

# Back to Basics: Are You Aware of All the CAP Bugs?

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## Community-Acquired Respiratory Tract Infections (What are the key pathogens?)

- **Sinusitis, Otitis Media (OM), and Acute Exacerbations of Chronic Bronchitis (AECB)**
  - Typical:
    - *S. pneumoniae*
    - *H. influenzae*
    - *M. catarrhalis*
- **Community-Acquired Pneumonia (CAP)**
  - Typical:
    - *S. pneumoniae*
    - *H. influenzae*
    - *M. catarrhalis*
  - Atypical:
    - *M. pneumoniae*
    - *C. pneumoniae*
    - *Legionella* spp.

Lynch JP, Zhanel GG. *Curr Opin Pulm Med.* 2010;16:217-225.  
Lynch JP, Zhanel GG. *Semin Respir Crit Care Med.* 2005;26:575-616.

## Community-Acquired Pneumonia (CAP)

- Leading cause of morbidity and mortality
  - 40,000 deaths per year in US
  - Especially in elderly and patients with comorbidities
- Incidence
  - General population: 1-12/1000/year
  - >65 years: 25-44/1000/year
- 5-6 million cases per year
  - Approximately 1 million admissions per year
    - 40% one-year mortality\*
  - >75% treated as outpatients
- Cost of treating CAP exceeds \$17 billion per year



File TM. *Lancet.* 2003;362:1991-2001.  
File TM, Tan JS. *JAMA.* 2005;294:2760-2763.  
File TM, Marrie TJ. *Postgrad Med.* 2010;122:130-141.  
\*Kaplan V, et al. *Arch Intern Med.* 2003;163:317-323.



## CAP Topics

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- ***Etiology***
- Diagnosis
- Site of Care
- Initial Empirical Treatment
- Prevention

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## Etiologic Diagnosis of CAP

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- Symptoms, signs and laboratory features are **not specific** in identifying a particular pathogen
- Manifestations of pneumonia may reflect the host response more than the actual pathogen
- Sputum cultures: rarely rewarding for outpatients
- Blood cultures: not practical for outpatients
- Serology: not helpful in acute management

Mandell L, et al. *Clin Infect Dis*. 2007;44(Suppl 2):S27-72.



## CAP Pathogens

### Outpatients (80%)

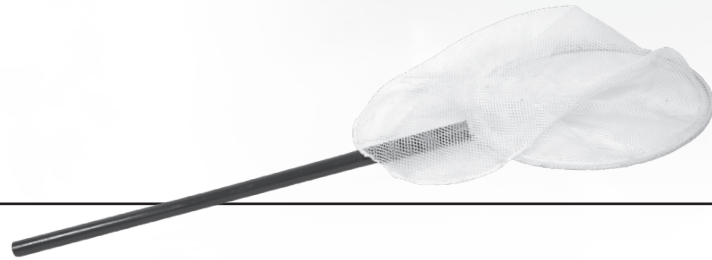
- *S. pneumoniae*
- *M. pneumoniae*
- *C. pneumoniae*
- *H. influenzae*
- CA-MRSA
  
- Viruses

### Inpatients (20%)

- *S. pneumoniae*
- *H. influenzae*
- *M. pneumoniae*
- *C. pneumoniae*
- *Legionella* spp.
- GNR
- *S. aureus* (CA-MRSA)
- Viruses

GNR, Gram-negative rods  
Mandell L, et al. *Clin Infect Dis.* 2007;44(Suppl 2):S27-72.  
File TM. *Lancet.* 2003;362:1991-2001.





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# The Current Challenge of CAP

## **Emerging Etiology of CAP**

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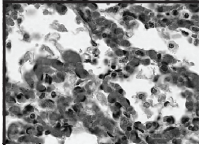
**David S. Burgess, PharmD, FCCP**

Professor and Chair  
Department of Pharmacy Practice and Science  
University of Kentucky College of Pharmacy  
Lexington, KY

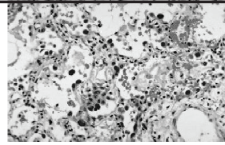


## CAP Epidemiology

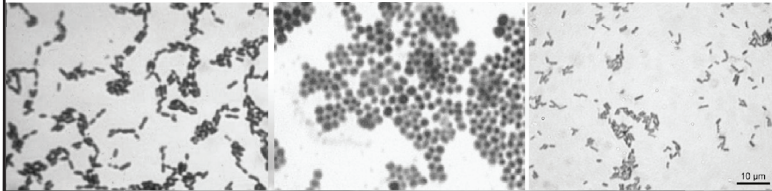
- Pneumonia is the only infectious disease consistently among the top 10 causes of death worldwide.
  - Outpatient mortality rate: ~1–5%
  - Inpatient mortality rate: ~6–12%
  - ICU mortality rate: ~37–50%
- Pneumonia is the 2<sup>nd</sup> leading cause of hospital admission.
  - ~500,000 hospital admissions or ~20% of patients



## Etiology of CAP



- Over 100 microorganisms can cause CAP
  - Bacteria, viruses, fungi, and parasites
- However, only a handful of organisms account for the majority of the cases



**Which of the following is the most common cause of CAP in adult outpatients?**

- A. *S. pneumoniae*
- B. *H. influenzae*
- C. *M. pneumoniae*
- D. *S. aureus*
- E. Viruses



## Community-Acquired Pneumonia Pathogens

### Outpatients

- *S. pneumoniae*
- *M. pneumoniae*
- *C. pneumoniae*
- *H. influenzae*
- *S. aureus* (CA-MRSA)
- Viruses

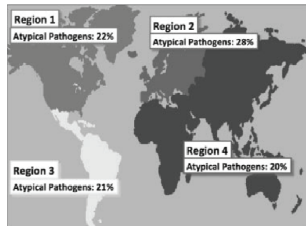
### Inpatients

- *S. pneumoniae*
- *H. influenzae*
- *M. pneumoniae*
- *C. pneumoniae*
- *Legionella* spp.
- Gram-negative rods
- *S. aureus* (CA-MRSA)
- Viruses

Mandell L, et al. *Clin Infect Dis.* 2007;44(Suppl 2):S27-72.  
File TM. *Lancet.* 2003;362:1991-2001.

## Atypical Pathogens

- *Chlamydophila pneumoniae*
- *Legionella pneumophila*
- *Mycoplasma pneumoniae*



Wiemken TL, et al. *Semin Respir Crit Care Med.* 2012;33:213-219.

