FUTURE OF PEDIATRICS TALKS!
A VIRTUAL SUMMER SERIES

Pediatric Health Network
Children's National
Know when to say when: Antimicrobial stewardship case studies

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We will be using PollEverywhere
Please go to pollev.com/ranahamdy216 on your smartphone/laptop web browser NOW
Learning Objectives

1. Describe the benefits of shorter antibiotic courses when appropriate
2. Identify clinical scenarios where shorter courses of antibiotics are appropriate as well as when prescribing no antibiotics is appropriate
   1. Community Acquired Pneumonia
   2. Cellulitis
   3. UTI
   4. AOM

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What are you supposed to be?

An unfinished course of antibiotics.

I can lead to antibiotic resistance. Aren't I terrifying?!

And Beatrice was never invited to a Halloween party ever again.

Beatrice the Biologist
Actually, multiple studies have shown that longer durations of therapy are more likely to lead to development of antibiotic resistance.

Is it time to stop counselling patients to “finish the course of antibiotics”?

Bradley J. Langford, BScPhm, ACPR, PharmD, BCPS and Andrew M. Morris, MD, SM(Epi), FRCPC
Antibiotic use is the #1 driving factor leading to antibiotic resistance

1. Lots of germs. A few are drug resistant.
2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.
3. The drug-resistant bacteria are now allowed to grow and take over.
4. Some bacteria give their drug-resistance to other bacteria, causing more problems.

- Broader spectrum antibiotics
- Inadequate doses
- Longer durations

Antibiotic resistance
Bacteria have developed resistance to every single antibiotic that has been developed.
Antibiotic resistance is affecting outpatient pediatrics: 

*Staphylococcus aureus*

Clindamycin Resistance, *S. aureus* from outpatient pediatrics isolates

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Antibiotic Resistance is affecting our pediatric patients: *Streptococcus pneumoniae*
Antibiotic resistance is affecting our pediatric patients: Gram negative infections

Antibiotic Resistance is “one of the world’s most pressing health problems”
Resistance aside ...  
Antibiotic prescribing decisions should focus on risks/benefits for the individual patient  

Adverse Effects of Antibiotics  

1 in 5 ED visits for adverse drug events is due to an antibiotic  
10%–25%: antibiotic-associated diarrhea  
2%: skin reaction  
1 in 5,000: anaphylactic reaction  

Overall:  
- number needed to harm (NNH) = 13  
- NNH = 6, including diarrhea  
- Each additional day of abx → 7% ↑ odds of AE
Community Acquired Pneumonia
3-year old p/w cough, fever to 38.5°C x 2 days. Patient is well-appearing and well-hydrated with a RR of 44 and mild intercostal retractions, rt lung base w/ crackles exam. You diagnose with community-acquired pneumonia and prescribe amoxicillin for:

- 10 days
- 7 days
- 5 days
- 3 days
Question #1:

3-year old previously healthy child is seen with cough, fever to 38.5C for 2 days. Patient is well-appearing and well-hydrated with a respiratory rate of 44 and mild intercostal retractions, right lower lobe noted to have crackles on auscultatory exam. You make a diagnosis of Community-Acquired Pneumonia and prescribe high-dose amoxicillin. How long should the antibiotic course be?

a) 7 days
b) 10 days
c) 5 days
d) 3 days
Community-Acquired Pneumonia - Adults

- Uncomplicated Community-Acquired pneumonia → treat for 3-5 days\(^1\)
- Longer if:
  - Initial therapy not active against identified pathogen
  - Loculated fluid collections
  - Complications with extrapulmonary infection

Supplemental Figure 4. Duration of antibiotic therapy by antibiotic category for community acquired pneumonia (CAP) in A) Children (<18 years) and B) Adults (≥18 years), IQVIA National Disease and Therapeutic Index (NDTI) 2017.
• 2-center RCT in Ontario: 2016-2019

• **Included**: 6 months – 10 years previously healthy with radiographic-confirmed pneumonia diagnosed in ER, not requiring hospitalization

• **Excluded**: comorbidities predisposing to severe disease and/or pneumonia of unusual origin, previous beta-lactam antibiotic therapy

• **Intervention**: 5-day high dose amox therapy followed by 5-day placebo vs. 5-days high dose amox followed by different formulation of the same (control)

• **Outcome**: Clinical cure at 14-21 days

• **Results**: Clinical cure similar between the two groups (88.6 vs. 90.8%)

• **Conclusion**: short-course therapy comparable to standard of care
Cellulitis
10 yo p/w a 2x3cm area of erythema on his rt lower leg x 2-3 days, + induration, + warmth, + tenderness. Pt is otherwise well-appearing, well-hydrated, interactive, Tm 38.3, other VS normal. What is your next management plan of choice?

