UWTASP tele-antimicrobial stewardship program | echo

February 7, 2023

ID and Stewardship in Pediatrics: Considerations for Adult Clinicians

Project ECHO

Antimicrobial prescribing is common in non-pediatric settings

Antibiotic use common in non-pediatric settings

- Non-pediatric EDs care for >85% of pediatric ED patients (>25 million visits annually) → antibiotics are more commonly prescribed in non-pediatric EDs than pediatric

Inappropriate prescribing in pediatrics is common

- ED → 32% = 2.1 million per year were generally **not** indicated
- Ambulatory practices → antibiotic prescribing compliance with guidelines for otitis media, pharyngitis, and sinusitis = 21%

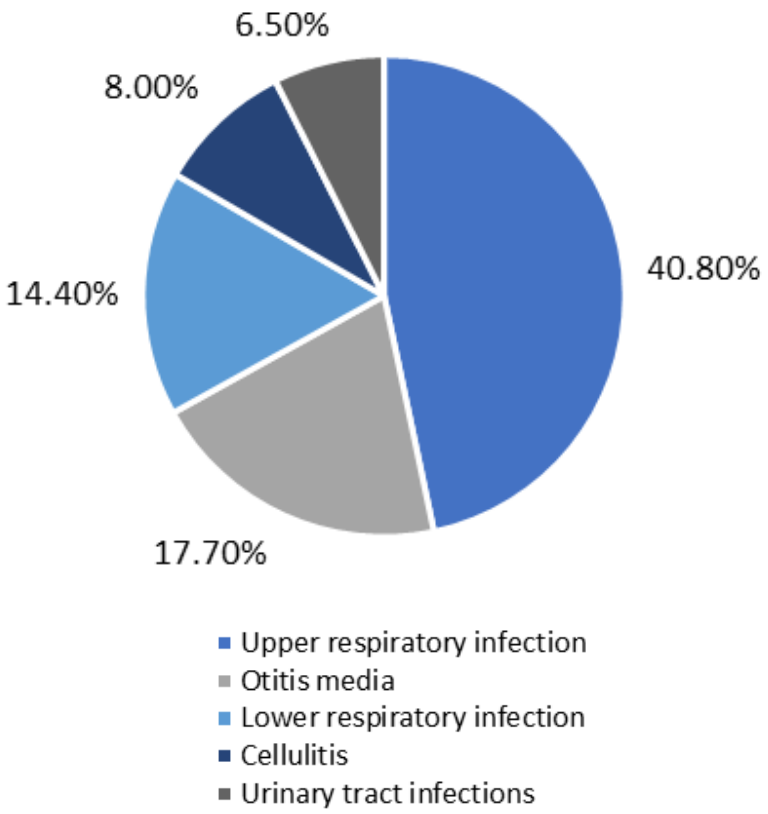
Use is associated with harm

- 70,000 children are harmed annually due to antibiotics necessitating an ED visit