## Viruses

- Recognized as causes of CAP in infants and children
- Recently associated with CAP in adults
- Molecular diagnostic test has increased the ability to identify viruses in adults
- Incidence ranges from
  - 11% in summer
  - 32% in winter

Johansson N, et al. *Clin Infect Dis.* 2010;50:202-209.  
Wiemken TL, et al. *Semin Respir Crit Care Med.* 2012;33:213-219.



## Viral Pneumonia

- Most common viruses causing pneumonia
  - Influenza A virus
  - Respiratory Syncytial Virus (RSV)
  - Adenoviruses
  - Parainfluenza viruses
  - Influenza B virus
  - Human metapneumovirus
- Viral pneumonia alone: ~13-50%
- Mixed bacteria and viral pneumonia: ~10-27%
- Mixed infections with bacteria and viruses usually result in more severe pneumonia

Marrie TJ, et al. *Semin Respir Crit Care Med.* 2012;33:244-256.  
 Johansson N, et al. *Clin Infect Dis.* 2010;50:202-209.

## Risk Factors for Resistant Organisms

- Previous antibiotic treatment
- Previous hospital admission
- Nursing home
- Comorbidities – cardiovascular disease, HIV, chronic respiratory disease, kidney disease
- Hemodialysis
- Home wound care (past 30 days)
- Family member with resistant organism



Herrero FS, et al. *Semin Respir Crit Care Med.* 2012;33:220-231.

## Antibiotic Resistance Among Common Pathogens Causing CAP

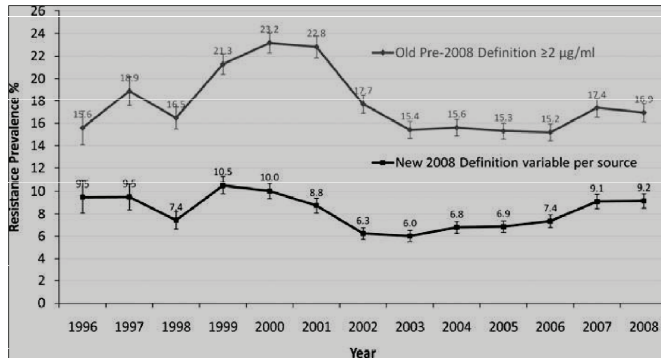
Microorganism	Antibiotic Class	Common Mechanisms of Resistance
<i>Streptococcus pneumoniae</i>	Beta-lactam	• Alterations to penicillin-binding proteins (PBPs)
	Macrolide	• Efflux pump ( <i>mef A</i> gene) • Ribosomal methylation mechanism ( <i>erm B</i> gene)
	Fluoroquinolone	• Mutations in fluoroquinolone resistance determining regions ( <i>par C</i> and <i>gyr A</i> ) • Efflux pump
<i>Mycoplasma pneumoniae</i>	Macrolide	• Point mutation in domain V of the 23S rRNA gene
<i>Haemophilus influenzae</i>	Beta-lactamase	• Beta-lactamase production (TEM-1, ROB-1, and poorly defined others) • Macrolide efflux pump
<i>Moraxella catarrhalis</i>	Beta-lactamase	• Beta-lactamase production (BRO-1, BRO-2, BRO-3)
<i>Staphylococcus aureus</i>	"Methicillin"	• <i>mec A</i> gene
Gram-negative rods	Various	• Beta-lactamase production, including extended spectrum beta-lactamase (ESBL) • Various other mechanisms

Feldman C, Anderson R. *Semin Respir Crit Care Med.* 2012;33:232-243.





## *Streptococcus pneumoniae* Susceptibility



Mera RM, et al. *Microb Drug Resist.* 2011;17:47-52.

## Community-Associated MRSA

- Tend to occur in younger, healthy patients
- Mainly cause skin and soft tissue infections
- May cause necrotizing form of pneumonia
- CA-MRSA account for >50% of staphylococcal infections in the outpatient setting

## Methicillin-Resistant *S. aureus*

### CA-MRSA

- SCC mec types (IV, V, or VII)
- Resistant to all beta-lactams
- Less resistant to non-beta-lactams
- Panton-Valentine Leukocidin (PVL) positive

### HA-MRSA

- SCC mec types (I, II, and III)
- Resistant to all beta-lactams
- Resistant to non-beta-lactams
- Panton-Valentine Leukocidin (PVL) negative



**Which of the following CAP pathogens commonly exhibits antimicrobial resistance?**

- A. *S. pneumoniae*
- B. *S. aureus*
- C. *P. aeruginosa*
- D. *E. coli*
- E. *K. pneumoniae*
- F. Three of the above
- G. All of the above

**Emerging CAP Pathogens**

The CDC has identified 6 pathogens that pose a national security threat

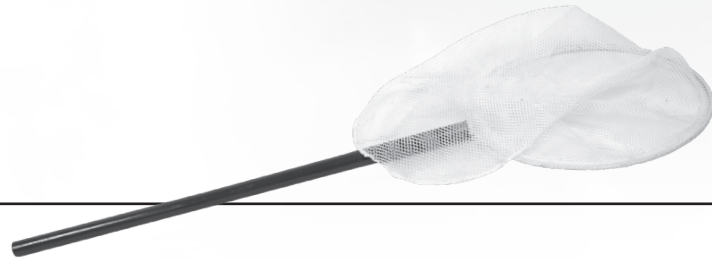
- A. *Bacillus anthracis* – anthrax
- B. *Francisella tularensis* – tularemia
- C. *Yersinia pestis* – plague
- D. Ebola – viral hemorrhagic fever
- E. Marburg – viral hemorrhagic fever
- F. *Clostridium botulinum* – respiratory failure

Wiemken TL, et al. *Semin Respir Crit Care Med.* 2012;33:213-219.

**Conclusion**

- CAP is still a major cause of morbidity and mortality worldwide today.
- New resistant and emerging pathogens continue to arise everyday.
- Molecular diagnostic testing allows for better identification of pathogens.





# The Current Challenge of CAP

## **The One-Two Punch to Managing CAP: Risk Factors & Resistance**

**Debra A. Goff, PharmD, FCCP**

Clinical Associate Professor  
Infectious Disease Specialist  
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Columbus, OH



## Risk Factors for Bacterial Resistance in CAP

- $\beta$ -lactam (penicillins and cephalosporins)
- Macrolide
- Fluoroquinolone
  
- Risk factors for antimicrobial resistance

## Definition of Resistance

- MDRSP (multidrug resistant *S. pneumoniae*)  
Resistance to  $\geq 2$  of the following:  
penicillin, ceftriaxone, erythromycin, tetracycline, levofloxacin, TMP/sulfamethoxazole
- MDR *S. aureus*  
Resistance to oxacillin, erythromycin, clindamycin, levofloxacin, tetracycline and TMP/sulfamethoxazole

Farrell DJ, et al. *Clin Inf Dis*. 2012;55(Suppl 3):S206-214.

