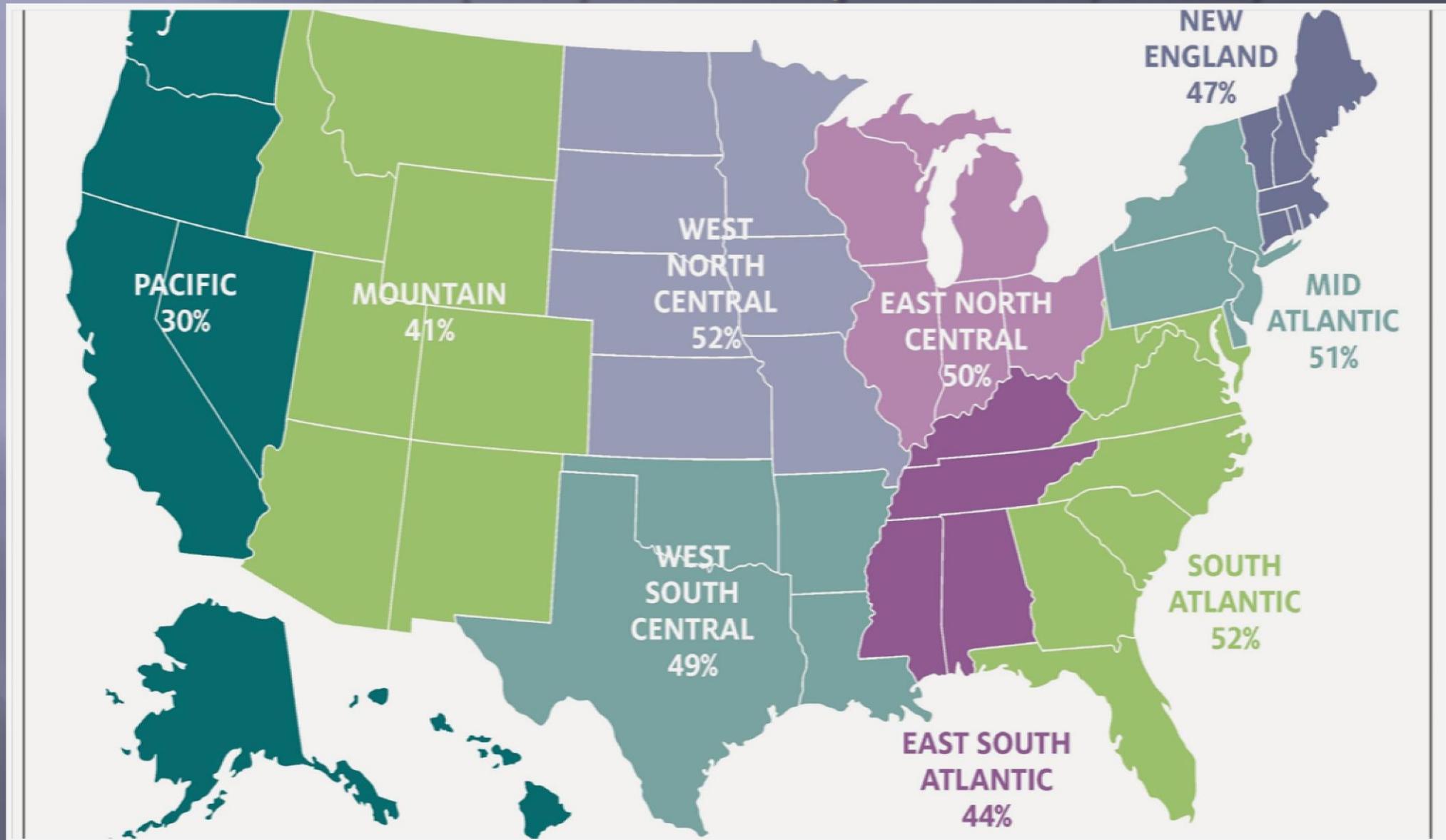
7,000 deaths per year

Public health threat

19,000 excess hospitalizations per year (\$10,000 = avg. cost per admission) <sup>13</sup>

13. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. Atlanta, GA; Centers for Disease Control and Prevention, U.S. Department of Health and Human Services.

