1. In 1898, William Osler described community-acquired pneumonia as:

a. An ailment that often leads to suffocation and death.

b. A friend of the aged.

c. A common and mortal disease which can be diagnosed by simple observation and percussion of the chest.


"Pneumonia may well be called the friend of the aged. Taken off by it in an acute, short, not often painful illness, the old man escapes those 'cold gradations of decay' so distressing of himself and to his friends."

-- William Osler, M.D., 1898
“Brad, pneumonia sucks.”
-- Mary R. Sharpe
November 2011

**CAP, HCAP, HAP, VAP**

**Roadmap**

- Background
- Community-acquired pneumonia (CAP)
- Healthcare-associated pneumonia (HCAP)
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)
Specific Goals:

- Describe the most common causes of pneumonia in different settings
- Initiate appropriate antibiotics in the treatment of CAP, HCAP, HAP, and VAP
- State the optimal duration of therapy in pneumonia in different settings

Caveats

- Will not talk about other types of pneumonia (in HIV, aspiration, etc.)
- Will not discuss admission decision (complex)
- Syllabus or specific questions: sharpeb@medicine.ucsf.edu

Roadmap

- Background
  - Community-acquired pneumonia (CAP)
  - Healthcare-associated pneumonia (HCAP)
  - Hospital-acquired pneumonia (HAP)
  - Ventilator-associated pneumonia (VAP)

Definition of Pneumonia(s)

- Community-acquired (CAP): pneumonia acquired outside of hospitals or healthcare setting
- Healthcare-associated (HCAP): pneumonia in a patient with significant healthcare exposure
Definition of Pneumonia(s)

- Hospital-acquired (HAP): pneumonia acquired > 48-72 hours after admission
- Ventilator-associated (VAP): pneumonia acquired > 48-72 hours after intubation

Why does it matter?

- Risk factors for changing microbiology

Roadmap

- Background
- Community-acquired pneumonia (CAP)
  - Clinical, microbiology, treatment
- Healthcare-associated pneumonia (HCAP)
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)
**CAP: Background**

- Cough: 90%*
- Dyspnea: 66%
- Sputum: 66%
- Pleuritic chest pain: 50%

* Yet, only 4% of all visits for cough are pneumonia


**Clinical Presentation: Geriatrics**

- Less “classic” presentations
  - 10% have NONE of the classic signs or symptoms
- Up to 35% will **not** have fever
- Up to 50% will have altered mental status
- Up to 50% will have “asthenia”

**Microbiology of CAP**

- Many studies examining microbiology

Evolving Understanding of the Causes of Pneumonia in Adults, With Special Attention to the Role of Pneumococcus

### Etiology of CAP

<table>
<thead>
<tr>
<th>Outpatients (mild)</th>
<th>Non-ICU inpatients</th>
<th>ICU inpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <em>S. pneumoniae</em></td>
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<tr>
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</tr>
<tr>
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</tr>
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</tr>
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<td>• Resp. Viruses (?)</td>
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</tbody>
</table>


### Diagnosis of CAP

1. Select clinical features  
   (e.g. cough, fever, sputum, pleuritic chest pain)  
   
   AND

2. Infiltrate by CXR or other imaging

---

### Chest Radiograph – Gold Standard

- All expert guidelines state should have positive CXR to make diagnosis  
  - History & exam not good enough (50% sensitive)
- In outpt setting, should see an infiltrate.  
  - Order CXR if you are concerned about CAP  
  - If CXR negative, may *not* treat for CAP
- In the inpatient setting, can see pneumonia with a negative CXR (~30%)

**Chest Radiograph – Gold Standard?**

- Should (generally) order CXR in all patients with suspected pneumonia.
- In the hospital, a positive CXR is **not necessary** to treat as CAP (but consider other diagnoses).

**Etiology of CAP**

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</tr>
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</tr>
</tbody>
</table>

**Antimicrobials for Respiratory Tract Infections**

H. Joseph Gogbilmano, Pharm.D.
Professor and Dean
School of Pharmacy
University of California San Francisco

A 72 year-old man with a PMH of gout and HTN presented to your clinic with cough and shortness of breath. Based on the history, exam, and CXR (RML infiltrate), he is diagnosed with community-acquired pneumonia. He is well enough to be treated as an outpatient. He has no allergies.

Which of the following is the best treatment regimen?

