

Evidence-based Medicine 2009: Community Acquired Pneumonia

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Case of KPB

- 62 yr old female daycare worker presents with fever, chills, sweats and productive cough of reddish sputum for 24 hours prior to presentation
- PMHX: hyperlipidemia;
- Social history: nonsmoker; social ETOH;
- No recent travel
- Medications: lovastatin; aspirin;

Case of KPB

- Examination: T 103F; RR 28; P 138; BP 100/64
 - Oropharynx: mild erythema; EAC's, TM's normal;
 - no cervical adenopathy;
 - chest examination:
 - Symmetrical expansion
 - Resonance to percussion
 - No tracheal shift
 - Crackles present anteriorly, lower right chest
 - No wheezing; no E-A change
- O₂ saturation: 92% on room air



Case of KPB

- Considerations:
 - Pathophysiology?
 - Microbiology?
 - Classification of severity?
 - Hospitalization or ambulatory treatment?
 - Potential for antibiotic resistance? Treatment?
 - Potential for complications?

**Infectious Disease Society of America /
American Thoracic Society
Consensus Guidelines**

**Management of Community-
Acquired Pneumonia in Adults**
*Clinics Infectious Diseases, 2007;
44(2): S27-S72*

CAP: IDSA/ATS: EBM Guideline 2007

- Why use guidelines?
 - Causative agent frequently not isolated
 - Empiric therapy, based upon likely pathogens, has resulted in reduced morbidity and mortality for patients with CAP;
 - Locally adapted guidelines should be implemented to improve process of care variables and outcomes (LEVEL I evidence)

Levels of Evidence

- **Level I (high)** Evidence from well-conducted, randomized controlled trials.
- **Level II (moderate)** Evidence from well-designed, controlled trials without randomization (including cohort, patient series, and case-control studies).
 - Level II studies also include any large case series in which systematic analysis of disease patterns and/or microbial etiology was conducted, as well as reports of data on new therapies that were not collected in a randomized fashion.
- **Level III (low)** Evidence from case studies and expert opinion.

CAP: IDSA/ATS: EBM Guideline 2007

- Decision to hospitalize?
 - Severity of illness scores (e.g CURB-65) should be used to determine which patients can be treated safely as outpatients. **LEVEL I evidence**
 - CURB-65: Confusion; Uremia; Respiratory Rate; Low blood pressure; age > **65** years)

Ambulatory treatment or hospitalization? CURB-65 score (Level I evidence)

Clinical Factor	Points
Confusion?	1
Respiratory Rate ≥ 30 ?	1
BUN > 19 mg/dL **	1
Systolic BP < 90 mm OR Diastolic BP ≤ 60 mm	1
Age ≥ 65 years	1
TOTAL points	

***Am J Medicine* 2005; 118:384-92; *Thorax* 2003; 58:377-82;**

Interpretation of CURB-65

CURB-65 score	% mortality	Hospitalize?
1	0.6%	LOW Risk; consider home treatment
2	2.7%	
3	6.8%	Short inpatient hosp. <u>OR</u> closely supervised OP RX
4	14%	<u>Severe pneumonia;</u> hospitalize and consider ICU admission for close monitoring
5	27.8%	

CAP: ICU admission?

- **Major criteria**: septic shock with need for vasopressors;
Mechanical ventilation (Level II evidence)
- **Minor criteria**: (3 or more of these criteria suggest need for ICU admission—validation in process): (Level II evidence)
 - Respiratory rate >30 /min;
 - PaO₂/FiO₂ ratio <250 ;
 - Multilobar infiltrates;
 - Confusion/disorientation;
 - Uremia (BUN level, 20 mg/dL);
 - Leukopenia
 - Thrombocytopenia (platelet count, $<100,000$ cells/mm³)
 - Hypothermia (core temperature, $<36^{\circ}\text{C}$)
 - Hypotension requiring aggressive fluid resuscitation

CAP: Diagnostic testing

- Diagnostic testing remains controversial; it may be undertaken IF it is believed that it would lead to deviation from empiric, guideline-based therapy, when there is suspicion of unusual pathogens based upon clinical or epidemiological clues (Level II evidence)
- For ambulatory patients, diagnostic testing is optional (typically respond well to empirical therapy); Level III evidence)

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
Failure of outpatient antibiotic therapy		X	X	X	
Cavitary infiltrates	X	X			X
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
Positive <i>Legionella</i> UAT result		X ^d	NA		
Positive pneumococcal UAT result	X	X		NA	
Pleural effusion	X	X	X	X	X

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	<i>Streptococcus pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydia pneumoniae</i> Respiratory viruses ^a
Inpatient (non-ICU)	<i>S. pneumoniae</i> <i>M. pneumoniae</i> <i>C. pneumoniae</i> <i>H. influenzae</i> <i>Legionella</i> species Aspiration Respiratory viruses ^a
Inpatient (ICU)	<i>S. pneumoniae</i> <i>Staphylococcus aureus</i> <i>Legionella</i> species Gram-negative bacilli <i>H. influenzae</i>

NOTE. Based on collective data from recent studies [171]. ICU, intensive care unit.