Send to ER for ultrasound to ensure there is no abscess component

Prescribe Skin and soft tissue infection (SSTI)-appropriate antibiotic for a 10-day course

Prescribe SSTI-appropriate antibiotic for a 5-day course with specific return precautions/call-back instructions if not improving

Prescribe SSTI-appropriate antibiotic for a 5-day course and have patient return to office to monitor for improvement after 2 days

Prescribe SSTI-appropriate antibiotic for a 14-day course
Question #2

10-year old presents to clinic with a 2x3cm area of erythema on his right lower leg that has developed over the past 2-3 days, with associated induration but no fluctuance or purulent discharge. The area is warm and tender to touch. The patient is otherwise well-appearing, well-hydrated, interactive. He does have an elevated temperature to 38.3F in office but other vital signs are normal. What is your next management plan of choice?

1. Send to ER for ultrasound to ensure there is no abscess component
2. Prescribe Skin and soft tissue infection(SSTI)-appropriate antibiotic for a 10- day course
3. Prescribe SSTI-appropriate antibiotic for a 5-day course with specific return precautions/ call-back instructions if not improving
4. Prescribe SSTI-appropriate antibiotic for a 5-day course and have patient return to office to monitor for improvement after 2 days
5. Prescribe SSTI-appropriate antibiotic for a 14- day course
Cellulitis

- 5 days of antibiotic ("but should be extended if infection has not improved")
- Recommendation level, evidence grade: Strong, High
Comparison of Short-Course (5 Days) and Standard (10 Days) Treatment for Uncomplicated Cellulitis

MAJ Matthew J. Hepburn, MC, USA; COL David P. Dooley, MC, USA; MAJ Peter J. Skidmore, MC, USA; MAJ Michael W. Ellis, MC, USA; MAJ William F. Starnes, MSC, USA; LTC William C. Hasewinkle, MC, USA

- 5 days of levofloxacin followed by 5 more days of either placebo or additional levofloxacin
- Outcome measure: resolution of cellulitis at 14 days, absence of relapse by 28 days
- Results: No significant difference in clinical outcome between the two courses of therapy
Takeaways

You can SEE cellulitis improve (and so can the patient)

Treatment time can be variable, but 5 days is reasonable!

When erythema and induration have resolved, can discontinue antibiotics
Urinary tract infections
A previously healthy 16 y/o female p/w dysuria and urinary frequency without back pain or fever. A clean-catch UA reveals 2+ nitrites and 3+LE. You decide to treat with TMP/SMX 160/800mg empirically for UTI pending the urine culture result. Which of the

- 3 days
- 5 days
- 7 days
- 10 days
Question #3

- A previously healthy 16 y/o Female presents with dysuria and urinary frequency without back pain or fever. A clean-catch urinalysis reveals 2+ nitrites and 3+ leuk esterase. You decide to treat with TMP/SMX 160/800mg empirically for UTI. Pending the urine culture result, which of the following is the most appropriate duration of therapy?
  - 3 days
  - 5 days
  - 7 days
  - 10 days
Adult Data

- Nitrofurantoin 100mg twice daily for 5 days
- Bactrim 160/800mg twice daily for 3 days
- Fosfomycin 3g single dose
- IV Ceftriaxone or AG, single dose
- Alternatives:
  - Fluoroquinolones 3 days
  - Beta-lactams 3-7 days

