FUTURE OF PEDIATRICS TALKS!

A VIRTUAL SUMMER SERIES

Pediatric Health Network

Children's National.

Know when to say when: Antimicrobial stewardship case studies

Rana Hamdy, MD- Infectious Diseases CNH

Ariella Slovin, MD- General Pediatrics, Goldberg Center

David Sullivan, MD – General Pediatrics, Goldberg Center CNH

FUTURE OF PEDIATRICS 7/27/2021

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

We will be using PollEverywhere

Please go to pollev.com/ranahamdy216 on your smartphone/laptop web browser now

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.

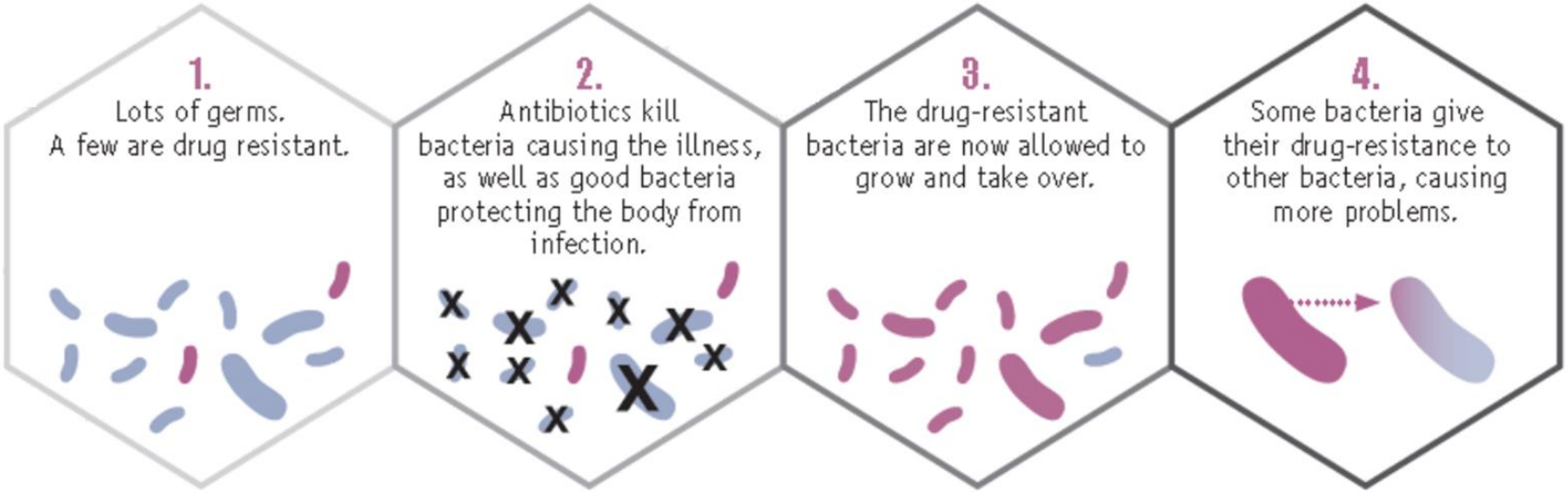
Can Pharm J (Ott). 2017 Nov-Dec; 150(6): 349–350.
Published online 2017 Oct 5. doi: 10.1177/1715163517735549