^a Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza.

Risks for drug-resistant pathogens

- ***S. pneumoniae* Beta-lactam resistance**

- *Age <2 and > 65*
- *B lactam therapy within 3 mos*
- *Alcoholism*
- *Medical comorbidities*
- *Immunosuppressive therapy*
- *Exposure to child in a daycare setting*

- **CA (community acquired) MRSA**

- *Cavitary pneumonia without other risks (e.g. alcoholism; gingivitis with aspiration; seizures; esophageal motility disorders)*

Risks for drug-resistant pathogens

- *Pseudomonas aeruginosa*
 - Structural lung disease, e.g. bronchiectasis
 - Repeated COPD exacerbations with use of steroids and/or antibiotics
 - Frequent antibiotic use
 - Alcoholism

Treatment of CAP

- Ambulatory treatment
- Previously healthy; no antibiotic therapy for 3 months; no risk for DRSP:
 - A: **Macrolide: azithromycin,** clarithromycin, erythromycin** (Strong recommendation: **Level I evidence**) ** *preferred for H. influenzae*
 - B: Alternative: **Doxycycline** (Weak recommendation: **Level III evidence**)

Treatment of CAP

- **Ambulatory treatment (continued)**
- **Comorbidities, OR previous use of an antibiotic within 3 months or other risks for DRSP:**
 - **A: Respiratory fluoroquinolone: moxifloxacin, gemifloxacin, levofloxacin (750 mg); (Strong recommendation: **Level I evidence**)**
 - **B: Beta lactam PLUS macrolide (Strong recommendation: **Level I evidence**)**
 - High dose Amoxicillin (1 gm TID)
 - Amoxicillin/Clavulanate (2 gms BID)
 - Alternatives: Cefuroxime; Cefpodoxime; Ceftriaxone (500 mg BID)
 - **?Telithromycin (... Hepatotoxicity)**

Treatment of CAP

- Ambulatory treatment (continued)
- In areas where there is $>25\%$ (MIC >16) **macrolide resistance**, consider choices A and B above for individuals without comorbidities (moderate recommendation, **Level III evidence**)

Treatment of CAP

- Inpatient admission, NON-ICU
 - Respiratory fluoroquinolone: Strong recommendation: **Level I evidence**
 - Preferred choice for penicillin allergic patients
 - Beta lactam PLUS macrolide (Strong recommendation: **Level I evidence**)
 - Preferred agents: ceftriaxone; cefotaxime; ampicillin; ertapenem** for selected patients;
***activity against anaerobes, DRSP and most GNR enterics;
(awaiting more clinical experience)*
 - Doxycycline as an alternative to macrolide (Level III evidence)

Treatment of CAP

Inpatients, ICU treatment

A β -lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **plus** either azithromycin (level II evidence) **or** a respiratory fluoroquinolone (level I evidence) (strong recommendation) (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended)

If *Pseudomonas* is a consideration

An antipneumococcal, antipseudomonal β -lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg)

or

The above β -lactam plus an aminoglycoside and azithromycin

or

The above β -lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above β -lactam)

(moderate recommendation; level III evidence)

If CA-MRSA is a consideration, add vancomycin or linezolid
(moderate recommendation; level III evidence)

Case of KPB

- 62 yr old female **daycare worker** presents with fever, chills, sweats and productive cough of reddish sputum for 24 hours prior to presentation
- PMHX: hyperlipidemia;
- Social history: nonsmoker; social ETOH;
- No recent travel
- Medications: lovastatin; aspirin;
- T 103F; RR 28; P 138; BP 100/64



Choice of Treatment for KPB

- **Respiratory fluoroquinolone: moxifloxacin, gemifloxacin, levofloxacin (750 mg); (Strong recommendation: **Level I evidence**)**
- **B: Beta lactam PLUS macrolide (Strong recommendation: **Level I evidence**)**
 - High dose Amoxicillin (1 gm TID)
 - Amoxicillin/Clavulanate (2 gms BID)
 - Alternatives: Cefuroxime; Cefpodoxime; Ceftriaxone (500 mg BID)