International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases
<table>
<thead>
<tr>
<th>System</th>
<th>Condition</th>
<th>Common Pathogens</th>
<th>Empiric Antibiotic Therapy</th>
<th>Antibiotic Duration</th>
<th>Notes</th>
<th>Key Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genitourinary</td>
<td>UTI - pyelonephritis</td>
<td><em>Escherichia coli</em></td>
<td>Cephalexin</td>
<td>7–10 days</td>
<td>Drug selection should be based on local antibiogram or patient’s prior urine isolates</td>
<td>Roberts et al&lt;sup&gt;7&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td><em>Klebsiella</em> species</td>
<td>OR</td>
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<td></td>
<td></td>
<td><em>Proteus</em> species</td>
<td>TMP-SMX</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><em>Enterobacter</em> species</td>
<td>Ampicillin PLUS</td>
<td>3–5 days (simple cystitis in adolescents)</td>
<td>Initial short course of IV therapy (2–4 days) is as effective as longer courses of IV therapy</td>
<td>Gupta et al&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Citrobacter</em> species</td>
<td>Gentamicin</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><em>Enterococcus</em> species</td>
<td>OR</td>
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<tr>
<td></td>
<td></td>
<td><em>Staphylococcus</em> <em>saprophyticus</em></td>
<td>Ceftriaxone</td>
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<td>OR</td>
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<td></td>
<td></td>
<td></td>
<td>Ciprofloxacin</td>
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</tbody>
</table>

**Table 4.12. Systems-based Treatment Table, continued**

**Notes**: Avoid nitrofurantoin for upper urinary tract infection or bacteremia.
Asymptomatic bacteriuria

NO ANTIBIOTICS!!!

Exceptions:
• Pregnancy
• Renal transplant
• Undergoing urinary procedural manipulation
Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

“The clinician should choose 7 to 14 days as the duration of antimicrobial therapy”

“The committee attempted to identify a single, preferred, evidence-based duration, rather than a range, but data comparing 7, 10, and 14 days directly were not found”

Fox MT et al. JAMA Network Open. 2020

- Children 6mo-18 yrs with urine culture growing *E. coli*, *Klebsiella* spp, or *P. mirabilis* with lab & clinical criteria for pyelonephritis
- Compared short course (6-9 d) vs. long course (10+ d)
- Inverse probability of treatment weighted propensity analysis
- 791 children enrolled, avg 8 d for short course, 11 d for long course.
- Overall, 10% experienced treatment failure (11.2% for short-course, 9.4% for long-course; OR 1.22, 95% CI: 0.75-1.98)
### Choice of antibiotic: children and young people under 16 years

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage and course length</th>
</tr>
</thead>
<tbody>
<tr>
<td>If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the <a href="https://www.nice.org.uk/guidance/ng133">NICE guideline on acute pyelonephritis</a> for antibiotic choices.</td>
<td></td>
</tr>
<tr>
<td>Refer children under 3 months to paediatric specialist and treat with intravenous antibiotics in line with the <a href="https://www.nice.org.uk/guidance/ng130">NICE guideline on fever in under 5s</a>.</td>
<td></td>
</tr>
</tbody>
</table>

#### Children aged 3 months and over - First choice\(^3\)\(^4\)

| Trimethoprim: if low risk of resistance\(^5\) | 3 to 5 months, 4 mg/kg (maximum 200 mg per dose) or 25 mg twice a day for 3 days  
6 months to 5 years, 4 mg/kg (maximum 200 mg per dose) or 50 mg twice a day for 3 days  
6 to 11 years, 4 mg/kg (maximum 200 mg per dose) or 100 mg twice a day for 3 days  
12 to 15 years, 200 mg twice a day for 3 days |
|------------------------------------------------|----------------------------------------------------------------------------------|

Nitrofurantoin: if estimated glomerular filtration rate (eGFR) ≥ 45 ml/minute\(^6\)

| 3 months to 11 years, 750 micrograms/kg four times a day for 3 days  
12 to 15 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days |                                    |

#### Children aged 3 months and over - Second choice (worsening lower UTI symptoms on first choice taken for at least 48 hours or when first choice not suitable)\(^3\)\(^4\)

| Nitrofurantoin: if eGFR ≥ 45 ml/minute\(^6\) and not first choice | 3 months to 11 years, 750 micrograms/kg four times a day for 3 days  
12 to 15 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days |
|---------------------------------------------------------------|--------------------------------------------------------------------------|
| Amoxicillin (only if culture results available and susceptible) | 1 to 11 months, 125 mg three times a day for 3 days  
1 to 4 years, 250 mg three times a day for 3 days  
5 to 15 years, 500 mg three times a day for 3 days |
| Cefalexin                                                      | 3 to 11 months, 12.5 mg/kg or 125 mg twice a day for 3 days  
1 to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 3 days  
5 to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 3 days  
12 to 15 years, 500 mg twice a day for 3 days                  |
## Pyelonephritis (acute): antimicrobial prescribing