PMCID: PMC5661683
PMID: 29123590

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

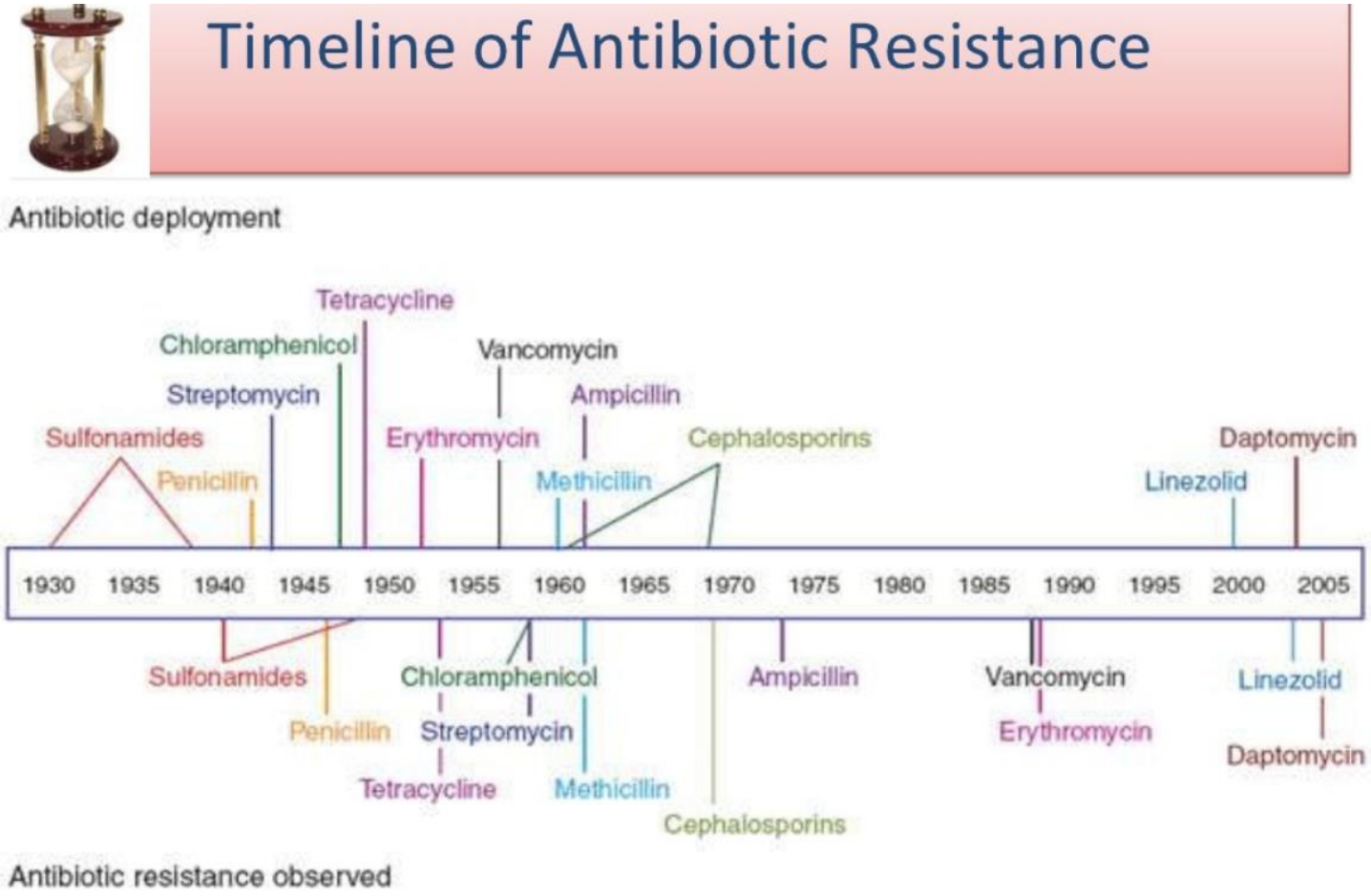


- **Broader spectrum antibiotics**
- **Inadequate doses**
- **<u>Longer durations</u>**