## S. Pneumoniae Regional Resistance Rates to Macrolides (azith/clarithromycin – Z-Pak, Biaxin)



# UCAOA Position Statement on Antibiotic Stewardship

- ▣ Improving Antibiotic Stewardship in Urgent Care: Antibiotic resistance is a serious public health concern that affects patient care, safety, and healthcare costs. The Urgent Care Association of America (UCAOA) is proud to represent thousands of urgent care clinics and professionals in one of the United States most rapidly growing healthcare markets, urgent care medicine. Urgent care clinics treat more than 160 million patients each year, the vast majority of whom present with acute, infectious disease-related symptoms, such as cough, sore throat, and fever. The proportion of patients with such symptoms seen in the urgent care setting is significantly higher than those seen in traditional office based primary care and internal medicine clinics.
- ▣ As such, the UCAOA recognizes the vitally important role our clinicians can play in the responsible use and preservation of antibiotics while focusing on the health of patients. **The UCAOA is committed to ensuring urgent care medicine supports the White House National Strategy for Combatting Antibiotic-Resistant Bacteria. We will strive to meet the White House plan's year 2020 goal of reducing inappropriate outpatient antibiotic use for monitored conditions/agents by 50% from 2010 levels.** We will do so via patient education, training and education of both clinical and non-clinical staff, clinical decision support tools, data collection, evidence-based antibiotic stewardship practices and research.
- ▣ The Antibiotic Resistance Crisis: Antibiotic resistance is driven by the inappropriate use of antibiotics in humans, animals and agriculture. Leading medical and public health organizations from around the world, including the World Health Organization (WHO) and the U.S. Centers for Disease Prevention and Control (CDC), have warned of a “post-antibiotic” era in which common infections and minor injuries which have been treatable for decades can once again become deadly. The CDC and WHO consider antibiotic resistance to be an increasingly emergent threat to national and global health with potential and likely dire consequences if antibiotic use in all settings (humans, animals, and agriculture) is not reduced.

# UCAOA Statement cont.,

- ▣ The White House Combatting Antibiotic-Resistance Bacteria vision statement is included below:
- ▣ Vision: The United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic-resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections.” This vision will require all sectors of the healthcare system (hospitals, long-term care settings, primary care, urgent care, telemedicine and animal/agriculture) that prescribe or use antibiotics to do their part in finding solutions to reducing inappropriate antibiotic use and helping to preserve the utility of these life-saving drugs.
- ▣ Improving Antibiotic Stewardship in Urgent Care: As a rapidly expanding healthcare sector, urgent care provides an estimated 160 million patient visits each year. Compared to other specialties urgent care providers see a significant percentage of patients with acute, infectious disease-related symptoms. This results in both appropriate antibiotic prescribing as well as a greater opportunity for antibiotic stewardship.

# UCAOA Position Statement on Antibiotic Stewardship



- ▣ UCAOA is committed to leading the Urgent Care sector in improving its antibiotic prescription practices through the following four areas:
  - 1) Education and training: Improve provider, staff, and patient literacy on antibiotic resistance and enhance provider training on antibiotic stewardship.
  - 2) Clinical decision support: Lead the effort to provide clinical decision support technologies for Urgent Care providers through electronic health records and e-prescribing systems.
  - 3) Antibiotic use data collection: Provide guidance and support for Urgent Care practices to collect data on antibiotic use and incorporate quality control measures on inappropriate antibiotic uses.
  - 4) Evidence-based practice: Advance evidence-based stewardship practices in Urgent Care through innovative clinical research and stewardship program evaluation.

