2020 Pediatric Antibiotic Prescribing Update
Teri Moser Woo PhD, ARNP, CPNP-PC, CNL, FAANP
Professor and Director of Nursing
Saint Martin’s University

Speaker Introduction
• Dr. Teri Moser Woo is professor and director of nursing at Saint Martin’s University in Lacey, Wash. She completed her BSN, MSN and post master’s PNP Certificate at Oregon Health Sciences University, and her PhD in nursing at University of Colorado Denver College of Nursing in Dec. 2008. She is lead author of Pharmacotherapeutics for Advanced Practice Registered Nurses 4th Ed. (2016) and 5th Ed. (2019) and has written and lectured extensively in the area of pediatric pharmacology. She serves on the NAPNAP Executive Board as a member-at-large and the PNCB Pharmacology CE committee. She holds national certification as a pediatric nurse practitioner in primary care and is a Fellow in the American Academy of Nurse Practitioners. Dr. Woo practices as a pediatric nurse practitioner in Urgent Care at Woodcreek Mary Bridge in Puyallup, Wash.

Disclosures
No personal or financial disclosures

Learning Objectives
• Discussion general principles regarding antibiotic resistance in 2020
• Determine local antimicrobial resistance patterns when making prescribing decisions.
• Review of common pediatric primary care conditions that require antibiotics and recommendations for prescribing
• Review core principles of an antibiotic stewardship program and resources for practice

Urgent Threats (CDC, 2019)
• Carbapenem-resistant Acinetobacter
• Drug-resistant Candida auris (C. auris)
• Clostridioides difficile (C. difficile)
• Carbapenem-resistant Enterobacteriaceae (CRE)
• Drug-resistant Neisseria gonorrhoeae (N. gonorrhoeae)
Serious Threats (CDC, 2019)
- Drug-resistant Campylobacter
- Drug-resistant Candida
- ESBL-producing Enterobacteriaceae
- Vancomycin-resistant Enterococci
- Multidrug-resistant Pseudomonas aeruginosa
- Drug-resistant non-typhoidal Salmonella
- Drug-resistant Salmonella serotype Typhi
- Drug-resistant Shigella
- Methicillin-resistant Staphylococcus aureus (MRSA)
- Drug-resistant Streptococcus pneumoniae
- Drug-resistant Tuberculosis

Concerning Threats
- Erythromycin-resistant Group A Streptococcus
- Clindamycin-resistant Group B Streptococcus

Watch List
- Azole-resistant Aspergillus fumigatus
- Drug-resistant Mycoplasma genitalium (M. genitalium)
- Drug-resistant Bordetella pertussis (B. pertussis)
Upper Respiratory Pathogens (AOM/Sinusitis)

- *S. pneumoniae* (15-25%)
- Non-typeable *H. influenzae* (50-60%)
- *M. catarrhalis* (12-15%)
- Sterile (15-20%)

***Viruses***

Wald & DeMuri, 2018

AOM/Sinusitis Guidelines

Acute Otitis Media (Lieberthal, AS et al., 2013)
- First line: High dose amoxicillin
- Second line:
  - High-dose amoxicillin-clavulanate
  - Cefdinir (14 mg/kg/day)
  - Cefuroxime (30 mg/kg/day)
  - Cefpodoxime (50 mg/kg IM)
- PCN Allergy:
  - First line: Cefdinir or Cefuroxime
  - Second line: cefpodoxime or ceftriaxone

Bacterial Sinusitis (Baud et al., 2010)
- First line:
  - Amoxicillin 45 mg/kg/day
  - High risk of resistance use high dose amoxicillin
  - If age 2 yrs, no daycare and no antibiotics for 4 weeks use high dose amoxicillin-clavulanate
- Second line:
  - High-dose amoxicillin-clavulanate
  - Cefdinir (14 mg/kg/day)
  - Cefuroxime (30 mg/kg/day)
  - Cefpodoxime (50 mg/kg/day)
  - Ceftriaxone (50 mg/kg IM)
- PCN allergic:
  - Cefdinir, cefuroxime or cefpodoxime
  - Moderate to severe sinusitis in children < 2 yrs with Type I allergy: Clindamycin and ceftriaxone

US outpatient oral antibiotic prescriptions per 1000 persons by state, 2016.