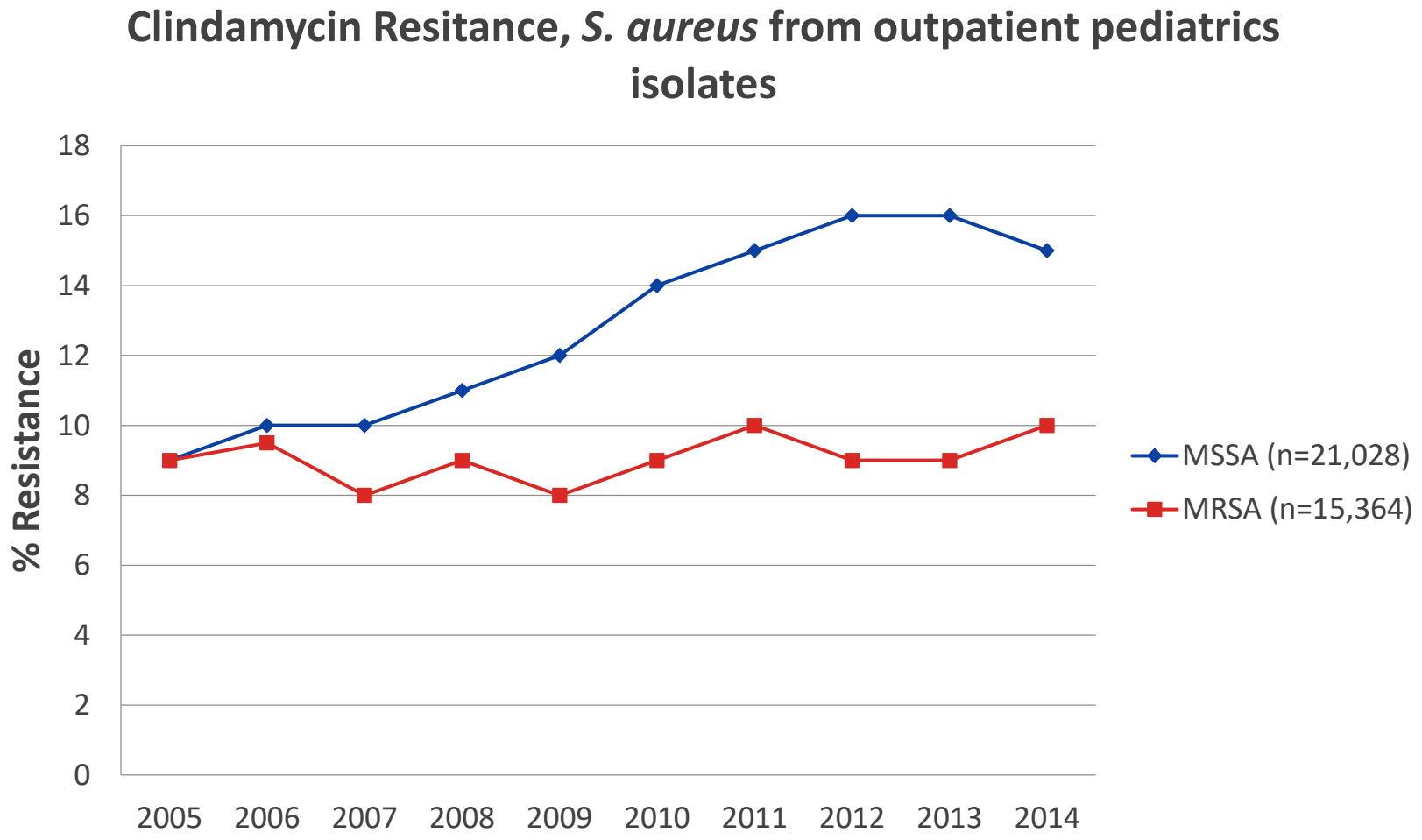
→

Antibiotic resistance

Bacteria have developed resistance to every single antibiotic that has been developed



Antibiotic resistance is affecting outpatient pediatrics: *Staphylococcus aureus*