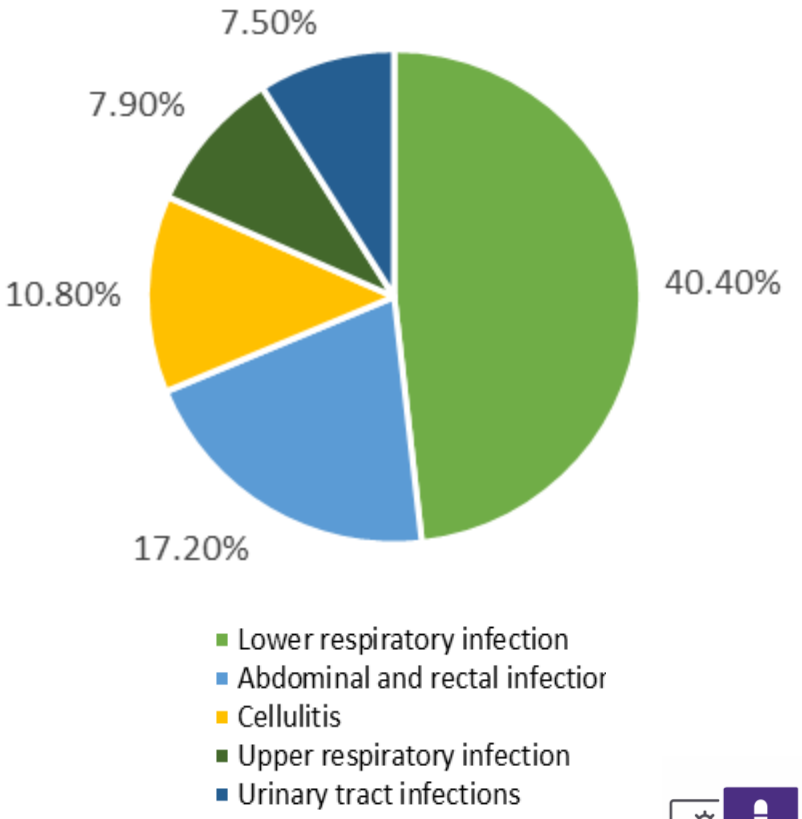
Kohei, et al. *The Pediatric Infectious Disease Journal*. 2015.
Kronman, et al. *Pediatrics*. 2014.
Abuali, et al. *American Journal of Infection Control*. 2019.

Respiratory infections are main driver of visits

Most frequent visits by ID subgroup

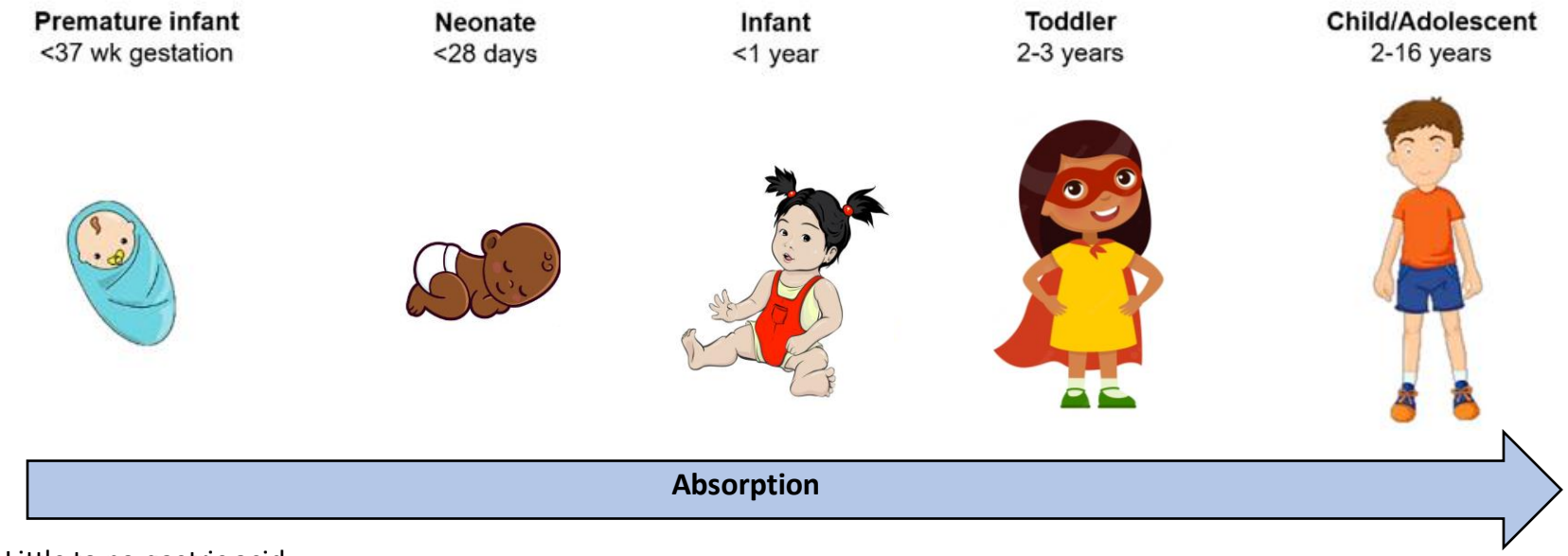


Hospitalizations by ID subgroup



Kohei, et al. *The Pediatric Infectious Disease Journal*. 2015.