A. Levofloxacin PO  
B. Azithromycin PO  
C. Ertapenem  
D. Amoxicillin/clavulanate PO and azithromycin PO  
E. Piperacillin/tazobactam & Vanco & Flagyl
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E. Piperacillin/tazobactam & Vanco & Flagyl

**Risk Factors for DRSP**

- Age > 65 years old
- Chronic disease
  - Heart, lung, renal, liver
- Diabetes mellitus
- Alcoholism
- Malignancy (active)
- Immunosuppression
- Antibiotics in the last 3 months

**Treatment CAP**

<table>
<thead>
<tr>
<th>Outpatient, Risk factors for resistant Strep. pneumoniae</th>
<th>Oral fluoroquinolone OR Oral β-lactam + doxy OR β-lactam + macrolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-lactam: High-dose amoxicillin (1gm PO bid)</td>
<td>Amoxicillin/clavulanate (875mg PO bid)</td>
</tr>
</tbody>
</table>

**NOTE:** Macrolides are not indicated for outpatients with DRSP risk factors (US resistance > 40%).

**2007 IDSA/ATS Recommendations: Outpatient Treatment of CAP**

- Presence of co-morbidities or receipt of antimicrobials within the past 3 months in which case an alternative from another class should be used:
  - A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, 750 mg levofloxacin): strong recommendation and level I evidence
  - Beta-lactam plus macrolide: level I evidence
A 37 year-old man with no PMH presented to your clinic with fever, cough, and shortness of breath. Based on the history, exam, and CXR (RML infiltrate), he is diagnosed with community-acquired pneumonia. He is well enough to be treated as an outpatient. He has no allergies.

Which of the following is the best treatment regimen?

A. Levofloxacin PO  
B. Azithromycin PO  
C. Doxycycline PO  
D. Amoxicillin/clavulanate PO and azithromycin PO  
E. Piperacillin/tazobactam & Vanco & Flagyl

---

Treatment CAP  
Outpatient, healthy, no risk factors for resistance  
Doxycycline or macrolide

2007* IDSA/ATS Recommendations: Outpatient Treatment of CAP

* Healthy, no use of antimicrobials within the past 3 months
* Doxycycline (level I evidence)
* Azithromycin (level III evidence)
* Update due Summer 2017

---

Risk Factors for DRSP

- Age > 65 years old
- Chronic disease: Heart, lung, renal, liver
- Diabetes mellitus
- Alcoholism
- Malignancy (active)
- Immunosuppression
- Antibiotics in the last 3 months
**Treatment of CAP**

- Outpatient, healthy, NO risk factors for resistance: Doxycycline or macrolide
- Outpatient, risk factors for resistant *Strep. pneumoniae*: Oral fluoroquinolone OR Oral β-lactam + doxy or β-lactam + macrolide

---

**Take Home Points**

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) 
3) 
4) 
5)
### Etiology of CAP

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### Treatment Inpatient CAP

**Inpatient, non-ICU**

- Fluoroquinolone OR 
- β-lactam + macrolide OR 
- β-lactam + doxycycline**

**At UCSF, we use ceftriaxone & doxycycline**

---


CAP: Current & Future

**CAP: A Practical Approach**

---

### Treatment Inpatient CAP

**Inpatient, non-ICU**

- Fluoroquinolone OR 
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CAP: Current & Future

**CAP: A Practical Approach**
### Treatment Inpatient CAP

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<th>Fluoroquinolone OR β-lactam + macrolide OR β-lactam + doxycycline**</th>
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<tr>
<td>Inpatient, ICU</td>
<td>IV β-lactam + macrolide + vancomycin OR IV β-lactam + fluoroquinolone + vancomycin</td>
</tr>
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** At UCSF, we use ceftriaxone & doxycycline

### Duration of therapy

**Meta-analysis of 15 RCTs, 2796 patients with mild to moderate CAP**

- Compared short-course (< 7 days) with longer courses.
- Looked at clinical failure, bacterial eradication, and mortality.


---

A 67 year-old man with CHF and diabetes is admitted to the hospital with CAP (non-ICU). He is treated with ceftriaxone and azithromycin and does well. The cultures are all negative. On hospital day 3 he is afebrile, feeling well and ready for discharge.

What is the optimal duration of total therapy for his CAP?

A. 14 days  
B. 10 days  
C. 7 days  
D. 5 days  
E. Who cares. He probably won’t take it anyway. I hate my job.
Duration of therapy?