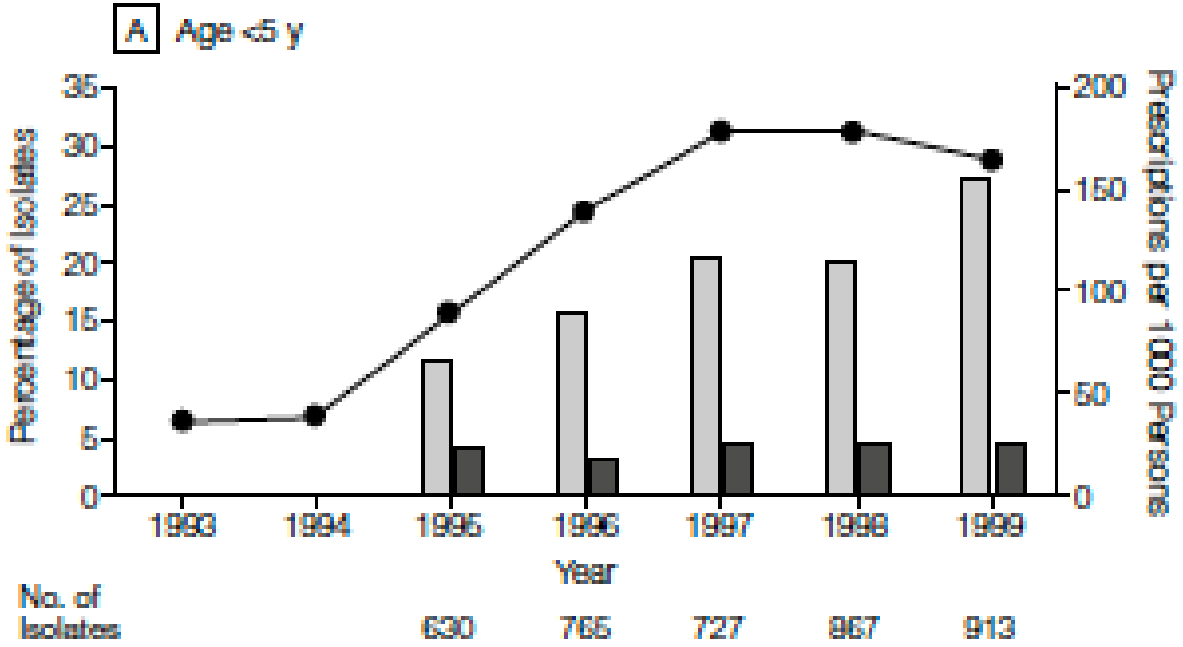


Sutter DE et al. *Pediatrics.* 2016. 137(3): e20153099

Antibiotic Resistance is affecting our pediatric patients:

Streptoco

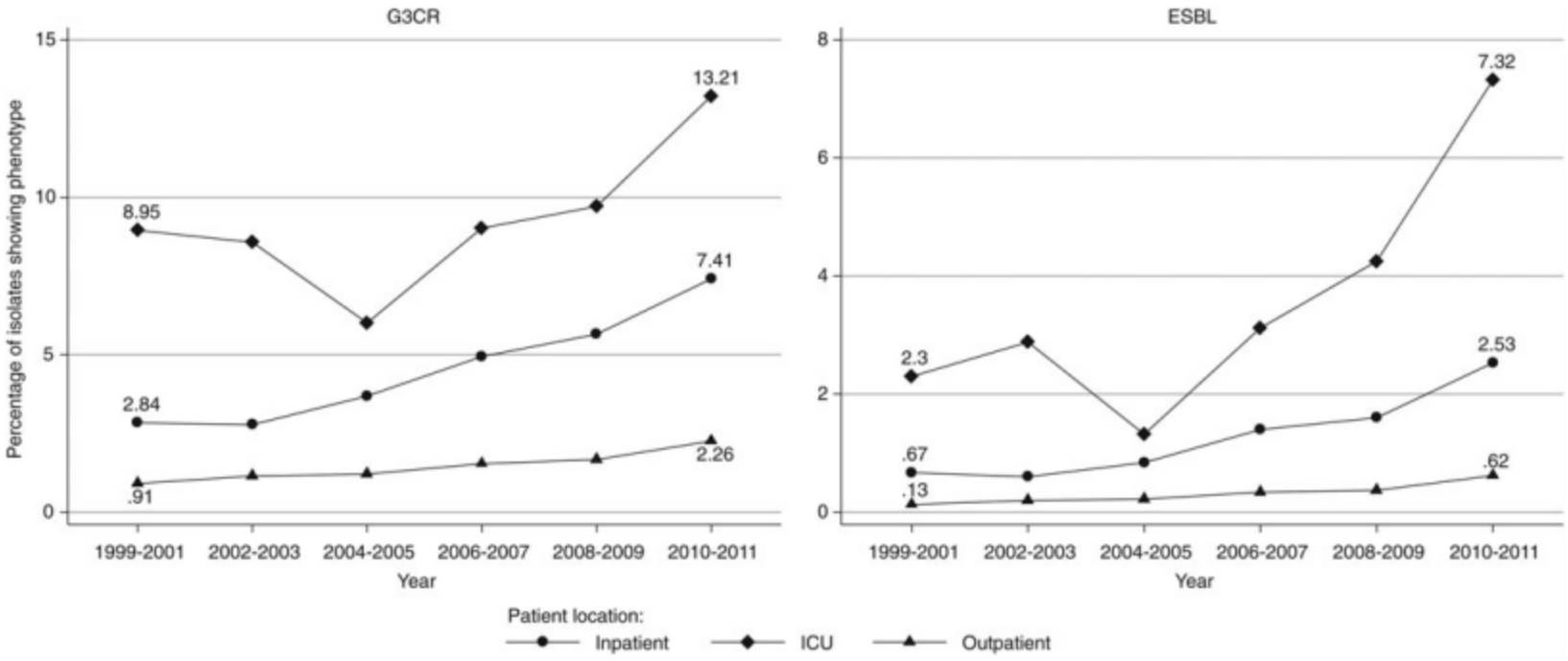
Macrolide Resistance Among Invasive *Streptococcus pneumoniae* Isolates



JAMA, October 17, 2001—Vol 286, No. 15

Antibiotic resistance is affecting our pediatric patients: Gram negative infections

Resistance to 3rd gen cephalosporins **ESBL**



Logan LK et al. *JPIDS.* 2014. 3(4): 320-8.