CAP: IDSA/ATS Consensus Guidelines
Weblink

[http://www.thoracic.org/
sections/publications/statements/
pages/mtpi/idsaats-cap.html](http://www.thoracic.org/sections/publications/statements/pages/mtpi/idsaats-cap.html)

CAP: Non-response to therapy

- Occurs in 6-15%
- Mortality rate in non-responders:
25-49%

CAP: Non-response to therapy

Risk factor	Overall failure ^a	
	Decreased risk	Increased risk
Older age (>65 years)
COPD	0.60	...
Liver disease	...	2.0
Vaccination	0.3	...
Pleural effusion	...	2.7
Multilobar infiltrates	...	2.1
Cavitation	...	4.1
Leukopenia	...	3.7

CAP: Non-response to therapy

Early failure^b

Risk factor	Early failure ^b	
	Decreased risk	Increased risk
Older age (>65 years)	0.35	...
COPD
Liver disease
Vaccination
Pleural effusion
Multilobar infiltrates	...	1.81
Cavitation
Leukopenia
PSI class	...	2.75
<i>Legionella</i> pneumonia	...	2.71
Gram-negative pneumonia	...	4.34

CAP: Non-response to therapy

- Consider reevaluation of diagnosis and treatment
 - Erroneous diagnosis? Failure to consider risks for resistant organism or alternative organism? HIV infection?
 - Antibiotic resistance?
 - Iatrogenic error?
 - Previously undiscovered effusion/empyema?
 - Major airway obstruction?
 - Foreign body?
- Are additional imaging/invasive procedures indicated?
 - Thoracentesis?
 - Bronchoscopy?

Commonly encountered pathogens

- **Alcoholism:**

- *S. pneumoniae*
- Oral anaerobes
- *K. pneumoniae*
- *Acinetobacter spp.*
- *M. tuberculosis*

- **Aspiration:**

- Gram negative enterics
- Oral anaerobes

- **COPD, and/or smoking:**

- *H. influenzae*
- *P. aeruginosa*
- *Legionella spp.*
- *S. pneumoniae*
- *M. catarrhalis*
- *C. pneumoniae*

Commonly encountered pathogens

- **Lung abscess**

- CA-MRSA
- Oral anaerobes
- Endemic fungal infections
- *M. tuberculosis*
- Atypical Mycobacteria

- **Bat or bird droppings**

- *H. capsulatum*

- **Exposure to birds**

- *C. psittaci*
- If poultry: *avian influenza*

- **Exposure to rabbits**

- *Franciscella tularensis*

- **Exposure to parturient cats or farm animals**

- *C. burnettii*

Commonly encountered pathogens

- **HIV infection (early)**

- *S. pneumoniae*
- *H. influenzae*
- *M. tuberculosis*

- **HIV infection (late)**

- Above, PLUS:
 - *Pneumocystis jirovecii*
 - *Cryptococcus, Histoplasmosis, Aspergillus*
 - *Atypical Mycobacteria*
 - *P. aeruginosa*

- **Hotel or cruise ship stay within last 2 weeks**

- *Legionella*

- **Exposure to rabbits**

- *Franciscella tularensis*

- **Travel to or resident of SW USA**

- *Coccidioides spp.*
- *Hantavirus*

Commonly encountered pathogens

- **Travel to or resident of Southeast, East Asia**
 - *Burkholderia pseudomallei*
 - *Avian influenzae*
 - *SARS*
- **Influenza active in the community**
 - *Influenzae*
 - *S. pneumoniae*
 - *H. influenzae*
 - *S. aureus*
- **Cough > 2 weeks with whoop or posttussive emesis**
 - *B. pertussis*
- **Structural lung disease (e.g. bronchiectasis)**
 - *P. aeruginosa*
 - *S. aureus*
 - *Burkholderia cepacia*

Commonly encountered pathogens

- **Injection drug use**

- *S. aureus*
- *M. tuberculosis*
- *Anaerobes*
- *S. pneumoniae*

- **In the context of bioterrorism**

- Anthrax (*B. anthracis*)
- Plague (*Y. pestis*)
- Tularemia (*F. tularensis*)

- **Endobronchial obstruction**

- *Anaerobes*
- *S. pneumoniae*
- *H. influenzae*
- *S. aureus*



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