### Choice of antibiotic: children and young people under 16 years

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<th>Antibiotic</th>
<th>Dosage and course length</th>
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<tr>
<td><strong>Refer children under 3 months to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Children aged 3 months and over - First choice oral antibiotic</strong></td>
<td></td>
</tr>
<tr>
<td>Cefalexin</td>
<td>3 to 11 months, 12.5 mg/kg or 125 mg twice a day for 7 to 10 days; 25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections 1 to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 7 to 10 days; 25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections 5 to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 7 to 10 days; 25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections 12 to 15 years, 500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days</td>
</tr>
<tr>
<td>Co-amoxiclav (only if culture results available and susceptible)</td>
<td>3 to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 1 to 5 years, 0.25 ml/kg of 125/31 suspension or 5 ml of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 6 to 11 years, 0.15 ml/kg of 250/62 suspension or 5 ml of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 12 to 15 years, 250/125 mg or 500/125 mg three times a day for 7 to 10 days</td>
</tr>
<tr>
<td><strong>Children aged 3 months and over - First choice intravenous antibiotics (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if susceptibility or sepsis a concern</strong></td>
<td></td>
</tr>
<tr>
<td>Co-amoxiclav (only in combination or if culture results available and susceptible)</td>
<td>3 months to 15 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>3 months to 15 years, 20 mg/kg three times a day (maximum 750 mg per dose), increased to 50 to 60 mg/kg three or four times a day (maximum 1.5 g per dose) for severe infections</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>3 months to 11 years (up to 50 kg), 50 to 80 mg/kg once a day (maximum 4 g per day); 9 to 11 years (50 kg and above), 1 to 2 g once a day; 12 to 15 years, 1 to 2 g once a day</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Initially 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration</td>
</tr>
</tbody>
</table>
Takeaways

3-5 days for cases of cystitis

No abx for asymptomatic bacteriuria, please

7-14 days, try for 7 in cases of pyelonephritis
Otitis Media
In which of the following scenarios would you choose observation with pain control without the use of antibiotics?

A. 4 mo old w/ unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

B. 15-mo old with bilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

C. 20-mo old with unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, fever (temperature of 39.3°C [102.8°F]), and otalgia.

D. 30 mo old with unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, fever (temperature of 39.4°C [103.0°F]), and otalgia.

E. 3-year-old with a unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.
In which of the following scenarios would you choose observation with pain control without the use of antibiotics?

A. A 4-month-old with unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

B. A 15-month-old with bilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

C. A 20-month-old with unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, fever (temperature of 39.3°C [102.8°F]), and otalgia.

D. A 30-month-old with unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, fever (temperature of 39.4°C [103.0°F]), and otalgia.

E. A 3-year-old with a unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.
2010 Cochrane review

- Wait and watch approach for:
  - >6 months, non-severe disease
  - If treatment warranted, shorter courses → fewer side effects & higher compliance
Otitis Media: To Treat, To Refer, To Do Nothing: A Review for the Practitioner

7 days if 2-5 years
5 days if not severe in > 6 years

10 days
Justification for withholding antibiotic treatment from selected children with AOM is based upon analysis of numerous clinical trials over 30 years.

Review of these trials suggests most children with AOM do well without antimicrobial therapy.

Observation only for children with AOM who are likely to improve on their own reduces common adverse effects of antibiotics, such as diarrhea and diaper dermatitis.

The length of treatment with oral antibiotics should be 10 days for children < 2 years of age, 7 days for children ages 2 to 5 years, and 5 to 7 days for children 6 years and older.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Length of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-Acquired Pneumonia</td>
<td>5 days</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>5 days</td>
</tr>
<tr>
<td>UTI:</td>
<td></td>
</tr>
<tr>
<td>Simple Cystitis</td>
<td>3-5 days</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>7 days</td>
</tr>
<tr>
<td>Asymptomatic bacteriuria</td>
<td>0 days</td>
</tr>
<tr>
<td>AOM:</td>
<td></td>
</tr>
<tr>
<td>&lt;2 years</td>
<td>10 days</td>
</tr>
<tr>
<td>2-5 years</td>
<td>7 days</td>
</tr>
<tr>
<td>≥ 6 years</td>
<td>5 days</td>
</tr>
</tbody>
</table>
References


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