- No difference in clinical failure
- No difference in bacterial eradication
- No difference in mortality

- In subgroup analysis, trend toward favorable efficacy with short-course.


Duration of therapy?

“Patients with CAP should be treated for a minimum of 5 days (level I evidence)”

-- IDSA/ATS Guidelines 2007

Duration of therapy

- Start at 5 days total
  - If afebrile x 48 hours and clinically well
  - Can extend at your discretion
  - Most will need 7 days or less

A 67 year-old man with CHF and diabetes is admitted to the hospital with CAP (non-ICU). He is treated with ceftriaxone and azithromycin and does well. The cultures are all negative. On hospital day 3 he is afebrile, feeling well and ready for discharge.

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Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) 
3) 
4) 
5)
**Roadmap**

- Background
- Community-acquired pneumonia (CAP)
- **Healthcare-associated pneumonia (HCAP)**
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)

**Definition of HCAP**

- Hospitalized for ≥ 2 days in the last 90 days
- Live in a nursing facility (SNF)/Long-term care facility
- Chemo, wound care, antibiotics in the last 90 days*
- Attend hemodialysis clinic


---

**Healthcare-Associated Pneumonia**

- Definition did not predict resistant organisms
- Most patients with these risk factors have usual CAP organisms
- Yet, there are patients in the community at risk for resistant organisms


**Healthcare-Associated Pneumonia**

- Patients with pneumonia at risk for CAP organisms & drug-resistant organisms

### Etiology of CAP

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- **Outpatients (mild)**
  - S pneumoniae
  - Resp. viruses
  - M pneumoniae
  - Others
- **Non-ICU inpatients**
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  - Resp. viruses
  - M pneumoniae
  - H influenzae
  - Legionella spp
- **ICU inpatient**
  - S pneumoniae
  - Legionella
  - H influenzae
  - GNRs
  - S aureus
  - Resp. viruses (?)

### Drug-Resistant Organisms

- Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum
  - Citrobacter
  - Acinetobacter
  - Pseudomonas (however, ceftazidime strong)
  - ENRIS AND Enterobacter
  - Stenotrophomonas (and/or Serratia)
  - Methicillin-resistant Staph aureus (MRSA)

### Healthcare-Associated Pneumonia

- Patients with pneumonia at risk for CAP organisms & drug-resistant organisms:
  - Sick (ICU or close)
  - Old and frail
  - In and out of the hospital
  - Long time in the SNF

### Healthcare-Associated Pneumonia

- If sick, old and frail, in and out of the hospital, SNF + pneumonia
  - Treat like HAP + CAP (add atypical coverage)
- Otherwise, treat like CAP

---

Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3)
4)
5)

Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3) HCAP: Old, sick, readmissions, SNF... treat like HAP + CAP
4)
5)

Roadmap

- Background
- Community-acquired pneumonia (CAP)
- Healthcare-associated pneumonia (HCAP)
- Hospital-acquired pneumonia (HAP)
  - Microbiology, Diagnosis, Treatment
- Ventilator-associated pneumonia (VAP)
**Definition of Pneumonia(s)**

- **Hospital-acquired (HAP):** pneumonia acquired > 48-72 hours after admission
- **Ventilator-associated (VAP):** pneumonia acquired > 48-72 hours after intubation

**Microbiology of HAP**

A 83 year old man with CAD, CHF, and diabetes was admitted with a CHF exacerbation. On hospital day 7, he developed a hospital-acquired pneumonia (HAP).

Which of the following is NOT a likely cause?

A. *Staphylococcus aureus*
B. *Streptococcus pneumoniae*
C. Rhinovirus
D. *Pseudomonas aeruginosa*
E. Hey, can we stop with the microbiology questions. I hate microbiology.
**Microbiology of HAP**

**Bacteria in HAP**

1. *Staph aureus*
2. Gram-negative rods (e.g. *E. coli*)
3. *Pseudomonas aeruginosa*
4. *Acinetobacter* spp
5. Others


**Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum**

- *Citrobacter*
- *Acinetobacter*
- *Pseudomonas* (however, ceftazidime strong)
- ENRls AND *Enterobacter* and *E. Coli*
- Stenotrophomonas (and/or Serratia)
- Methicillin-resistant *Staph aureus* (MRSA)
Viruses in HAP

- Total of 174 cases, cultures positive in 46%
  - Bacteria = ~50%
  - Viruses = ~50%
- Rhinovirus was the most common

