Antibiotic Update: Smart Prescribers Smart Choices

Amelie Hollier, DNP, FNP-BC, FAANP
President, APEA

Before you prescribe an antibiotic....
There is a question you MUST ask

What bug is causing my patient’s infection?
What are the most likely bugs?

Most of the time we guess!
Empiric Treatment!

There are times....

- We HAVE to get a culture
- The patient can’t afford treatment failure!

Since we can’t culture every bug.....
We have to be pretty good at Empiric Treatment!
**Lung Infections**

- Community Acquired Pneumonia (CAP)
- CAP post influenza
- Acute Bronchitis

**Patient #1**

52 year old female, ND, a retired school teacher, has been diagnosed with CAP. She is a non-smoker, has normal BMI, takes no meds. She walks 3 miles, 4-5 times weekly.

What’s the most likely pathogen for her CAP?
1. *Strept pneumoniae*
2. Atypical pathogen
3. *Staph aureus*
4. Viral pathogen


**Patient #1**

52 year old female, ND, a retired school teacher, has been diagnosed with CAP. She is a non-smoker, has normal BMI, takes no meds.

Most common cause is an atypical pathogen: *Mycoplasma pneumoniae*; could be viral; could be *S. pneumonia* but these 2 are much less likely


**Patient #1**

What is an acceptable treatment for the most likely pathogen?
1. Azith 500 mg once, then 250 mg x 4 days
2. Azith 2g once
3. Doxy 100 mg PO BID
4. Amox-clav 875 PO mg BID


**Patient #1**

If Mycoplasma is documented as the pathogen, what is the best treatment?
1. Azith 500 mg once, then 250 mg x 4 days
2. Azith 2g once
3. Doxy 100 mg PO BID
4. Amox-clav 875 PO mg BID

JAC 68:506, 2013

**Patient #1**

- Increasing macrolide resistance with *Mycoplasma*
- *Doxy* is a superior choice

JAC 68:506, 2013
**Patient #1**

Suppose ND developed **CAP post influenza infection**?  
What’s the most likely pathogen for her CAP?  

1. *Strept pneumoniae*  
2. Atypical pathogen  
3. *Staph aureus*  
4. Viral pathogen


**Patient #1**

What’s an acceptable treatment for the most likely pathogen?  

1. Levofloxacin 750 mg PO daily  
2. Azith 2g once  
3. Doxy 100 mg PO BID  
4. Amox-clav 875 mg PO BID


**Patient #1**

Suppose she was quinolone allergic or couldn’t take a quinolone (and had post-flu pneumonia)?  

- Azith or Clarith *Plus* HD amox, HD amox-clav, cefdinir (Omnicef), cefpodoxime (Vantin), cefprozil (Cefzil)  
FYI: if use a ceph, always give the BID dose!


**Patient #1**

How much amox is considered HIGH DOSE?  

- Amox: 1 gram PO TID  
- Amox-clav: Use Amox-clav ER (1000/62.5)  
Prescribe 2 tabs BID


**Patient #1**

52 year old female, ND, a retired school teacher, has been diagnosed with CAP.  
Suppose she has COPD and smokes 1 PPD.


**Patient #1**

What’s the most likely pathogen for her CAP if she has COPD?  

1. *Strept pneumoniae*  
2. *M. catarrhalis*  
3. *H. influenzae*  
4. Viral pathogen

So, knowing the most likely bug is helpful in choosing the best antibiotic!

What’s an easy way to remember which antibiotic to give for CAP?

CAP in an Adult

Give a macrolide or doxy first line UNLESS.....

The patient has a co-morbid:
• Alcoholism
• Bronchiectasis
• COPD
• Post-CVA aspiration
• Post-influenza
• Significant chronic disease

If co-morbid is present:
Respiratory quinolone
• Gemifloxacin (Factive) 320 mg
• Levofloxacin (Levaquin) 750 mg
• Moxifloxacin (Avelox) 400 mg

Respiratory Quinolones
Ciprofloxacin no longer considered a respiratory quinolone R/T increased rates of resistance:
• S. pneumoniae
• Pseudomonas aeruginosa
• C. difficile
• N. gonorrhoeae
• MRSA, MSSA
• S. aureus
What do Tequin, Raxar, Zagam, and Trovan all have in common?

Hint: They all “were” quinolones.

Remember These?

- Tequin (gatifloxacin): blood sugar irregularities
- Zagam (sparfloxacin): phototoxicity and QT prolongation
- Trovan (trovafloxacin): hepatotoxicity

Quinolones as a Class

- Blood sugar level issues!
- QT prolongation
- CNS adverse effects (dizziness, etc.)
- Tendon rupture (rare)

Things to Remember!

- None approved in children*
- Do not use in pregnant patients
- Separate from Mg, Al, sucralfate, Fe, Zn (Ca probably OK but not with cipro): drug specific
- No sig CYP450 interactions except with cipro

Ciprofloxacin

- Ciprofloxacin is a 1A2 med
- Combined with theophylline, xanthines (CAFFEINE), results in increased plasma concentrations of the co-administered drug
- So what happens???