Developmental changes in pediatrics

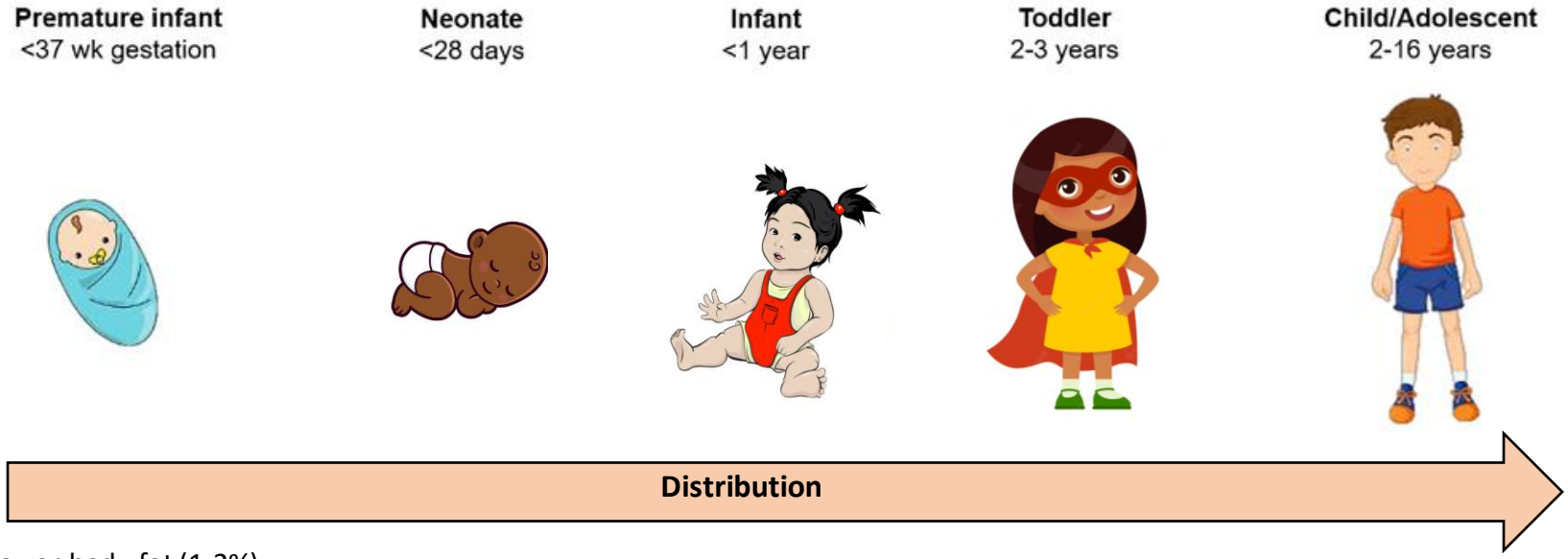


PK Implications

- Weakly acidic drugs: ↓ bioavailability
  - Example drugs: ganciclovir
- Weakly basic drugs: ↑ bioavailability
  - Example drugs: penicillin, ampicillin, nafcillin

Lu, et al. *Developmental Pharmacokinetics*. 2019.
Batchelor et al. *British Journal of Pharmacology*. 2013.
Yellepeddi et al. *Advanced Drug Delivery Reviews*. 2019.