Microbiology of HAP

- Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum
  - Citrobacter
  - Acinetobacter
  - Pseudomonas (however, ceftriaxone strong)
- ENRIs AND Enterobacter and E. Coli
- Stenotrophomonas (and/or Serratia)
- Methicillin-resistant Staph aureus (MRSA)
- Viruses

Diagnosis of HAP

1) Select clinical features
   (e.g. shortness of breath, fever, cough, altered mental status, hypoxia, sepsis)
   AND

2) Infiltrate by CXR or other imaging
You work at a hospital with high rates of MRSA. An 82 year old woman with dementia was admitted with acute kidney injury and encephalopathy. On hospital day 4, she developed a fever and new hypoxia and was found to have a right lower lobe (RLL) infiltrate. She is diagnosed with a hospital-acquired pneumonia. Which is an appropriate empiric treatment regimen?

A. Ceftriaxone and azithromycin  
B. Levofloxacin  
C. Vancomycin  
D. Cefepime and Vancomycin  
E. Pepperup Potion made of Bicorn Horn and Mandrake Root

Treatment Hospital-Acquired Pneumonia

- Broad-spectrum coverage but not too broad  
- No RCTs or great evidence  
- Based on severity of illness and risk factors
Microbiology of HAP

Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum
- Citrobacter
- Acinetobacter
- Pseudomonas (however, ceftazidime strong)
- ESBLs AND Enterobacter and E. Coli
- Stenotrophomonas (and/or Serratia)
- Methicillin-resistant Staph aureus (MRSA)
- Viruses

Treatment Hospital-Acquired Pneumonia

Hospital-acquired pneumonia (HAP) with:
1. Lots of MRSA (> 20%)
2. IV antibiotics in the last 90 days
   - Cefepime OR Piperacillin/tazobactam
   - Vancomycin

Treatment Hospital-Acquired Pneumonia

Critically-ill (e.g. septic shock, respiratory failure) with Hospital-acquired pneumonia
- Cefepime OR Piperacillin/tazobactam
- Tobramycin OR Levofloxacin
- Vancomycin
Hospital-acquired pneumonia (HAP) with:
1. Lots of MRSA
2. IV antibiotics in the last 90 days

Cefepime OR Piperacillin/tazobactam
+ Vancomycin

Take Home Points
1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3) HCAP: Old, sick, readmissions, SNF... treat like HAP + CAP
4)
5)
Healthcare-Associated Pneumonia

- If sick, old and frail, in and out of the hospital + pneumonia
  - Treat like HAP + CAP (add atypical coverage)
- Otherwise, treat like CAP

Treatment Hospital-Acquired Pneumonia

Hospital-acquired pneumonia (HAP) with:
1. Lots of MRSA
2. IV antibiotics in the last 90 days

- Cefepime OR Piperacillin/tazobactam
  - + Vancomycin

Treatment HCAP

Healthcare-associated pneumonia (HCAP):
- Cefepime OR Piperacillin/tazobactam
  - + Vancomycin
  - + Azithromycin

Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
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Roadmap

- Background
- Community-acquired pneumonia (CAP)
- Healthcare-associated pneumonia (HCAP)
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)
  - Microbiology, diagnosis, treatment

Definition of Pneumonia(s)

- Hospital-acquired (HAP): pneumonia acquired > 48-72 hours after admission
- **Ventilator-associated (VAP):** pneumonia acquired > 48-72 hours after intubation

Microbiology of VAP

- Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum
  - Citrobacter
  - Acinetobacter
  - *Pseudomonas* (however, ceftazidime strong)
  - *ESBLs AND Enterobacter* and *E. Coli*
  - *Serratia* and/or *Serratia*
  - Methicillin-resistant *Staph aureus* (MRSA)
  - Viruses

Diagnosis of VAP

IDSACATS Guidelines. CID. 2016;63.
For all patients clinically diagnosed with ventilator-associated pneumonia (VAP), what percentage actually have VAP at autopsy?