Respiratory Quinolones

What would make you choose one over the other?

- Gemifloxacin (Factive) 320 mg
- Levofloxacin (Levaquin) 750 mg
- Moxifloxacin (Avelox) 400 mg
Levofloxacin

- Diminished activity against *Strept pneumoniae* and anaerobic pathogens
- Levofloxacin originally dosed at 500 mg daily but increased to 750 mg daily to improve coverage against resistant organisms

**Respiratory Fluoroquinolones**

**3rd Generation**

*Levofloxacin* (Levaquin)

- Gram Positives, Gram Negatives, Atypical Pathogens, DRSP, many aerobes, some anaerobes

**4th Generation**

*Moxifloxacin* *(Avelox)*

- Gemifloxacin (Factive), Gatifloxacin (Zymar ophth)

- Gram Positives, Atypical Pathogens, *superior pneumococcus and anaerobic coverage*

- *Staph: MSSA*
- *Listeria*
- Not urinary pathogens

**Take Home Point**

- A 4th generation quinolone would be a better choice than a 3rd gen quinolone for DRSP

**Patient #2**

38 year old male, otherwise healthy has been diagnosed with acute bronchitis. He is a non-smoker, has BMI 29, has well controlled HTN, lipids.

What’s the most likely pathogen for his acute bronchitis?

1. *Strept pneumoniae*
2. Atypical pathogen
3. *Staph aureus*
4. Viral pathogen


**Patient #2**

**Acute Bronchitis**

- 90% viral
- 5% *M. pneumoniae*
- 5% *C. pneumoniae*

Antibiotics are NOT indicated usually!

*JAMA 312:2678, 2014*
When might antibiotics be indicated?

- Associated sinusitis
- Heavy growth on throat culture for *S. pneumoniae*, Group A Strept, *H. influenzae*
- No improvement in 1 week
- Otherwise, treatment is SYMPTOMATIC!

Acute Bronchitis

- Purulent sputum is not an indication for antibiotic treatment
- Expect cough to last 2 weeks (<20 days)

Quiz

Why do most patients with acute bronchitis have purulent looking sputum?

Purulent Sputum

IF patient has fever, rigors, systemic symptoms, get chest x-ray

Urinary Tract Infection

If Local resistance rate < 20%
- TMP-SMX BID x 3 days
- *Add phenazopyridine (Pyridium)*

Local resistance rate correlates with clinical failure

TMP/SMX Drug Interactions

- You’ll see this as a New Drug Interaction in your Smart Phone Apps!
- Possible HYPERKALEMIA when TMP-SMX combined with meds that increase potassium
- ACEs, ARBs, potassium sparing diuretics, NSAIDs

Prescribers Letter; January 2015, Vol 31
TMP/SMX Drug Interactions

- Trimethoprim decreases excretion of potassium (acts on the distal nephron, blocking the epithelium Na channel which leads to reduction in renal excretion of K)
- Hyperkalemia develops 4-5 days after taking TMP/SMX, so 3 day dose likely OK

Prescribers Letter; January 2015; Vol 31

TMP/SMX Drug Interactions

- 81.5% had significant increase in serum K from baseline
- 18% had hyperkalemia > 5 meq/L
- 6% had hyperkalemia > 5.5 meq/L
- Reversible once TMP/SMX is d/c'd


Drug Interactions

- 6% of patients on TMP/SMX develop hyperkalemia
- Hospitalizations increase 7-fold when elders take TMP-SMX with ACE, ARB, etc
- Even higher when combined in patients who take ACEs, ARBs, or spironolactone

Prescribers Letter; January 2015; Vol 31

Care in These Patients!

- Elderly
- Renal insufficiency
- DM
- Heart failure

***If no alternative to TMP/SMX, check K level after day 3

Prescribers Letter; January 2015; Vol 31

So... UTI

If Local resistance rate < 20%
- TMP-SMX BID x 3 days
- Add phenazopyridine (Pyridium)

Local resistance rate correlates with clinical failure

JAMA 312:1677, 2014

Why are we adding phenzopyridine?

JAMA 312:1677, 2014
Urinary Tract Infection

IF Local resistance rate > 20% or sulfa allergy:
- Ciprofloxacin 250mg BID or 500 mg ER q24h
- Levofoxacin 250 mg q24
- Nitrofurantoin 100 mg PO BID x 5 days
- Fosfomycin single 3g dose

Add phenazopyridine (Pyridium)

JAMA 312:1677, 2014

Why aren’t the 4th generation quinolones used to treat UTIs?

Drug package inserts: Moxifloxacin, Gemifloxacin

Mrs. Jones is 75 years old. She is diagnosed with a UTI. Her CrCl is 50 mL/min.

What drug might be a good choice for her?

2012 Beers Criteria Update Expert Panel
J AM Geriatr Soc. 2012;60(4):616-631

Mrs. Jones is 75 years old. She is diagnosed with a UTI. Her CrCl is 50 mL/min.

Which anti-infective should be avoided in her because of inadequate drug concentration in the urine?

1. Sulfa drug (none as long as CrCl > 30 mL/min)
2. Ciprofloxacin (none as long as CrCl > 30 mL/min)
3. Nitrofurantoin (AVOID!)