Developmental changes in pediatrics



Lower body fat (1-2%)

High body water (80-90%)
Body fat 10-15%
Low serum protein levels (86% of adults)

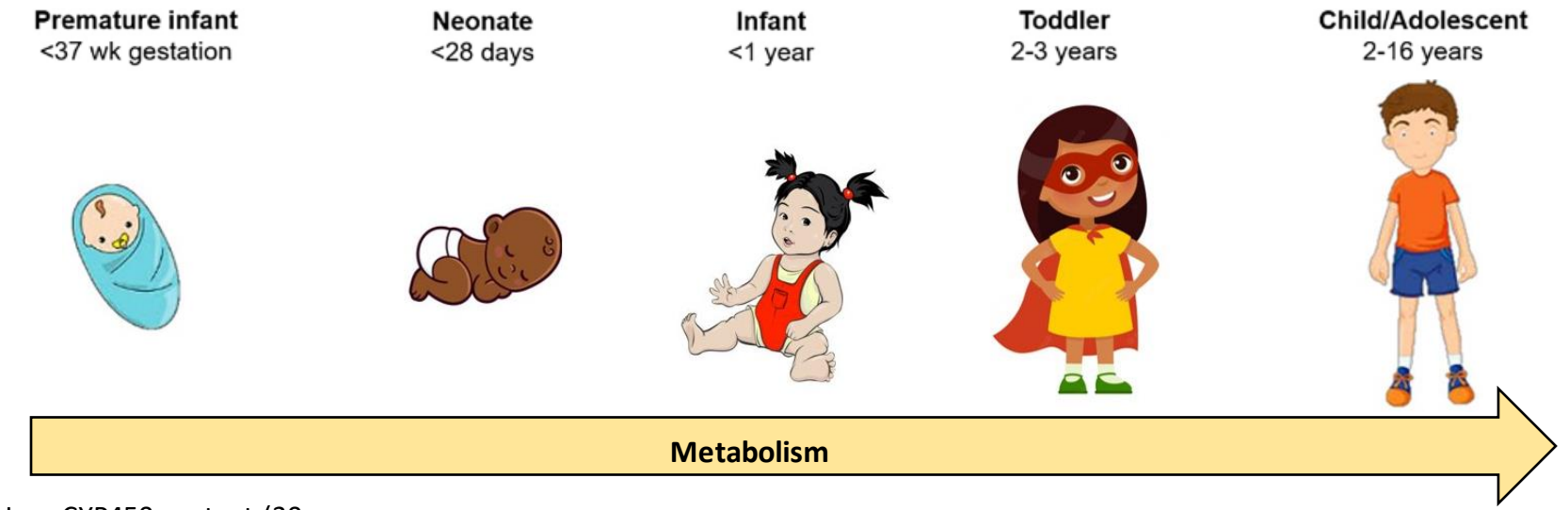
Decreased total body water (60%)
Body fat 20-25%

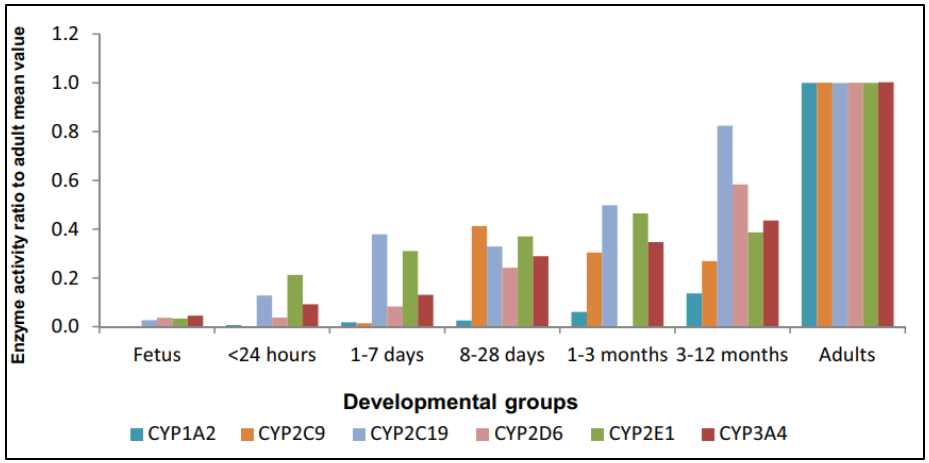
Normal body water (55-60%)
Normal body fat 11-30%
Near adult serum protein levels