US outpatient oral antibiotic prescriptions per 1000 persons, by age group (in years), 2011–2016.
Duration of Therapy

**Acute Otitis Media (Lieberthal, AS et al., 2013)**
- < 2 yrs: 10 days
- 2 yr to 5 yr olds with mild to moderate symptoms: 7 days
- ≥ 6 yrs with mild to moderate symptoms: 5 to 7 days
- Shortened course (5 days) not effective in children < 2 yrs (Hoberman et al., 2016)

**Bacterial Sinusitis (Wald et al., 2013)**
- Wald (2013) “optimal duration has not received systematic study”
- AAP (2013) 10 days or 7 days after improvement
- majority have improvement in 3 days
- ISDA (2012) 5 to 7 days
- AAO (2015) 5 to 10 days

Time to rethink the guidelines?
- Prevalence of S. pneumoniae primary pathogen has decreased from 40-45% in 1999 to 15-25% in 2017 (Wald & DeMuri, 2018)
- High-dose amoxicillin was based on penicillin resistant S. pneumoniae
- H. flu and M. catarrhalis are resistant to amoxicillin
- Regular dose amoxicillin-clavulanate will treat resistant H. flu and M. catarrhalis – no need for high dose amoxicillin clavulanate
- Consider amoxicillin-clavulanate 45 mg/kg/d in 2 divided doses of 400 mg/57 mg

Community Acquired Pneumonia
- S. pneumoniae is the most common cause of bacterial pneumonia in patients of all ages
- Infants 4 to 16 weeks – Consider chlamydia
- Respiratory viruses most common in first 2 to 3 years of life (80% of CAP)
- Over 5 yrs through adolescence: – Consider mycoplasma
- CA-MRSA
- Virus
- New ISDA Pediatric CAP guidelines under development

Pneumonia antibiotic choices in Children (Bradley et al., 2011)

**Infants and children < age 5 years**
- Fully immunized with bacterial pneumonia (S. pneumoniae)
- Amoxicillin 80-90 mg/kg/day
- PCN allergy: Clindamycin or a macrolide
- Unimmunized for Hib or PCV
- Ceftriaxone 50 mg/kg
- Infant with suspected chlamydial pneumonia

**Children 5 yrs or older**
- Guidelines say amoxicillin 90 mg/kg to max 4 gm per day
- Treat for 10 days
- Mycoplasma or other atypical most likely
  - Azithromycin
  - Erythromycin
  - Doxycycline if > 7 yrs

Following Guidelines for CAP – March 2017
- Outpatient pediatric primary care (N = 10,414) (Handy et al, 2017)
  - 40.7% received amoxicillin
  - 42.5% received macrolides (≥ age 5, recent antib, private insurance)
  - 16.8% received broad spectrum antibiotics (suburbs, private insurance)
- 28 children’s hospitals (Williams et al, 2017)
  - Before ISDA guideline penicillin for CAP was rare (<10%)
  - Increase after guideline to 27.6% (29.5% vs 20.1%)
- 53 hospitals (3802 charts) (Parikh et al, 2017)
  - Implemented evidence-based tools to promote judicious use of antibiotics
  - Narrow spectrum antibiotic use increased by 67% in the ED, 43% in the inpatient setting, and 25% at discharge
  - Macrolides decreased by 22% in the ED and 27% in the inpatient setting
Following pneumonia guidelines (Poole, Shapiro, Kronman & Hersh, 2019)

- Cross-sectional retrospective study of patients aged 90 days–18 years with an outpatient clinic or emergency department (ED) visit with dx of CAP
- Amoxicillin was prescribed in 23% (95% CI 18–30%)
- Azithromycin was prescribed in 47% (95% CI 41–54%)
- Cephalosporins were prescribed in 26% (95% CI 21–31%)
- Midwest and South more likely to be prescribed azithromycin
- Azithromycin more likely in ED than private offices

Strep Pharyngitis

- Pathogen: *Streptococcus pyogenes*
- Strep 20-30% of pharyngitis
- Most rapid strep tests are 90 to 95% accurate
- Rapid tests and throat cultures cannot differentiate between GAS pharyngitis and GAS carriers
- Likelihood of positive strep is higher with fewer viral symptoms (cough, rhinorrhea)
- patients with any viral feature were ~30% less likely to have GAS, and patients with ≥2 features were >40% less likely to have GAS (Shapiro et al, 2017)

Strep Pharyngitis

Treatment (Red Book, 2018; ISDA, 2012):