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

When poll is active, respond at **pollev.com/ranahamdy216**

Text **RANAHAMDY216** to **22333** once to join

3-year old p/w cough, fever to 38.5C 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**

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

1.Metlay JP, et al. Clin Infect Dis 2019;200(7):e45-67.

Clinical Infectious Diseases

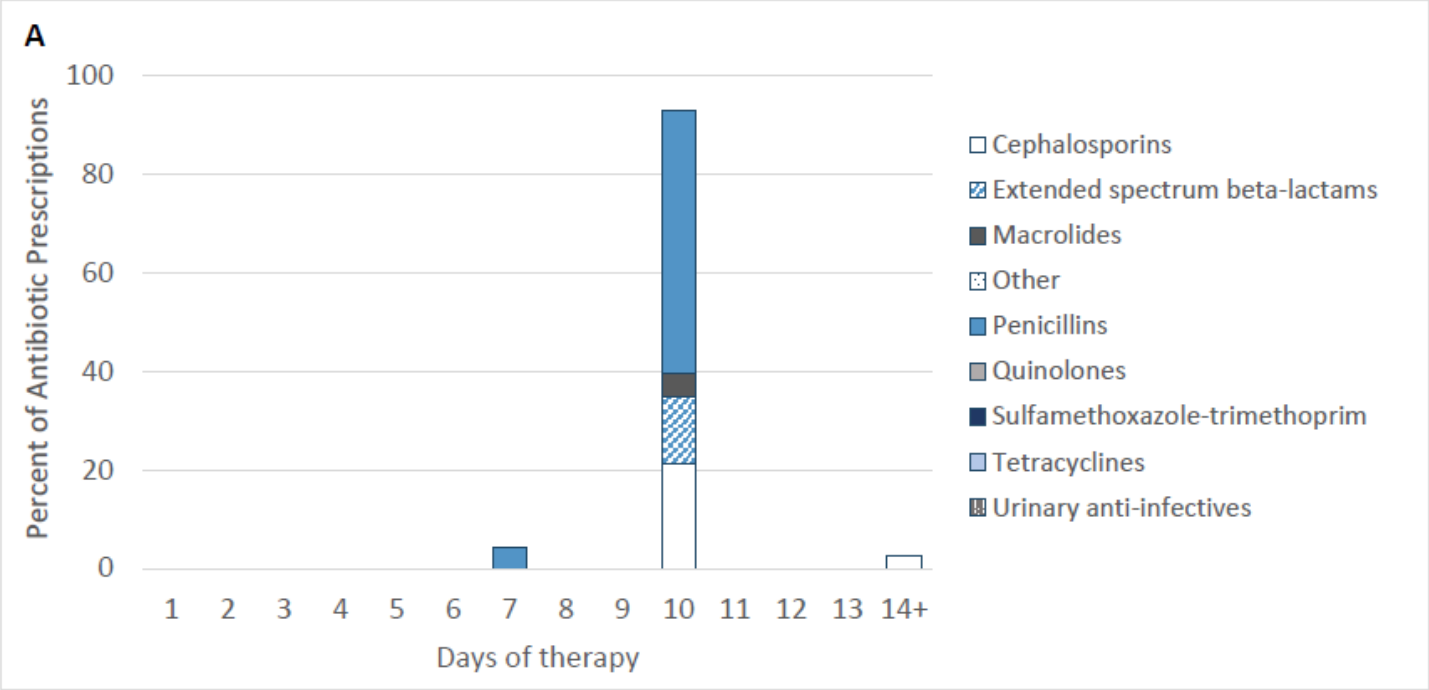
BRIEF REPORT

Duration of Outpatient Antibiotic Therapy for Common Outpatient Infections, 2017

Laura M. King,[1] Adam L. Hersh,[2] Lauri A. Hicks,[1] and Katherine E. Fleming-Dutra[1]

[1]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and [2]Division of Pediatric Infectious Diseases, University of Utah, Salt Lake City, Utah, USA

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



Research

JAMA Pediatrics | Original Investigation

Short-Course Antimicrobial Therapy for Pediatric Community-Acquired Pneumonia
The SAFER Randomized Clinical Trial

Jeffrey M. Pernica, MD; Stuart Harman, MD; April J. Kam, MD; Redjana Carciumaru, MSc; Thuva Vanniyasingam, PhD; Tyrus Crawford, BSocSc; Dale Dalgleish, RN, BHScN; Sarah Khan, MD; Robert S. Slinger, MD; Martha Fulford, MD; Cheryl Main, MD; Marek Smieja, MD, PhD; Lehana Thabane, PhD; Mark Loeb, MD