## History of *S. pneumoniae* Resistance

- Before 1990s:  
Majority of isolates were inhibited by penicillin  $< 0.1$  mg/L
- 1997-1998 surveillance study  
13% resistance (MIC  $\geq 2$ mg/L)
- 1999-2000 multicenter study  
21.5% resistance (MIC  $\geq 2$ mg/L)

File TM. *Clin Inf Dis* 2002;34(Suppl 1):S17-26.



## Drug-Resistant *Streptococcus pneumoniae* (DRSP)

- Nonmeningeal breakpoints
- Changed in 2008
- In the US, most drug-resistant *S. pneumoniae* are intermediate type

	New MIC (mg/L)	Old MIC (mg/L)
Susceptible	≤2	≤0.06
Intermediate	4	0.12-1.0
Resistant	≥8	≥2

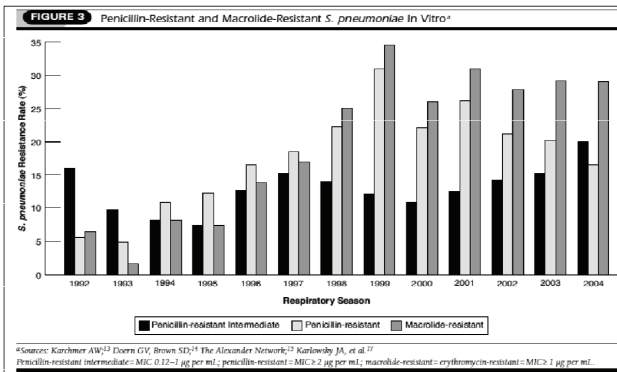
## Risk Factors for Drug-Resistant *S. pneumoniae*



Risk Factors for Drug-Resistant <i>S. pneumoniae</i>
Antimicrobial use in the past 90 days
Extremes of age (<5 and >65 years)
Chronic heart, lung, liver, or kidney disease
Diabetes mellitus
Alcoholism
Malignancies
Asplenia
Immunosuppressive conditions or use of immunosuppressive drugs
Community or household exposure
Epidemiologic/geographic association
Institutionalization
Clonal dissemination in crowded environments (eg. day care centers, hospitals, jails, long-term care facilities)

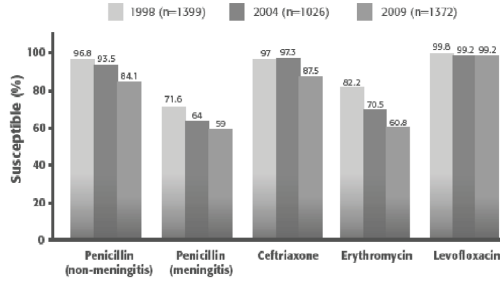
Vanderkooi OG, et al. *Clin Inf Dis.* 2005;40(9):1288-1297.

## DRSP Historical Data & Old Breakpoints, 1992-2004



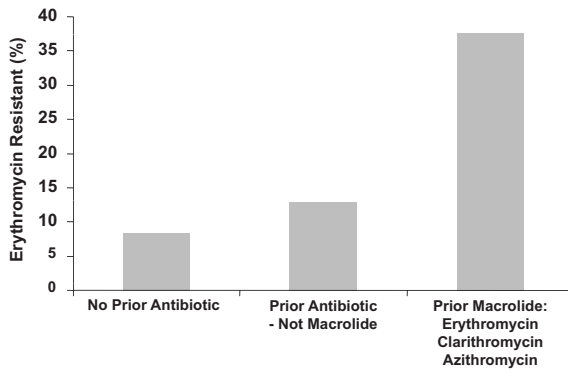
## Susceptibility Trends for *S. pneumoniae*

### US SENTRY Program, 1998-2009



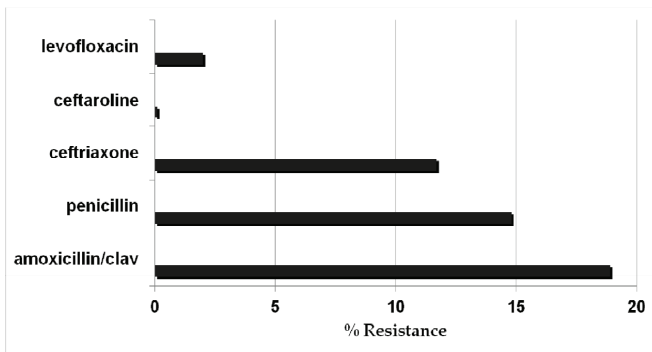
Jones RN, et al. *Diagn Microbiol Infect Dis.* 2010;68:334-336.

## Relative Risk of Infection With Macrolide-Resistant Pneumococci, by Prior Antibiotic Use



Vanderkooi OG, et al. *Clin Infect Dis.* 2005;40:1288-1297.

## Resistance Trends Among *S. pneumoniae*: US SENTRY Program, 1998-2011

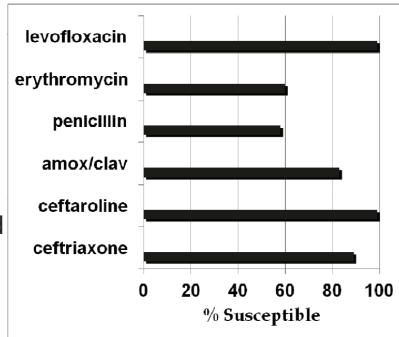


Jones RN, et al. *Diagn Microbiol Infect Dis.* 2012. [Epub ahead of print. Sept doi10.1016]



## AWARE Surveillance Program (2008-2010) *S. pneumoniae* Susceptibility in the US

- 71 US hospitals
- Ceftaroline was 16-fold more potent than ceftriaxone
- Among 70 ceftriaxone-resistant pneumococcal isolates, all were inhibited by  $\leq 0.5$   $\mu\text{g/mL}$  ceftaroline



Pfaller MA, et al. *Clin Infect Dis.* 2012;55(Suppl 3):S187-193.

## Risk Factors MRSA Pneumonia

- Influenza-like prodrome
- Severe respiratory symptoms
- Hemoptysis
- CXR multilobar infiltrates
- Recent contact with CA-MRSA
- Belong to a group associated with increased rates of CA-MRSA

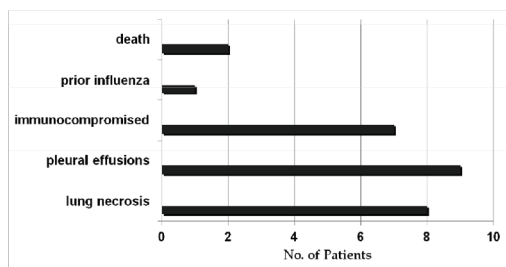
Karampela I, et al. *Minerva Anestesiologica.* 2012;78:930-940.