# Antibiotic Stewardship

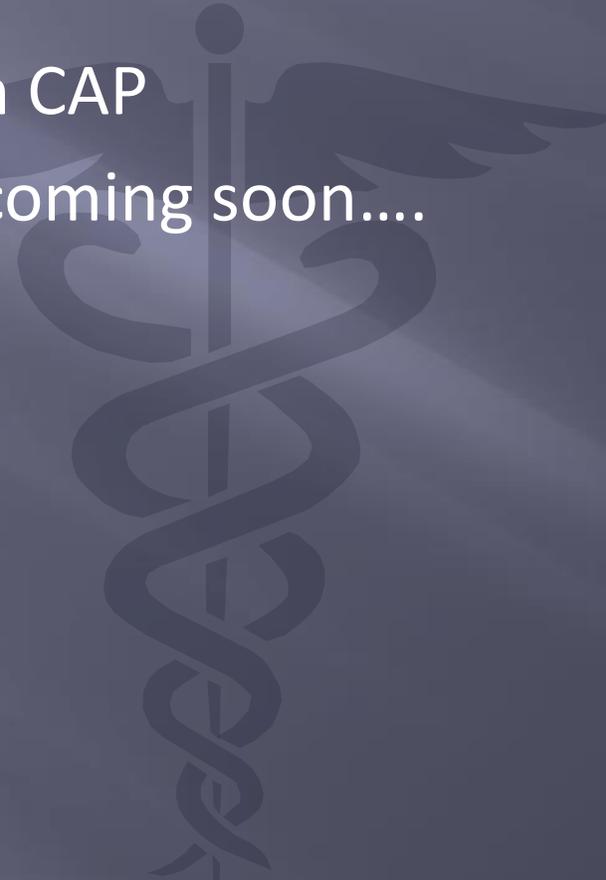
- ▣ The White House recently released its National Strategy for Combatting Antibiotic-Resistant Bacteria including the 2020 goal of reducing inappropriate outpatient antibiotic use for monitored conditions/agents by 50% from 2010 levels.
- ▣ Political/Social/Medical awareness increasing rapidly
- ▣ Studies have concluded that 30% of pneumococcal isolates are just one mutation away from fluoroquinolone resistance.
- ▣ Another study revealed that antibiotic resistant pneumonia infections more than doubled ICU admissions and increased complications by 51%.<sup>14</sup>

# Antimicrobial Stewardship

- ▣ Primary goal: optimize clinical outcomes while minimizing unintended consequences of antibiotic use
  - Toxicity
  - Selection of pathogenic organisms (i.e. *Clostridium difficile*)
  - Emergence (selection) of resistance
- ▣ Avoid unnecessary antibiotics
- ▣ Decrease length of antibiotic therapy
- ▣ De-escalate (IV to oral)
- ▣ “Right bug, right drug!” –Non culture based POC testing
- ▣ Use of local antibiograms
- ▣ New IDSA/TSA guidelines soon....

# Antibiotic Resistance

- ▣ Use of local antibiograms
- ▣ Need for new antibiotics in CAP
- ▣ New IDSA/TSA guidelines coming soon....



# Benefits of Identifying Targeted Pathogen

Reduce overuse of broad spectrum antibiotics, which may reduce selection pressure and antimicrobial resistance

Optimize antibiotic selection

Reduce adverse events

Reduce costs

# CMS Antibiotic Stewardship: Potential Guidelines

- ▣ CMS sets the table for regulation requiring antibiotic stewardship programs
- ▣ In a recently released report, the President's Council of Advisors on Science and Technology (PCAST), recommended that a regulatory requirement for antibiotic stewardship be in place by the end of 2017.

# CMS Antibiotic Stewardship: Potential Guidelines

- ❑ The hospital has written policies and procedures whose purpose is to improve antibiotic use (antibiotic stewardship)
- ❑ The hospital has designated a leader (e.g., physician, pharmacist, etc.) responsible for program outcomes of antibiotic stewardship activities at the hospital
- ❑ The hospital's antibiotic stewardship policy and procedures requires practitioners to document in the medical record or during order entry an indication for all antibiotics, in addition to other required elements such as dose and duration
- ❑ The hospital has a formal procedure for all practitioners to review the appropriateness of any antibiotics prescribed after 48 hours from the initial orders (e.g., antibiotic time out)
- ❑ The hospital monitors antibiotic use (consumption) at the unit and/or hospital level

# Conclusions

- ▣ Streptococcus pneumoniae is the most common cause of community-acquired pneumonia worldwide.
- ▣ Strep pneumo resistance to current macrolides approaching alarming levels
- ▣ Influenza is a predisposing factor for acquiring pneumonia, especially in older adults and those with comorbid conditions.
- ▣ It is important that urgent care physicians are aware of the correlation between pneumonia and influenza and how to diagnose and treat them appropriately.

# Conclusions

- ▣ Antibiotic resistance is a growing threat that urgent care providers need to be more aware of.
- ▣ The nature of our specialty makes us more likely than other outpatient-based specialties to assess patients with acute infections. This leads to higher antibiotic prescription rates than other specialties.
- ▣ Still, we must carefully evaluate the need for an antibiotic medication and join the fight to decrease the number of unnecessary antibiotic prescriptions.
- ▣ Additional diagnostic testing and pathogen identification is a consideration when appropriate pre-test indications are present.



Questions??