PK Implications

- Hydrophilic drugs: ↑ volume of distribution = drug dosing in neonates requires higher mg/kg amount compared to adults
    - Example drugs: gentamicin, vancomycin
- Lipophilic drugs: ↓ volume of distribution
- Lower protein concentrations and affinity in <1 year = lower binding to highly protein bound agents

Developmental changes in pediatrics





PK Implications

- Lower enzyme activity: ↓ hepatic clearance

Lu, et al. *Developmental Pharmacokinetics*. 2019.
Batchelor et al. *British Journal of Pharmacology*. 2013.
Yellepeddi et al. *Advanced Drug Delivery Reviews*. 2019.

Developmental changes in pediatrics

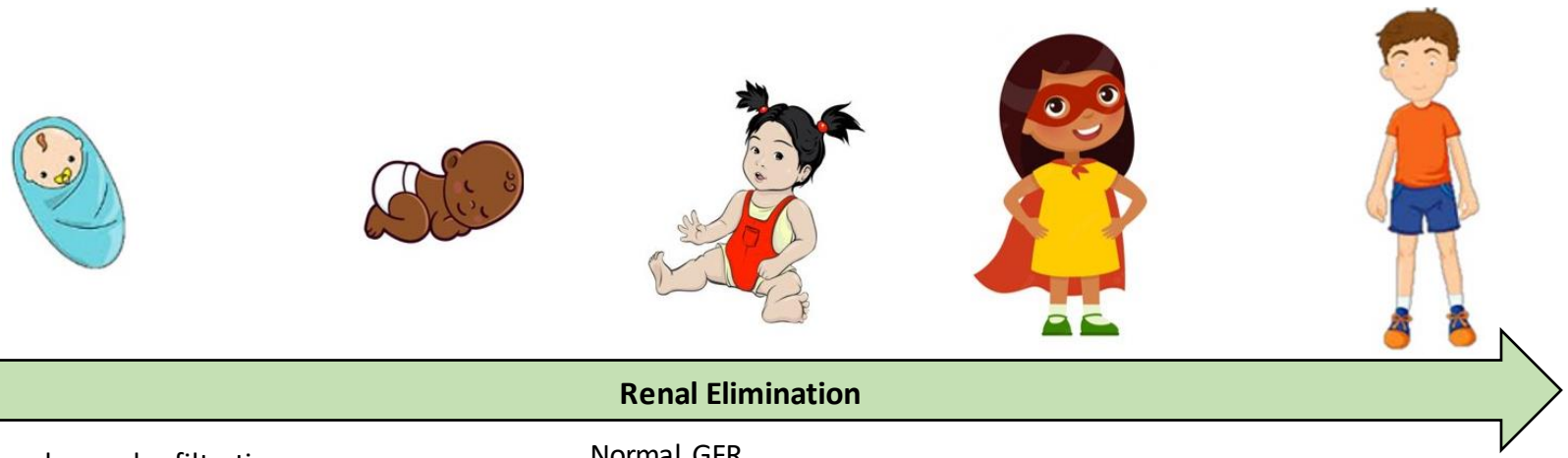
Premature infant
<37 wk gestation

Neonate
<28 days

Infant
<1 year

Toddler
2-3 years

Child/Adolescent
2-16 years

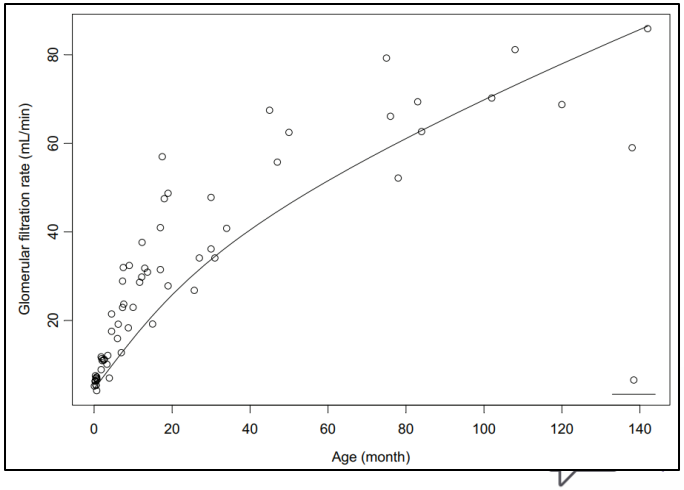


Renal Elimination

Lower glomerular filtration rate (GFR): 5-10 mL/min/m2

Low GFR: 10-15 mL/min/m2
Lower renal tubular secretion

Normal GFR
Normal renal tubular secretion



PK Implications

- Lower GFR: ↓ renal clearance
- Lower renal tubular secretion: ↓ renal clearance
- Example drugs: aminoglycosides, penicillins, cephalosporins

Lu, et al. *Developmental Pharmacokinetics*. 2019.
Batchelor et al. *British Journal of Pharmacology*. 2013.
Yellepeddi et al. *Advanced Drug Delivery Reviews*. 2019.

Developmental changes in pediatrics

Key takeaways

- In neonates and young infants (<2 months), age-specific dosing regimens are needed
- In infants ≥2 months, use weight-based dosing and adjust in those with impaired renal function
- Pediatric dosing handbooks are a must

Antibiotics			
Amikacin IV	Cefoxitin IV	Ciprofloxacin IV	Metronidazole IV
Amoxicillin PO	Cefpodoxime PO	Clindamycin IV/PO	Nafcillin IV