## Risk Factors

- Athletes (contact sports)
- IV drug users
- Military personnel
- Prisoners
- Pig farmers
- History of skin abscesses (past 6 months)



## CA-MRSA Pneumonia 28-month study, 15 patients



Lobo LJ, et al. *Chest*. 2010;138:130-136.

## Risk Factors MRSA Pneumonia

- Study: Prospective study (12 EDs) adults hospitalized with CAP 2006-2007
- 627 patients  
MRSA: 14 patients (2.4%)

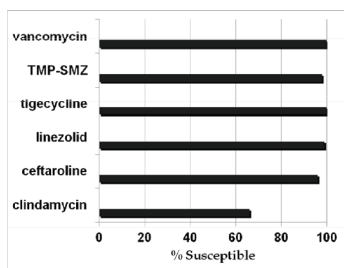
### Risk Factors Identified

- Nursing home admission in previous year
- History of MRSA
- Multiple infiltrates or cavities on CXR
- Close contact with someone with a skin infection

Moran GJ, et al. *Clin Infect Dis*. 2012 54:1126-1133.

## AWARE Surveillance Program (2008-2010) *S. aureus* Susceptibility in the US

- 72 US hospitals
- 8,469 *S. aureus* isolates
- 634 from patients hospitalized with pneumonia



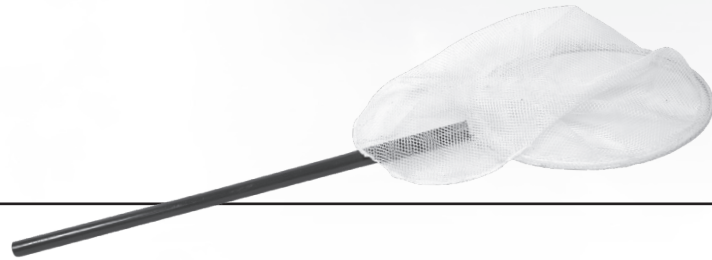
Farrell DJ, et al. *Clin Infect Dis*. 2012;55(Suppl 3):S206-214.

## One-Two Punch

- **One:** know your local resistance rates
- **Two:** identify the patient with risk factors for resistance to help target the most appropriate antimicrobial







# The Current Challenge of CAP

## **From Guidelines to Bedside: Therapeutic Approaches and Stewardship Tactics**

**Thomas M. File, Jr.**  
**MD, MS, MACP, FIDSA, FCCP**

Chair, Infectious Disease Division

Summa Health System

Akron, OH

Professor, Internal Medicine

Master Teacher; Chair, Infectious Disease Section

Northeast Ohio Medical University

Rootstown, OH





## From Pirates of the Caribbean

Curse of the Black Pearl 2003



- Jack Sparrow: I thought you were supposed to keep to the code
  - (referring to the pirates code that “Any man that falls behind stays behind”... when the Black Pearl waits for him to escape)
- Mr. Gibb: We figured they were more like **guidelines** rather than actual rules

**The majority of recommendations in clinical practice guidelines are based on high level evidence.**

- A. True
- B. False

### EDITORIAL COMMENT

#### Guiding in the Face of Minimal Evidence

*A Strength, Not a Weakness, of Graded Clinical Practice Guidelines*

*Thomas M. File, Jr, MD*

- Strength of most recommendations NOT robust
  - Recent sinusitis guideline: 1/24 recommendations based on “high” level evidence
- “We are often called upon to make decisions for which there is less than robust evidence, yet for the sake of the patient care, we need to respond and often expeditiously...even though randomized controlled trials may not be available, the clinical question may be so relevant that it would be delinquent to not include it in the guideline.”



**The initial objective of performance measures is:**

- A. To correlate reimbursement by CMS for hospitalized patients with appropriate care of infections
- B. To penalize poor practice of antimicrobial use
- C. To measure improvement of implementation of processes of care to maximize outcomes
- D. To develop evidence-based guidelines of care

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**Guidelines and Core Performance Measures**

Core Measures: Effort to improve care of patients by measuring improvement

- Process of care measures: reflect evidence-based components of encounter between HCP and patients
  - Based on guideline recommendations
  - Within control of the HCP
- Outcome measures: mortality, readmission rate
- Provide method to assess improvement of care
- Now tied to reimbursement (Pay for Performance)

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**CAP: Joint Commission/CMS Performance Measures for Inpatients 2012**

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|---|---|
| <ul style="list-style-type: none"> <li>• <b>Blood cultures<sup>a</sup></b> <ul style="list-style-type: none"> <li>- For all ICU patients;<sup>a</sup> <i>optional for general ward patients</i></li> <li>- Prior to antibiotics if obtained in emergency department<sup>a</sup></li> </ul> </li> <li>• <b>Empiric antimicrobials according to guidelines<sup>a</sup></b> <ul style="list-style-type: none"> <li>- <i>Exceptions: pathogen-directed therapy, clinical trials, diagnostic uncertainty</i></li> </ul> </li> <li>• <b>Timely administration of antibiotics (6 h; 2008)<sup>b</sup></b></li> <li>• <b>Measurement of blood gases or pulse oximetry<sup>c</sup></b></li> <li>• <b>Assessment/administration—pneumococcal and influenza vaccine<sup>d</sup></b></li> <li>• <b>Smoking-cessation counseling</b></li> <li>• <b>CAP mortality (July 2008)</b></li> <li>• <b>30-d readmission rate for pneumonia<sup>e</sup> (2013)</b></li> </ul> | <ul style="list-style-type: none"> <li><sup>a</sup>2012 Core Measure</li> <li><sup>b</sup>Retired as CAP measure</li> <li><sup>c</sup>Retired 2009</li> <li><sup>d</sup>Now global measure</li> <li><sup>e</sup>Complements Core Measures as part of the Hospital Readmissions Reduction Program—hospitals with higher than expected 30-d readmission rates for AMI, heart failure and pneumonia and will incur penalties against their total Medicare payments beginning in FFY 2013.</li> </ul> |
|---|---|

Centers for Medicare and Medicaid Services and the Joint Commission. Specifications manual for national hospital inpatient quality measures. Available at: [www.jointcommission.org/specifications\\_manual\\_for\\_national\\_hospital\\_inpatient\\_quality\\_measures.aspx](http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx). Accessed November 7, 2012. File TM, et al. *Clin Infect Dis*. 2011;53(Suppl 1):S15-S22.