- 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

When poll is active, respond at **pollev.com/ranahamdy216**

Text **RANAHAMDY216** to **22333** once to join

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

IDSA GUIDELINE

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,[1] Alan L. Bisno,[2] Henry F. Chambers,[3] E. Patchen Dellinger,[4] Ellie J. C. Goldstein,[5] Sherwood L. Gorbach,[6] Jan V. Hirschmann,[7] Sheldon L. Kaplan,[8] Jose G. Montoya,[9] and James C. Wade[10]

ORIGINAL INVESTIGATION

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

IDSA GUIDELINES

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

2021 Redbook

Table 4.12. Systems-based Treatment Table, continued

System	Condition	Common Pathogens	Empiric Antibiotic Therapy	Antibiotic Duration	Notes	Key Resources
Genitourinary	UTI - pyelonephritis	***Escherichia coli*** *Klebsiella* species *Proteus* species *Enterobacter* species *Citrobacter* species *Enterococcus* species *Staphylococcus saprophyticus*	Cephalexin OR TMP-SMX OR Ampicillin PLUS Gentamicin OR Ceftriaxone OR Ciprofloxacin	7–10 days 3–5 days (simple cystitis in adolescents) Longer durations may be required for complicated cases such as renal abscess without drainage	Drug selection should be based on local antibiogram or patient's prior urine isolates Initial short course of IV therapy (2–4 days) is as effective as longer courses of IV therapy Avoid nitrofurantoin for upper urinary tract infection or bacteremia	Roberts et al[7] Gupta et al[8]

Asymptomatic bacteriuria

NO ANTIBIOTICS!!!

Exceptions:

- Pregnancy
- Renal transplant
- Undergoing urinary procedural manipulation

IDSA GUIDELINES

Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults

Lindsay E. Nicolle,[1] Suzanne Bradley,[2] Richard Colgan,[3] James C. Rice,[4] Anthony Schaeffer,[5] and Thomas M. Hooton[6]

[1]University of Manitoba, Winnipeg, Canada; [2]University of Michigan, Ann Arbor; [3]University of Maryland, Baltimore; [4]University of Texas, Galveston; [5]Northwestern University, Chicago, Illinois; and [6]University of Washington, Seattle

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

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"

Pediatrics 2011; 128:595-610.

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)

JAMA Network Open

Original Investigation | Infectious Diseases

Comparative Effectiveness of Antibiotic Treatment Duration in Children With Pyelonephritis

Miriam T. Fox, MPH; Joe Amoah, MD, MPH; Alice J. Hsu, PharmD; Carrie A. Herzke, MD, MBA; Jeffrey S. Gerber, MD, PhD, MSCE; Pranita D. Tamma, MD, MHS

NICE National Institute for Health and Care Excellence

Simple Cystitis

Choice of antibiotic: children and young people under 16 years

Antibiotic[1]	Dosage and course length[2]
If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the NICE guideline on acute pyelonephritis for antibiotic choices	
Refer **children under 3 months** to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s	
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

NICE National Institute for Health and Care Exce

Choice of antibiotic: children and young people under 16 years

Antibiotic[1]	Dosage and course length[2]
Refer **children under 3 months** to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s	
Children aged 3 months and over - First choice oral antibiotic[3]	
Cefalexin	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
Co-amoxiclav (only if culture results available and susceptible)	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
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[3, 4, 5]	
Co-amoxiclav (only in combination or if culture results available and susceptible)	3 months to 15 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)
Cefuroxime	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
Ceftriaxone	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
Gentamicin	Initially 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration[6]

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.