Amoxicillin-clavulanate PO	Ceftaroline IV	Daptomycin IV	Nitrofurantoin PO
Ampicillin IV	Ceftazidime IV	Doxycycline IV/PO	Penicillin G IV
Ampicillin-sulbactam IV	Ceftazidime-avibactam IV	Ertapenem IV	Piperacillin-tazobactam IV
Azithromycin IV/PO	Ceftriaxone IV	Gentamicin IV	Rifampin IV/PO
Aztreonam IV	Cefuroxime Axetil PO	Imipenem IV	TMP-SMX IV/PO
Cefazolin IV	Cefuroxime IV	Levofloxacin IV/PO	Tobramycin IV
Cefepime IV	Cephalexin PO	Linezolid IV/PO	Vancomycin IV
Cefixime PO	Ciprofloxacin PO	Meropenem IV	
Antifungals			
Amphotericin B, liposomal IV	Itraconazole PO	Pentamidine IV	Voriconazole IV/PO
Fluconazole IV/PO	Micafungin IV	Posaconazole IV/PO	
Antivirals			
Acyclovir IV	Foscarnet IV	Oseltamivir PO	Valgancyclovir PO
Cidofovir IV	Ganciclovir IV	Peramivir IV	Zanamivir INH
Notes			
Footnotes		References	

https://www.med.umich.edu/asp/peds.html

Doxycycline use in pediatrics: time to change?

- Tooth discoloration appreciated in early 1960s with tetracycline
- Doxycycline exhibits less calcium binding (19%) compared to tetracycline (39.5%-75.4%)
- Re-evaluation of doxycycline in children found no evidence of doxycycline associated tooth discoloration

Red Book updated recommendation in 2018: "These reassuring data support the recommendation by AAP that doxycycline can be administered for short duration (ie, 21 days or less) without regards to the patient's age."

https://publications.aap.org/aapnews/news/14899

Stewardship Considerations

- Tailor stewardship efforts by age and diagnosis
  - Delayed antibiotic prescriptions for certain diagnosis, such as acute otitis media
- Clinicians are protocol driven with conditions less likely encountered
- Family partnerships are key
  - Communication coupled with contingency plans can improve care and satisfaction