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## Empiric Therapy in CAP: IDSA/ATS<sup>1</sup>

Healthy Outpatient	Outpatient at Risk for DRSP*	Inpatient, non-ICU	Inpatient, ICU†
Macrolide OR Doxycycline	Respiratory fluoroquinolone OR Beta-lactam plus macrolide	Respiratory fluoroquinolone OR Beta-lactam plus macrolide	Beta-lactam plus azithromycin or fluoroquinolone; consider MRSA, Pseudomonas

### CMS list of options<sup>2</sup>

Inpatient, non-ICU	Inpatient, non-ICU; Pseudomonal Risk	Inpatient, ICU†
Ceftriaxone, cefotaxime, ampicillin/sulbactam, ertapenem, ceftaroline. Erythromycin, clarithro, azithro. Levofloxacin 750 mg, moxifloxacin, gemifloxacin Tigecycline	Cefepime, imipenem, meropenem, piperacillin/tazobactam, doripenem. Ciprofloxacin, levofloxacin 750 mg. Gentamicin, tobramycin, amikacin. Levofloxacin 750 mg, moxifloxacin, gemifloxacin. Erythromycin, clarithromycin, azithromycin.	Erythromycin, azithromycin. Ceftriaxone, cefotaxime, ampicillin/sulbactam. Cefepime, imipenem, meropenem, piperacillin/tazobactam, doripenem. Levofloxacin 750 mg, moxifloxacin. Gentamicin, tobramycin, amikacin. Ciprofloxacin, levofloxacin 750 mg.

1. Mandell L, et al. *Clin Infect Dis.* 2007;44(Suppl 2):S27-S72.  
 2. CMS and the Joint Commission. Specifications manual for national hospital inpatient quality measures. Available at: [www.jointcommission.org/specifications\\_manual\\_for\\_national\\_hospital\\_inpatient\\_quality\\_measures.aspx](http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx). Accessed Nov. 7, 2012.

## CMS Measures and Stewardship

- Should be complementary to improve patient outcomes
  - Appropriate use per guidelines
  - Avoid overuse of ATB (e.g. antipseudomonal ATB if no pseudomonas indications)
- Improving Compliance and Stewardship
  - Order sets; Electronic Record (CPOE) to list only appropriate ABX
  - Clearly define CAP vs. HCAP
    - e.g., from ECF, prior hospitalization in 3 months
  - Define indications for anti-Pseudomonas Therapy
    - Structural lung disease (bronchiectasis); COPD with repeated ABX or steroids; any suggestion of Pseudomonas

File TM Jr, Gross PA. *Clin Infect Dis.* 2007;44:942-944.  
 Dellit TH, et al. *Clin Infect Dis.* 2007;44:159-177.  
 Shorr A, Owens R. *Am J Health-Syst Pharm.* 2009;66(Suppl 4):S8-14.

### EDITORIAL COMMENTARY

## Performance Measurement in Community-Acquired Pneumonia: Consequences Intended and Unintended

Thomas M. File, Jr.<sup>1,2</sup> and Peter A. Gross<sup>3,4</sup>

<sup>1</sup>Northeastern Ohio University College of Medicine, Rootstown, and <sup>2</sup>Summa Health System, Akron, Ohio; and <sup>3</sup>Hackensack University Medical Center, Hackensack, and <sup>4</sup>University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey

- Performance Measures based on “guidelines”
- Measures [*Guidelines*] need to be evaluated for ‘unintended’ consequences
- Need to assess affect of combined use of quality measures
- Deviation from recommendation is acceptable
  - “...specific performance measures [*guidelines*] cannot cover all host settings.”
- Changes recommended by National Pneumonia Medicare Improvement Project Panel
  - Blood cultures
  - Timing of first dose

File TM, Gross PA. *Clin Infect Dis.* 2007;44:942-944.



## CAP Processes of Care: Improving Stewardship

- De-escalation
  - Tailor ATB to diagnostic test results
    - “This information is often available at the time of consideration for a switch from parenteral to oral therapy and may be used to direct specific choices”<sup>1</sup>
- Duration of ATB
  - Based on multiple recent studies<sup>1-4</sup>
    - Minimum of 5 days if afebrile by 48-72 hrs for ‘core pathogens’
    - Longer for ‘other’ pathogens or evidence of extrapulmonary infection
  - Shorter course therapy
    - Reduced resistance, AE, cost

1. Mandell L, et al. *Clin Infect Dis.* 2007;44:S27-72. 2. File TM, Niederman MS. *Inf Dis Clinics North Am.* 2004;18:993-1016.  
3. el Moussaoui R, et al. *BMJ.* 2006;332:1355 4. Li JZ, et al. *Am J Med.* 2007;120:783-790 .

### Which of the following are included as part of Value-Based Purchasing Rule?

- A. Blood cultures prior to antimicrobial administration for CAP in ED patients
- B. Appropriate empirical antimicrobials for CAP
- C. Appropriate administration of pneumococcal vaccine
- D. All of the above
- E. A and B

## 2013 Measures: Value-Based Purchasing 20 Measures for FFY 2013

### Experience of Care Measures Encompassing 8 Key Topics

- Communication with nurses
- Communication with doctors
- Responsiveness of staff
- Pain management
- Communication
- Cleanliness and quietness
- Discharge information
- Overall rating of hospital



### 12 Clinical Process Measures

- Acute Myocardial Infection
- Heart Failure
- Pneumonia
  - Blood cultures
  - Approved Antimicrobials
- SCIP (SCIP 1,2,3 and 4 considered HAI)

FFY, Federal Fiscal Year.  
Medicare Program; Hospital Inpatient Value-Based Purchasing Program. Available at:  
<https://www.federalregister.gov/articles/2011/05/06/2011-10568/medicare-program-hospital-inpatient-value-based-purchasing-program>. Accessed June 5, 2012.



## 30-Day Readmission Rate

Posted: 8:15 p.m. Sunday, Oct. 21, 2012

### Too many readmissions to cost hospitals

By Misty Williams

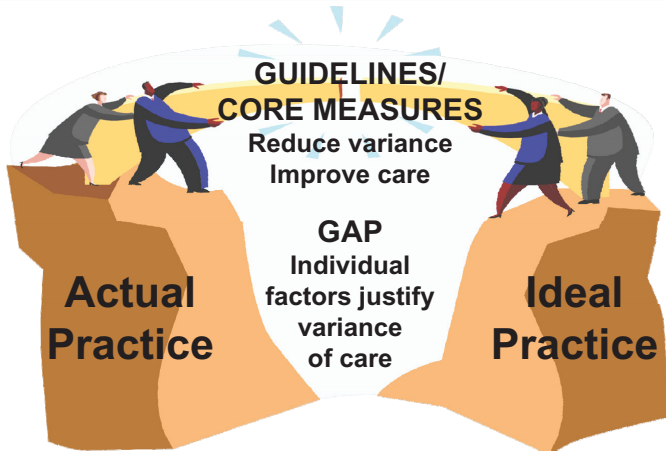
The Atlanta Journal-Constitution

Georgia hospitals face the loss of hundreds of thousands of dollars in federal funding for having too many Medicare patients come back through their doors just weeks – or sometimes days – after being sent home.