<table>
<thead>
<tr>
<th>Option</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>A.</td>
<td>88%</td>
</tr>
<tr>
<td>B.</td>
<td>72%</td>
</tr>
<tr>
<td>C.</td>
<td>43%</td>
</tr>
<tr>
<td>D.</td>
<td>33%</td>
</tr>
<tr>
<td>E.</td>
<td>Hey, can we stop with the math. I was told there would be no math.</td>
</tr>
</tbody>
</table>

**Diagnosis of VAP**

1) Select clinical features (e.g. fever, purulent sputum, hypoxia) **AND**
2) Infiltrate by CXR or other imaging **AND**
3) Positive sputum culture

**Take Home Points**

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3) HCAP: Old, sick, readmissions, SNF... Cefepime OR pip/tazo + vanco + azithromycin
4) HAP: Cefepime OR pip/tazo + vancomycin
5)
Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3) HCAP: Old, sick, readmissions, SNF...
   - Cefepime OR pip/tazo + vanco + azithromycin
4) HAP: Cefepime OR pip/tazo + vancomycin
5) VAP: Hard to diagnose

Treatment of VAP

A. True
B. False
Treatment of VAP

• Overall, complicated and depends on multiple risk factors

• Best to work with local guidelines and Infectious Disease

Microbiology of VAP

Third-generation Agents (Ceftriaxone): Holes in Gram-negative Spectrum

• Citrobacter
• Acinetobacter
• Pseudomonas (however, ceftazidime strong)
• ESBLs AND Enterobacter and E. Coli
• Stenotrophomonas (and/or Serratia)
• Methicillin-resistant Staph aureus (MRSA)
• Viruses

Treatment Ventilator-associated Pneumonia

For most patients with VAP:

Cefepime OR Piperacillin/tazobactam

+ Tobramycin OR Levofloxacin

+ Vancomycin
A 63 year old man with CAD and COPD is admitted with respiratory failure from a COPD exacerbation requiring intubation. He develops a VAP on hospital day 6 and is treated empirically with cefepime, levofloxacin, and vancomycin. Cultures eventually grow *Klebsiella* which is sensitive to levofloxacin. He clinically improves and is extubated. What is the appropriate total duration of treatment for his VAP?

A. 3 days  
B. 5 days  
C. 7 days  
D. 14 days  
E. 6 weeks of IV antibiotics

Treatment Duration for VAP

- Systematic review and meta-analysis in 2015  
- Total of 4 studies, 442 patients  
- Shorter course (7 days) vs. Longer (>14 days) was associated with:  
  - No difference in mortality, ICU LOS, etc.  
  - Fewer antibiotic days  
- Not true for *Staph aureus, Pseudomonas*

Treatment Duration for VAP

- For most patients with VAP (and HAP and HCAP), can start with 7 days*  
- Can extend based on patient illness or microbiology
Take Home Points

1) Outpatient CAP: Brad Pitt vs. Donald Rumsfeld
2) CAP: Start at 5 days
3) HCAP: Old, sick, readmissions, SNF...
   Cefepime OR pip/tazo + vanco + azithromycin
4) HAP: Cefepime OR pip/tazo + vancomycin
5) VAP: Hard to diagnose
6) VAP/HAP/HCAP: Treat for 7 days*

Roadmap

- Background
- Community-acquired pneumonia (CAP)
- Healthcare-associated pneumonia (HCAP)
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)

Specific Goals:

- Describe the most common causes of pneumonia in different settings
- Initiate appropriate antibiotics in the treatment of CAP, HCAP, HAP, and VAP
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   Cefepime OR pip/tazo + vanco + azithromycin
4) HAP: Cefepime OR pip/tazo + vancomycin
5) VAP: Hard to diagnose
6) VAP/HAP/HCAP: Treat for 7 days*
Healthcare-associated Pneumonia

CAP, HCAP, HAP, VAP

Brad Sharpe, M.D.
Professor of Clinical Medicine
Department of Medicine
UCSF
sharpeb@medicine.ucsf.edu

I have no relevant financial relationships to disclose.

Aspiration!

• Very common diagnosis
• Pneumonitis vs. pneumonia
• Pneumonitis
  • Syndrome of inflammation
  • “Jello on the lung”
  • Focal infiltrate or bilateral opacities
  • Patients recover quickly (hours)
Aspiration!

- Aspiration pneumonia
  - True bacterial infection
  - Usually focal infiltrate
  - Occurs 48 hours after aspiration event

- If true pneumonitis, don’t need antibiotics

De-Escalation in HCAP

- In general, can switch to a fluoroquinolone (levo or moxi)

- If fluoroquinolone allergy, can do Ceftriaxone + Azithromycin (or Augmentin + azithromycin at discharge)