Utilize resources from pediatric settings

Guidelines for common infections

UCSF University of California San Francisco

https://idmp.ucsf.edu/guidelines-for-empiric-therapy-pediatrics

Stanford MEDICINE Children's Health

https://www.stanfordchildrens.org/content-public/pdf/antimicrobial-stewardship-program/guidelines-for-initial-therapy-for-common-pediatric-nfections.pdf

Seattle Children's® HOSPITAL • RESEARCH • FOUNDATION

https://www.seattlechildrens.org/healthcare-professionals/gateway/clinical-resources/pathways/

MICHIGAN MEDICINE UNIVERSITY OF MICHIGAN

https://www.med.umich.edu/asp/peds.html

Children's Mercy KANSAS CITY

https://www.childrensmercy.org/siteassets/media-documents-for-depts-section/documents-for-health-care-providers/evidence-based-practice/clinical-practice-guidelines--care-process-models/outpatient-antibiotic-handbook.pdf

"Stewie Shares" Infographics

Children's Mercy KANSAS CITY

2022

- A Not Too DIFFicult C. Diff Review
- Strep Throat: A Common Conundrum
- Penicillin Allergies: What's True and What to Do?

2021

- Prescribing an Antibiotic? Tidbits to Teach Families
- A Consumer's Guide to Fluoroquinolones
- Dispose Antibiotics Safely. Prevent Resistance.
- Five Facts about Community Acquired Pneumonia
- Five Helpful Tips to Make Giving Antibiotics Easier for You
- Flu Who? Reviewing the Prevention and Treatment of Influ
- Four Vaccines You Didn't Know You Needed
- IV is not Always the Answer
- Preventing RSV... As Easy as 1,2,3
- "Tick" Talk

https://www.childrensmercy.org/health-care-providers/pediatrician-guides/antimicrobial-stewardship/provider-resources-for-antimicrobial-stewardship/

Differences in treatments by age

Diagnosis	Adult patients		Pediatric patients		
	Organization (publication year)	First-line therapy	Organization (publication year)	Pediatric population included	First-line therapy
Community acquired pneumonia	IDSA (2019)[28]	**No comorbidities:** (1) Amoxicillin (2) doxycycline (3) azithromycin **Comorbidities:** (1) Amoxicillin-clavulanate + macrolide OR doxycycline (2) Cefpodoxime OR cefuroxime + macrolide OR doxycycline (3) Levofloxacin OR moxifloxacin	IDSA (2011)[29]	Infants and Children	Antimicrobial therapy not routinely recommended for preschool-aged children **All ages:** Amoxicillin
Acute bacterial rhinosinusitis	IDSA (2012)[8]	**Children:** Amoxicillin-clavulanate **Adults:** Amoxicillin-clavulanate	AAP (2013)[9]	1-18 years	**Uncomplicated, mild to moderate, and ≥ 2 years:** Amoxicillin **Risk of resistance, moderate to severe, OR ≤ 2 years:** Amoxicillin-clavulanate
Uncomplicated cystitis and pyelonephritis in women	IDSA (2011)[30]	**Cystitis:** (1) Nitrofurantoin (2) Trimethoprim-sulfamethoxazole (3) Fosfomycin **Pyelonephritis:** (1) Ciprofloxacin (2) Levofloxacin (3) Trimethoprim-sulfamethoxazole Beta-lactams are NOT routinely recommended	AAP (2016)[31]	2 – 24 months	**Empiric Oral Antibiotics:** (1) Cephalexin (2) Cefixime (3) Cefpodoxime (4) Cefprozil (5) Amoxicillin-clavulanate (6) Trimethoprim-sulfamethoxazole

AAP, American Academy of Pediatrics; *IDSA*, Infectious Diseases Society of America.

Monsees, et al. *American Journal of Infection Control*. 2021.

Summarized Considerations for Adult Clinicians

1) Differences in physical size, body composition, and organ system maturation
2) Tailor stewardship efforts by age and diagnosis
3) Develop strong family partnerships
4) Utilize resources from pediatric institutions
5) Differences in infectious presentations, diagnoses, and treatments by age