Starting this month, more than 2,000 hospitals across the nation will be penalized for having too many discharged patients readmitted within 30 days as part of a massive effort to curb government health costs and improve the quality of care. Avoidable readmissions cost Medicare — the federal health program for people 65 and older — about \$17 billion each year.

**Hospitals will forfeit approx. \$280 million over next year**

## Link Between Evidence-based Guidelines, Core Measures & Outcomes



### Which of the following is (are) the likely barrier(s) to guideline implementation?

- A. Lack of guideline awareness
- B. Unawareness of impact on patient outcomes
- C. Lack of applicability to specific patient or local circumstances
- D. Lack of motivation
- E. All of the above





## Guidelines: Barriers and Solutions

Barriers	Solutions
Poor knowledge of guidelines	Disseminate info; Integrate in order sets; Involve Key Opinion Leaders
Lack of agreement	Assess evidence and strength of recommendation; individualize
Recommendations too complex	Establish clear recommendations
Not relevant to local situation	Adaptable to local situation
Lack of motivation	May be tied to performance measures (pay for performance)

Adapted from File TM Jr. Impact of guidelines on antimicrobial treatment of RTIs. In Owens and Lautenbach (eds) Antimicrobial Resistance: Problem pathogens and clinical countermeasures. Informa Healthcare, NY 2008.

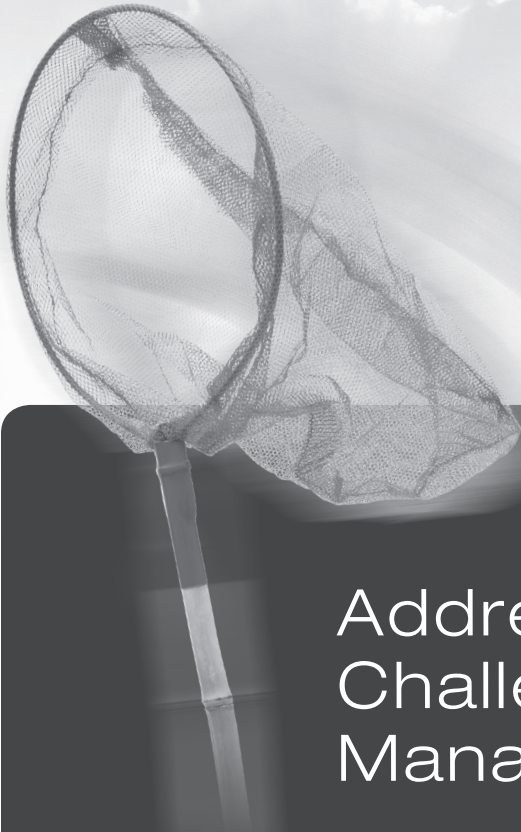
## Impact of CAP Guideline Interventions: Better Outcomes at Bedside

Study	Intervention	Outcome
Gordon et al. <sup>1</sup>	Initial choice of ATB	CAP Guidelines assoc with lower mortality
Menedez et al. <sup>1</sup>	Initial choice of ATB	CAP Guidelines assoc with less mortality
Dean et al <sup>1</sup>	Use of Guideline	Decreased mortality
Capelastegui et al. <sup>2</sup>	Use of Guideline	Improved processes of care
Bodi M, et al <sup>3</sup>	Use of Guideline ATB for Severe CAP	Decreased mortality

1. File TM. Impact of guidelines on antimicrobial treatment of RTIs. In Owens and Lautenbach (eds) Antimicrobial Resistance: Problem pathogens and clinical countermeasures. Informa Healthcare, NY 2008.  
 2. Capelastegui, et al. *Clin Infect Dis.* 2004; 39:955-963.  
 3. Bodi M, et al. *Clin Infect Dis.* 2005; 41:1709-1716.







# Addressing the Challenge in CAP Management

Using Patient- and Pathogen-  
Centered Approaches to Care

**A Series of Clinical Cases**

**Led by:**  
**George G. Zhanel, PharmD, PhD**

Professor  
Department of Medical Microbiology/Infectious Diseases  
Faculty of Medicine  
University of Manitoba  
Coordinator, Antibiotic Resistance Program  
Clinical Microbiology, Health Sciences Center  
Winnipeg, Canada



# Patient 1: Meet Ron



CXR Courtesy of TM File

- 66-year-old male
  - Smoker, diabetes, CHF
  - Treated with macrolide for 'sinusitis' 8 weeks ago
  - Grandfather, retired (farmer)
- Headache, fever, productive cough for 3 days, new confusion
- Temp: 101.8°F; Pulse: 110 BPM; RR: 28 breaths/min
- Auscultation: rhonchi in RLL
- O<sub>2</sub> sat: 92% in room air
- Patient is admitted to medical ward

What pathogens are you worried about?



## Back to CAP Pathogens

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### Outpatients

- *S. pneumoniae*
- *M. pneumoniae*
- *C. pneumoniae*
- *H. influenzae*
- *S. aureus* (CA-MRSA)
- Viruses

### Inpatients

- *S. pneumoniae*
- *H. influenzae*
- *M. pneumoniae*
- *C. pneumoniae*
- *Legionella* spp.
- GNR
- *S. aureus* (CA-MRSA)
- Viruses

Mandell L, et al. *Clin Infect Dis*. 2007;44(Suppl 2):S27-72.  
File TM. *Lancet*. 2003;362:1991-2001.

**What Empiric Antimicrobial Treatment Would You Recommend?  
Why?**



## IDSA/ATS CAP Recommendations Inpatients (non-ICU Treatment)

- ➔ Respiratory fluoroquinolone (moxifloxacin 400 mg, levofloxacin 750 mg) (Strong recommendation, Level I evidence)
- ➔ Beta-lactam (ceftriaxone, cefotaxime, ampicillin-sulbactam, ertapenem) PLUS a macrolide (Strong recommendation, Level I evidence)
- New antimicrobials with CABP indication:
  - Tigecycline
  - Ceftaroline

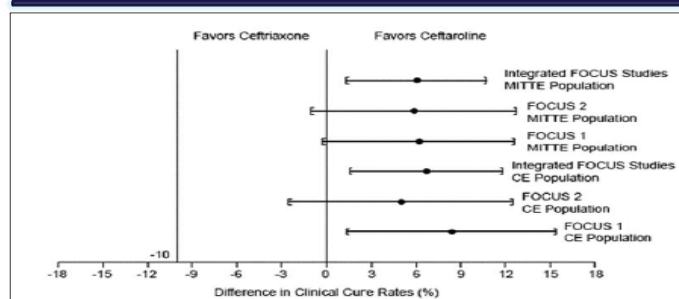
Mandell L, et al. *Clin Infect Dis*. 2007;44 (Suppl 2):S27-72.