- **Penicillin**
  - PO 250 mg ID if < 27 kg or 500 mg ID if > 27 kg
  - IM penicillin G benzathine single dose of 600 000 U (<27kg), > 27 kg and adults 1.2 million U
- Amoxicillin 50 mg/kg in a single daily dose (max 1gm)
- No statistical difference in negative cultures after treatment between QD, BID or TID dosing (Nako et al, 2019)
- **1st generation cephalosporin**
  - Cephalexin (Keflex) 40-50 mg/kg/day dosed BID (max 500 mg BID)
  - Cefadroxil (Duricef) 30 mg/kg/day (max 1 gm)
  - Clindamycin 7 mg/kg/dose tid (max 500 mg tid)

Group A Strep pharyngitis: PCN allergic

- **1st** generation cephalosporin (cephalexin)
- If immediate Type 1 hypersensitivity:
  - Clindamycin 20 mg/kg/day divided TID (max 1.8 gm/day)
  - Or macrolide
    - Azithromycin (12 mg/kg/day [maximum, 500 mg]) for 5 days
    - Macrolides have resistance (up to 23%)

GAS Carriers

- 20-25% of children may be asymptomatic carriers during the winter months (ISDA, 2012)
  - May be colonized by GAS pharyngitis for 26 months
- Children who are carriers are more likely to present with URI sx and atypical symptoms (Rick, Zaheer & Martin, 2020)
- Eradication therapy (Red Book, 2018; ISDA, 2012)
  - Clindamycin 30 mg/kg/day in 3 doses (max 300 mg/dose) x 10 days
  - Augmentin 40 mg amoxicillin/kg/d in 3 doses (max = 2000mg amoxicillin/d)
  - Pencillin V 50 mg/kg/d in 4 doses x 10 d (max = 2000 mg/d) PLUS rifampin: 20 mg/kg/d in 1 dose x last 4 d of treatment (max = 600 mg/d)
**Nongroup A Streptococcal Pharyngitis in Children**

- Large (N=116,578) retrospective study of children age 0 to 18 yrs (Frost et al., 2019)
  - Non-group A beta-hemolytic strep (NGAS) 3.1% vs 22.8% Group A strep (GAS)
  - NGAS lower rates of fever, throat erythema, and lymphadenopathy and higher rates of cough and rhinorrhea compared with those with GAS
  - Tx C or G
  - Not detected with rapid strep
  - Treatment:
    - Not known to trigger acute rheumatic fever
    - May treat if symptomatic (fever, tonsillar exudates, tender cervical lymphadenopathy)
    - Tx same as GAS: PCN, amoxicillin

**Skin and Soft Tissue Infections Guidelines**

- Impetigo
  - Bullous or non-bullous impetigo: mupirocin or retapamulin BID x 5 days (Stevens et al, 2014; AAP RedBook 2018)
  - Oral therapy for 7 days (dicloxacillin or cephalaxin)
  - MRSA is suspected or confirmed, doxycycline, clindamycin, or sulfamethoxazole-trimethoprim (SMX-TMP) is recommended (Stevens et al, 2014)

**Antibiotic choices for MRSA – outpatient**

- Based on antibiogram
- Purulent cellulitis
  - TMP-SMX
  - Clindamycin
  - If > 8 yrs: Doxycycline
- Non-purulent cellulitis
  - Cover for both CA-MRSA and β strep
  - Cephalexin and dicloxacillin
  - amoxicillin and/or TMP-SMX or a tetracycline
- Duration of therapy: 5 to 7 days

**Local Antibiogram – not everything is MRSA**

**LA County Antibiogram Gram Positive**

[Images and tables related to the above points are included.]
Prevalence of Inappropriate Antibiotic Prescribing

- Targets based on lowest prescribing regions for sinusitis, otitis media, streptococcal pharyngitis, and no antibiotics for asthma, allergy, bronchitis, bronchiolitis, influenza, URI
- For 0-19 yr olds: 29% of antibiotic prescriptions are inappropriate
  - 100% of URI/asthma/bronchitis
- For all ages: 50% of antibiotics are inappropriately prescribed
  
  Fleming-Dutra et al., 2016

Antibiotic Prescribing During Pediatric Direct-to-Consumer Telemedicine Visits

- Acute respiratory infections
- 4604 telemedicine, 38,408 urgent care, and 485,201 PCP visits
- 52% of telemedicine visits versus 42% urgent care and 31% PCP visits received antibiotics (P < .001 for both comparisons)
- Guideline-concordant antibiotic management
  - 59% of DTC telemedicine versus 67% urgent care and 78% PCP visits (P < .001 for both comparisons)
  
  Ray et al, 2019

Antibiotic Prescribing for Children in Emergency Departments

- 7 million antibiotic prescriptions for children in EDs annually
- When antibiotics were prescribed:
  - 44% (95% CI: 42%–45%) were broad spectrum,
  - 32% (95% CI: 30%–34%, 2.1 million per year) were generally not indicated.
- Non-pediatric EDs
  - higher frequency of prescribing macrolides (18% vs 8%, P < .0001)
  - lower frequency of first-line, guideline-concordant prescribing for the respiratory conditions studied (77% vs 87%, P < .001).
  