Mrs. Jones is 75 years old. She is diagnosed with a UTI. Her CrCl is 50 mL/min.

Beers Criteria recommends nitrofurantoin avoidance:
- CrCl < 60 mL/min
- For long-term suppression

2012 Beers Criteria Update Expert Panel
J AM Geriatr Soc. 2012;60(4):616-631
**Nitrofurantoin**

IF used for daily prophylaxis, may cause pulmonary toxicity, neuropathy, or hepatotoxicity.


Dailymed.nlm.gov; Nitrofurantoin product insert

---

**Etiology of Acute Sinusitis**

Most common???

**Etiology of Acute Sinusitis**

Obstruction of the sinus ostia by inflammation from virus or allergy

Treatment: Saline irrigation

---

**S/S Bacterial Infection**

- Fever
- Pain
- Purulent nasal discharge
- Still symptomatic after 10 days with no antibiotic
- Clinical failure despite antibiotic treatment

**IF Pathogen present:**

- *S. pneumoniae* 33%
- *H. influenzae* 32%
- *M. catarrhalis* 9%
- Anaerobes 6%
- Grp A Strep 2%
- Viruses 15-18%
- *S. aureus* 10%

---

**IF Pathogen present:**

- *S. pneumoniae* 33%
- *H. influenzae* 32%
- *M. catarrhalis* 9%
- Anaerobes 6%
- Grp A Strep 2%
- Viruses 15-18%
- *S. aureus* 10%
What Antibiotic for ABRS?

- Amoxicillin not a good first choice (too much resistance, less Strept pneumo, more incidence of H. flu)
- Empiric: Amoxicillin-clavulanate (500 TID or 875 BID)
- Amoxicillin-clavulanate (2g BID) in areas where DRSP likely

CID 54:e72, 2012

What Antibiotic for Peds?

- First line: Amoxicillin with or without clavulanate
- Alternatives: cefdinir, cefuroxime, cefpodoxime
- Avoid sulfa drugs, azithromycin


What if PCN allergic?

- Doxycycline (alternative first line tx PCN allergy)
- Resp FQ for PCN allergic patients
- No Macrolides: 30% resistance rate!
- TMPS, 2nd or 3rd gen cephs NOT recommended

What Antibiotic for Peds?

- First line: Amoxicillin with or without clavulanate
- Alternatives: cefdinir, cefuroxime, cefpodoxime
- Avoid sulfa drugs, azithromycin

Penicillins

Extended Spectrum PENICILLINS

<table>
<thead>
<tr>
<th>Amoxicillin/Clavulanic acid (Augmentin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Positives, Gram Negatives</td>
</tr>
<tr>
<td>B- lactamase, NOT MRSA</td>
</tr>
</tbody>
</table>

What bug do smokers harbor?

- H. influenza (40%)
- M. catarrhalis (90%)

CID 54:e72, 2012

Duration

- Eradication if on appropriate antibiotic in 72 hours but treat.....
- 5-7 days (no longer treat 10-14 days)
- With shorter courses: equal efficacy, fewer complications, no increased risk of relapse
- Better compliance!

Can PCN allergic patients safely receive cephalosporins?
2 Issues
There MUST be a PCN **allergic** reaction!!!

True Allergic Reaction
- IgE mediated
  (type 1 hypersensitivity reaction)

Morbilliform Rash
- Rash is macular or maculopapular, lesions are fixed, area expands over several days
- May itch
- More prevalent in children
- More common with aminopenicillins (amox and ampicillin)

Morbilliform Rash
- Usually T-cell mediated
  - Concurrent viral infections predispose patients to morbilliform rash
  - Unknown mechanism by which this occurs

The rash is Not IgE-mediated if **neither urticarial nor pruritic!!!**

And there is NO increased risk of the same rash recurring with repeated courses of the same antibiotic.

Second Issue
How significant is the cross-sensitivity reaction?

*Journal of Family Practice, Feb. 2006*
**Likely Allergy to Cephalosporins** *after allergy to PCN*

Very likely to have **SAME** allergic reaction with these drugs because they share a similar R side chain

- Pen G
- Cefaclor
- Cefadroxil
- Amoxicillin
- Cephalexin
- Ceftriaxone
- Ampicillin
- Cefazolin
- Cefuroxime

**UNLIKELY Allergy to Cephalosporins** *after allergy to PCN*

NOT likely to have **SAME** allergic reaction with these drugs because they are dissimilar in structure

- Cefazolin (1st gen IM)
- Cefuroxime (2nd gen)
- Cefdinir (3rd gen)
- Ceftibuten (3rd gen)

**RECOMMENDATION**

The risk of an allergic reaction is very low or non-existent if the side chains of the drugs are not similar.

**Summary and Take Home**
Take Home Point

Ask and be able to answer: What bug is causing my patient’s infection?

Take Home Point

Make Evidence-Based decisions when prescribing antibiotics

Thank you!
For questions or to contact me:

Dr. Amelie Hollier
amelie@apea.com
Advanced Practice Education Associates