## New Antimicrobials for Inpatient CAP

- Tigecycline (Tygacil®) IV<sup>1</sup>
  - Glycylcycline: broad spectrum activity, including *S. pneumoniae*, atypicals
  - Approved for intra-abdominal infections, bacterial skin infections, CAP (non-ICU)
    - CAP: Comparable to levofloxacin
  - Listed as option for CAP admitted to general ward
    - 100 mg initially, then 50 mg q12h;
    - Adverse effects: N/V
- Ceftaroline (Teflaro®) IV<sup>2</sup>
  - 600 mg q12h

1. Zhanel GG, et al. *Expert Rev Anti Infect Ther*. 2006;4(1):9-25.  
2. Zhanel GG, et al. *Drugs*. 2009;69(7):809-31.

## Ceftaroline Versus Ceftriaxone in Patients with CAP



- 1200+ patients; Average age: 61 years; all PORT III or IV
- Clinical Cure for *S. pneumoniae*:
  - Ceftaroline 59/69 (85.5%); Ceftriaxone 48/70 (68.6%)
- Ceftaroline has greater affinity for PBP-2a (4-fold > ceftriaxone)

File TM, et al. *Clin Infect Dis*. 2010;51:1395-1405.



## Patient Ron: Update

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The patient was treated with ceftriaxone + azithromycin.

### **Now Day 3:**

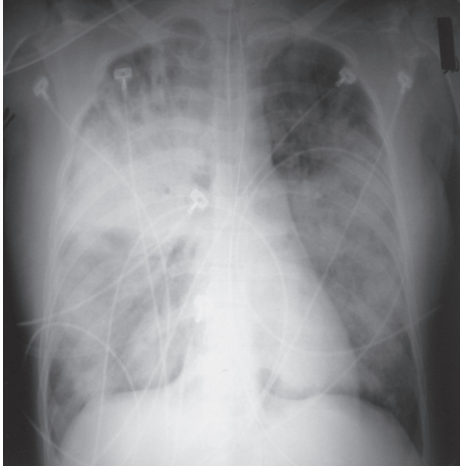
- Afebrile, other vital signs are stable
- Patient is alert with no unstable comorbidity
- O<sub>2</sub> sat: 98% in room air
- Sputum culture obtained on admission identified ***S. pneumoniae* (Pen S).**
- **Blood culture was negative.**

**How Would You Change Your Antimicrobial Regimen?**





# Patient 2: Meet Peg



CXR Courtesy of TM File

- **30-year-old female presents to ER at 0400 with respiratory distress**
  - **Immediate intubation**
  - **No prior medical problems, except for a recent ILI (influenza-like illness)**
  - **Stay-at-home mom (toddler twins)**
- **Sent to ICU**

**What pathogens are you worried about?**



## Back to CAP Pathogens

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### Outpatients

- *S. pneumoniae*
- *M. pneumoniae*
- *C. pneumoniae*
- *H. influenzae*
- *S. aureus* (CA-MRSA)
- Viruses

### Inpatients

- *S. pneumoniae*
- *H. influenzae*
- *M. pneumoniae*
- *C. pneumoniae*
- *Legionella* spp.
- GNR
- *S. aureus* (CA-MRSA)
- Viruses

Mandell L, et al. *Clin Infect Dis*. 2007;44(Suppl 2):S27-72.  
File TM. *Lancet*. 2003;362:1991-2001.

**What Empiric Antimicrobial Treatment Would You Recommend?  
Why?**





## IDSA/ATS CAP Recommendations Inpatients (ICU Treatment)

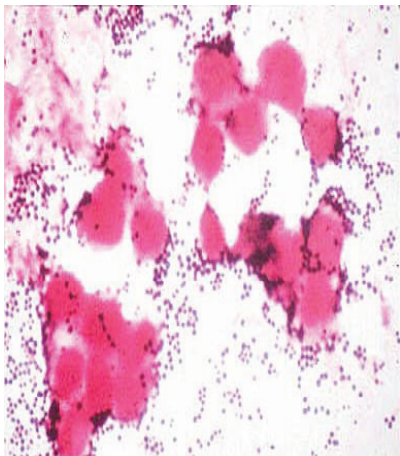
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- ➔ • A beta-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam) PLUS either azithromycin (Level II evidence) OR a respiratory fluoroquinolone (Level I evidence)
- ➔ • For penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended (Strong recommendation)
- Special considerations
  - *Pseudomonas* (bronchiectasis, steroids....)
- ➔ • CA-MRSA (recent influenza.....)

Mandell L, et al. *Clin Infect Dis*. 2007;44(Suppl 2):S27-72.

## Patient Peg: Update

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- Gram stain of respiratory secretions shows Gram-positive cocci clusters
- Bactec beeps after 24 hours
  - Blood smear shows Gram-positive cocci clusters



**What Pathogen Do You Think It Is?  
Gram-Positive Cocci in Clusters?**

## **Patient Peg: Update**

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The patient was treated with  
ceftriaxone + moxifloxacin + vancomycin

### **Now Day 3:**

- Patient is afebrile and alert, other vital signs are stable
- She has been extubated; O<sub>2</sub> sat: 96% in room air
- Sputum culture and blood culture grew *Staphylococcus aureus* and the Vitek II report reveals CA-MRSA



**How Would You Change Your Antimicrobial Regimen?**

Blank area for handwritten response to the question: How Would You Change Your Antimicrobial Regimen?

**How Long Would You Treat This Patient?**

Blank area for handwritten response to the question: How Long Would You Treat This Patient?



## CAP: Duration of Therapy Immunocompetent Host

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- Based on available data:
  - Minimum of 5 days if afebrile by 48-72 hrs for 'core pathogens'
  - Longer for other pathogens or evidence of extrapulmonary infection
    - *S. aureus*, *Pseudomonas*
- Shorter course therapy
  - Reduced resistance, AE, cost

File TM, Niederman MS. *Infect Dis Clinics North Am.* 2004;18:993-1016.  
Mandell L, et al. *Clin Infect Dis.* 2007;44(Suppl 2):S27-72.