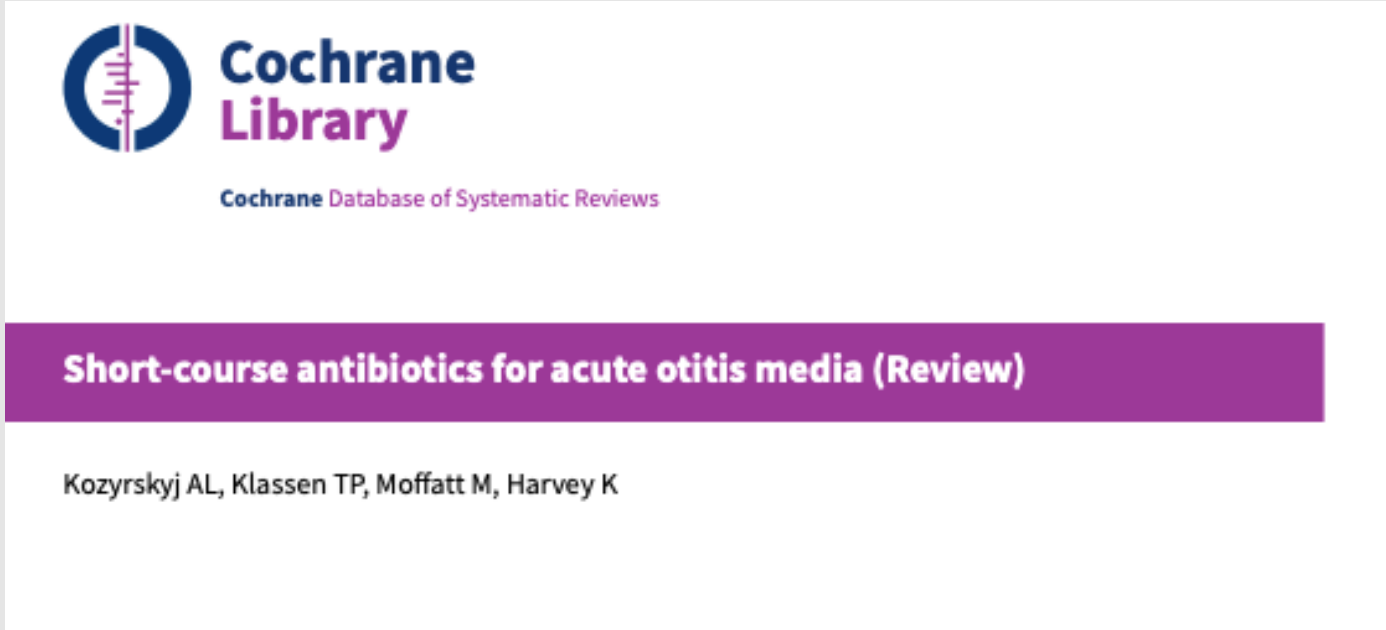
B. A 15-month-old with bilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

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.

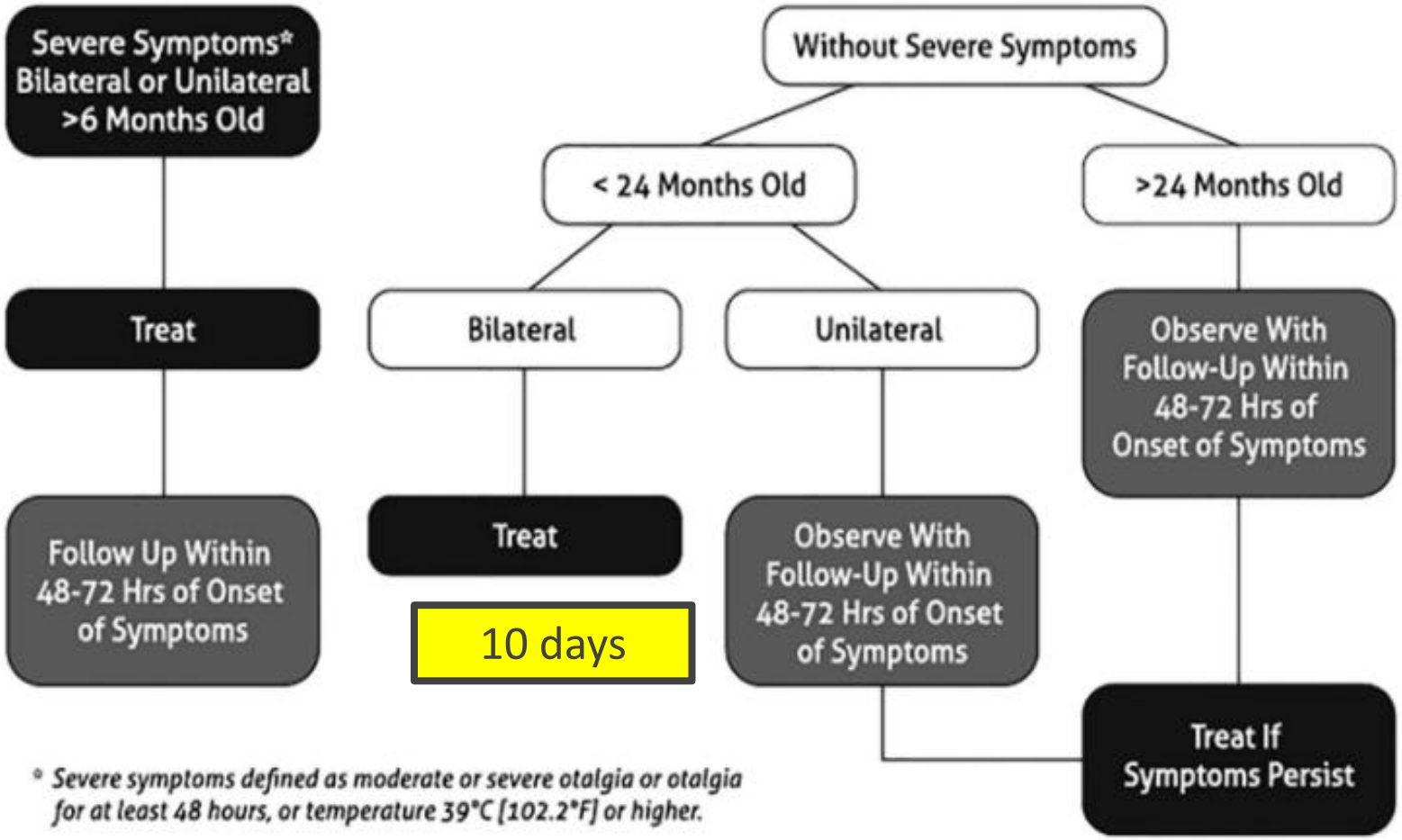
E. A 3-year-old with a unilateral purulent effusion, decreased tympanic membrane mobility with pneumatic otoscopy, minimal pain, no fever, and no other generalized symptoms.