  Poole, Shapiro et al, 2019

Antibiotic Prescribing in Children’s Hospitals (Tribble et al, 2020)

- 32 US children’s hospitals, 34,927 children, 11,784 receiving antibiotics for infections
- Antibiotic Stewardship Program (ASP) review found 21.0% of antibiotics were considered suboptimal
  - 27.5% were drug-bug mismatch
  - 17.6% surgical prophylaxis > 24 hrs
  - 11.2% overly broad
  - 11.0% unnecessary treatment
- ASP recommendations
  - 44.7% stop antibiotic
  - 19.7% narrow the spectrum

C. difficile

- ISDA C. difficile Guidelines now include children (McDonald et al, 2018)
- Routine testing not recommended in neonates or infants ≤ 12 months
  - The rate of C. difficile colonization among asymptomatic infants can exceed 40%
  - Avoid testing in 1-2 yr olds unless other sources of infectious and noninfectious causes of diarrhea have been excluded
  - ≥ 2 years of age testing recommended for prolonged or worsening diarrhea and risk factors
- Alcohol-based hand hygiene products do not inactivate C difficile spores
  - Soap and water handwashing

C. Difficile Treatment

- Stop antibiotics
- Moderate or severe disease: empirical antibiotic treatment
  - Metronidazole
    - 200 mg/kg per day, orally, in 6 divided doses, maximum 2 g/day
  - Oral vancomycin or vancomycin administered by enema
    - 150 mg/kg per day orally, 3–6 divided doses, to a maximum daily dose not to exceed 2 g
    - IV solution can be used orally (AAP Red Book, 2018, pg 288-290)
- Duration of therapy: 10 days
- Up to 30% of patients experience a recurrence after discontinuing therapy
- Usually responds to second course of same medication (AAP Red Book, 2018)
- Good hand washing to prevent spread

AAP Committee on Infectious Disease (2013). Clostridium difficile Infection in Infants and Children. Pediatrics, 131(1), 196‐200


AAP RedBook, 2018; McDonald et al, 2018
Penicillin Allergy

10% of the population reports a penicillin allergy but <1% of the whole population is truly allergic.

- Starts with accurate Hx & PE
- Characteristics of an IgE-mediated (Type I) reaction:
  - Reactions that occur immediately or usually within one hour
  - Hives: Multiple pink/red raised areas of skin that are intensely itchy
  - Angioedema: Localized edema without hives affecting the abdomen, face, extremities, genitalia, oropharynx, or larynx
  - Wheezing and shortness of breath
  - Anaphylaxis
- Amoxicillin rash
  - Occurs in 5% to 10% of children receiving amoxicillin
  - Appears 3 to 14 days from starting amoxicillin
  - Generalized dull, red, maculopapular rash
  - Begins on the trunk and spreads over most of the body. It tends to be most intense at pressure areas, elbows, and knees.
- Patients with EBV who receive amoxicillin may develop a non-allergic, non-pruritic rash

CDC Recommendations for Penicillin Allergy Testing

- “Penicillin skin testing and challenge doses are reliable and useful methods for evaluating for IgE-mediated penicillin allergy”
- Skin testing
  - Predictive value of 95%
  - 100% if followed by oral challenge
- Patients with severe hypersensitivity syndromes should not have skin testing
- Cephalosporins can be used in patients with penicillin allergy
- Pts with anaphylaxis may require allergy testing

What YOU Can Do

- Know what pathogen you are treating and prescribe appropriately
- Know your local resistance pattern
- Do not prescribe antibiotics for viral infection
  - Avoid “Vitamin Z”
- Appropriately identify penicillin allergy
  - Not all rashes are due to hypersensitivity
- Consider an antibiotic stewardship program for your facility
References


• Wald et al. (2013). Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years. Pediatrics, 132;e262-e280.