### NOTES

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## Common Clinical Abbreviations

<b>ABECB</b>	acute bacterial exacerbation of chronic bronchitis	<b>HAI</b>	hospital-acquired infection
<b>ABS</b>	acute bacterial sinusitis	<b>HAP</b>	hospital-acquired pneumonia
<b>ABSSSI</b>	acute bacterial skin and skin structure infections	<b>IAI</b>	intra-abdominal infection
<b>AECB</b>	acute exacerbation of chronic bronchitis	<b>ICU</b>	intensive care unit
<b>AMCL</b>	amoxicillin-clavulanate	<b>IDSA</b>	Infectious Diseases Society of America
<b>AMK</b>	amikacin	<b>IMI</b>	imipenem
<b>AMP</b>	ampicillin	<b>KPC</b>	<i>Klebsiella pneumoniae</i> carbapenemase
<b>ASP</b>	Antimicrobial Stewardship Program	<b>LOS</b>	length of stay
<b>ATS</b>	American Thoracic Society	<b>MDR</b>	multidrug resistant
<b>AUC</b>	area under the concentration-time curve	<b>MDRSP</b>	multidrug resistant <i>S. pneumoniae</i>
<b>AWARE</b>	Assessing Worldwide Antimicrobial Resistance Evaluation Program	<b>MIC</b>	minimal inhibitory concentration
<b>BAL</b>	bronchoalveolar lavage	<b>mMITT</b>	microbiological modified intent-to-treat
<b>BMT</b>	bone marrow transplantation	<b>MRSA</b>	methicillin-resistant <i>Staphylococcus aureus</i>
<b>BSI</b>	bloodstream infection	<b>MSSA</b>	methicillin-susceptible <i>Staphylococcus aureus</i>
<b>CA</b>	community-acquired or community-associated	<b>MV</b>	mechanical ventilation
<b>CABP</b>	community-acquired bacterial pneumonia	<b>NNIS</b>	National Nosocomial Infections Surveillance
<b>CAP</b>	community-acquired pneumonia	<b>OPAT</b>	outpatient parenteral antimicrobial therapy
<b>CASS</b>	continuous aspiration of subglottic secretions	<b>OXA</b>	oxacillin
<b>CAUTI</b>	catheter-associated urinary tract infection	<b>PAE</b>	post-antibiotic effect
<b>CFP</b>	cefepime	<b>PD</b>	pharmacodynamic
<b>CIP</b>	ciprofloxacin	<b>PICC</b>	peripherally inserted central catheter
<b>CLABSI</b>	central line-associated bloodstream infection	<b>PK</b>	pharmacokinetic
<b>CLSI</b>	Clinical and Laboratory Standards Institute	<b>PTZ</b>	piperacillin-tazobactam
<b>C<sub>max</sub></b>	peak concentration	<b>SHEA</b>	Society for Healthcare Epidemiology of America
<b>C<sub>min</sub></b>	trough concentration	<b>SHP</b>	Society of Health-System Pharmacists
<b>cMITT</b>	clinically modified intent-to-treat	<b>SICU</b>	surgical intensive care unit
<b>COPD</b>	chronic obstructive pulmonary disease	<b>SIDP</b>	Society of Infectious Diseases Pharmacists
<b>CPE</b>	carbapenemase-producing Enterobacteriaceae	<b>SSI</b>	surgical site infection
<b>CR-BSI</b>	catheter-related bloodstream infection	<b>SSSI</b>	skin and skin-structure infection
<b>CSF</b>	cerebrospinal fluid	<b>SSTI</b>	skin and soft tissue infection
<b>cSSSI</b>	complicated skin and skin structure infection	<b>%T&gt;MIC</b>	percent time above the MIC
<b>CTX</b>	ceftriaxone	<b>TBSA</b>	total burn surface area
<b>CTZ</b>	ceftazidime	<b>TOB</b>	tobramycin
<b>CVC</b>	central venous catheter	<b>UTI</b>	urinary tract infection
<b>DAP</b>	daptomycin	<b>VAN</b>	vancomycin
<b>DAT</b>	delayed antimicrobial therapy	<b>VAP</b>	ventilator-associated pneumonia
<b>ESBL</b>	extended-spectrum β-lactamase	<b>VAT</b>	ventilator-associated tracheobronchitis
<b>ETA</b>	endotracheal aspirate	<b>VISA</b>	vancomycin-intermediate <i>Staphylococcus aureus</i>
<b>ETT</b>	endotracheal tube	<b>VRE</b>	vancomycin-resistant enterococci
<b>FIC</b>	fractional inhibitory concentration		
<b>FQRP</b>	fluoroquinolone-resistant <i>P. aeruginosa</i>		
<b>GISA</b>	glycopeptides-intermediate <i>Staphylococcus aureus</i>		
<b>GNB</b>	gram-negative bacilli		
<b>GNR</b>	gram-negative rods		
<b>GPC</b>	gram-positive cocci		



# Continuing Professional Development (CPD): Reflect | Plan | Do | Evaluate

Managing the Many Bugs of CAP: An Ongoing Challenge!

Center for Independent Healthcare Education is committed to supporting pharmacists in their Continuing Professional Development (CPD) and lifelong learning. Please use this form to incorporate the learning from this educational activity into your everyday practice.

Continuing Professional Development: a self-directed, ongoing, systematic and outcomes-focused approach to learning and professional development that assists individuals in developing and maintaining continuing competence, enhancing their professional practice, and supporting achievement of their career goals.

## CPD Value Statement:

*“Pharmacists who adopt a CPD approach accept the responsibility to fully engage in and document their learning through reflecting on their practice, assessing and identifying professional learning needs and opportunities, developing and implementing a personal learning plan, and evaluating their learning outcomes with the goal of enhancing the knowledge, skills, attitudes and values required for their pharmacy practice.”*

## REFLECT

**Consider my current knowledge and skills in managing CAP, and self-assess my professional development needs and goals.**

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## **PLAN**

**Develop a “Personal Learning Plan” to achieve intended outcomes, based on what and how I want or need to learn.**

Develop objectives that are specific for you, measurable, achievable, relevant to the learning/practice topic, and define the time frame to achieve them.

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## **DO**

**Implement my learning plan utilizing an appropriate range of learning activities and methods.**

List learning activities that you will engage in to meet your goals.

List resources (e.g. materials, other people) that you might use to help achieve your goal.

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## **EVALUATE**

**Consider the outcomes and effectiveness of each learning activity and my overall plan, and what (if anything) I want or need to do next.**

Monitor progress regularly toward achievement of your goal.

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