2010 Cochrane review



- Wait and watch approach for:
- >6 months, non-severe disease
- If treatment warranted, shorter courses→ fewer side effects & higher compliance

Peds in Review 2015



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

Otitis Media: To Treat, To Refer, To Do Nothing: A Review for the Practitioner

Jose Rosa-Olivares, MD,* Amanda Porro, MD,* Marielys Rodriguez-Varela, MD,* Gloria Riefkohl, MD,* Iran Niroomand-Rad, DO*

Takeaways

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.

Diagnosis	Length of Treatment
Community-Acquired Pneumonia	5 days
Cellulitis	5 days
UTI: **Simple Cystitis** **Pyelonephritis** **Asymptomatic bacteriuria**	 3-5 days 7 days 0 days
AOM: **<2 years** **2-5 years** **≥ 6 years**	 10 days 7 days 5 days

References

1. Dunbar LM, et al. Curr Med Res Opin 2004;20:555.
2. Dunbar LM, et al. Clin Infec Dos 2003;37:752. Tellier G, et al. J Antimicrob Chemother 207;60:112. Leophonte P, et al. Med Mal Infect 2008;38:471. Li J, et al. Am J Med 2007; 120:783. Dimopoulos G, et al. Drugs 2008; 68:1841. El Moussaoui T, et al. BMJ 2006;331:1355. Montravers P, et al. Am Rev Respir Dis 1993;147:38.
3. Fitzgerald A, Mori R, Lakhanpaul M, Tullus K. Antibiotics for treating lower urinary tract infection in children. Cochrane Database Syst Rev 2012; :CD006857.
4. Gupta K, Hooton TM, Naber KG, et al. 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. Clin Infect Dis. 2011;52(5):e103-e120. DOI: https://doi.org/10.1093/cid/ciq257
5. Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. N Engl J Med. 2011;364(2):105–115pmid:21226576
6. Kozyrskyj AL, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. Cochrane Database Syst Rev. 2010;(9):CD001095pmid:20824827
7. Lieberthal A, et al. The Diagnosis and Management of Acute Otitis Media. Pediatrics Mar 2013, 131 (3) e964-e999; DOI: 10.1542/peds.2012-3488
8. Metlay JP, et al. Clin Infect Dis 2019;200(7):e45-67.
9. Roberts KB; Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128(3):595–610. DOI: https://doi.org/10.1542/peds.2011-1330 (Reaffirmed December 2016)
10. Tähtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. N Engl J Med. 2011;364(2):116–126pmid:21226577

Questions? Don’t hesitate to email/reach out

rhamdy2@cnmc.org

aslovin@cnmc.org

dsullivan@cnmc.org