Each year, physicians write over 50 million antibiotic prescriptions for pediatric patients (1). Many of these prescriptions are inappropriate, either due to incorrect indication, incorrect dosage, or incorrect choice. Since its inception in 2011 the CHCO antibiotic stewardship team has encountered several patterns of misconceptions regarding commonly prescribed antibiotics. We have compiled a list of some of the most helpful (but little-known!) antibiotic pearls to help both outpatient and inpatient providers choose the right medication every time!

1. Streptococcus pneumoniae treatment isn’t affected by adding a β-lactamase inhibitor. Since the 1970s, Streptococcus pneumoniae has become increasingly resistant to antimicrobial agents. Often, providers think that the addition of a β-lactamase inhibitor – broadening coverage from amoxicillin to amoxicillin-clavulanate (Augmentin®) – will increase the efficacy of their antibiotic choice. However, S. pneumoniae resistance is secondary to changes in penicillin-binding proteins, not because of the creation of a β-lactamase. Resistance secondary to the changes in penicillin-binding proteins can be overcome by using high dose penicillin/amoxicillin (2). The addition of a β-lactamase to amoxicillin broadens coverage to more anaerobes and gram negatives, and adds methicillin-susceptible Staphylococcus aureus (MSSA) coverage, as many of those organisms produce a β-lactamase. **Bottom line: Make sure you’ve prescribed high-dose penicillin/amoxicillin for optimal S. pneumoniae coverage.**

2. Oral cephalosporins are not a better choice than amoxicillin for S. pneumoniae. Many providers believe that switching to an oral cephalosporin (cefdinir, cefuroxime, or cefpodoxime) is an escalation of care for patients with S. pneumoniae. In reality, oral cephalosporins are a step-down compared to high dose penicillin/amoxicillin. As a class, the oral cephalosporins are poorly absorbed, highly protein bound (only unbound drug is active), and have low active levels in the serum. Conversely, high dose amoxicillin provides more coverage for S. pneumoniae given its higher active concentrations in the serum. **Bottom line: High dose amoxicillin (80-90 mg/kg/day divided BID for acute otitis media (AOM) and TID for other infections) continues to be the best oral treatment for suspected S. pneumoniae infections that can be treated orally.**

3. Susceptibility to ceftriaxone does not equate to susceptibility to cefdinir (or other oral cephalosporins). So a child with pneumonia gets better on ceftriaxone and is ready to go to oral, is it logical to go to the “third generation” oral cephalosporin, cefdinir? NO! Ceftriaxone has unbound fractions in the serum close to 20 mcg/mL and an 8 hour half-life, while cefdinir’s unbound concentration is about 0.8 mcg/mL, with a 1.5 hour half-life—even at its peak, this is hardly enough to kill most pathogens, particularly S. pneumoniae. For S. pneumoniae, stick with amoxicillin for an oral agent. For penicillin-resistant pathogens or penicillin-allergic patients, oral cephalosporins can be considered. Think about which organisms you are trying to treat before switching from IV to PO (3). **Bottom line: When narrowing from IV ceftriaxone, don’t assume an oral 3rd generation cephalosporin (i.e. cefdinir) is equivalent. Consider high dose amoxicillin, amoxicillin-clavulanate (Augmentin®), or outpatient IM ceftriaxone depending on the clinical picture and the organism isolated/suspected.**

4. For most pediatric infections, cephalexin (Keflex®) is best dosed QID. Cephalexin is commonly used to treat UTIs as well as skin and soft tissue infections. Although group A β-hemolytic Streptococcus (GAS) can be adequately treated by BID dosing due to its extremely low MIC, cephalexin is most effective when dosed QID for infections thought to be due to other organisms with higher MICs, especially MSSA. Because cephalexin is cleared renally, BID dosing is adequate for uncomplicated cystitis; however, QID dosing is recommended if treating febrile UTI/pyelonephritis to ensure adequate renal parenchyma concentrations of the drug. Like other oral cephalosporins, cephalexin has a short half-life (0.5-1.2 hours) and to maintain adequate concentrations above the MIC of an organism throughout the day, it makes sense to dose it more frequently. It can be dosed anywhere from 50-150 mg/kg/day divided into varying...
frequencies depending on severity of infection (4). **Bottom line: If treating anything other than uncomplicated cystitis or GAS infection, strongly consider higher dosing of cephalixin and divide the dose QID.**

5. **Beware of fluoroquinolones: difficult dosing and arthralgias.** In May 2016, the FDA released a new warning advising that in most cases, the risks of fluoroquinolones outweigh the benefits in most infections secondary to the increased risk of tendon and muscle damage (5). Although tendon rupture has yet to be described in pediatric patients, arthralgias and/or myalgias are common. Fluoroquinolones are also known contributors to antimicrobial resistance and to *Clostridium difficile* infection. In addition, fluoroquinolones need to be taken two hours before and after food, and can easily bind to metals such as calcium, aluminum, iron, and magnesium (present in infant formulas, supplements, and foods) (6). **Bottom line: The FDA’s newer warnings, the risk of driving antimicrobial resistance, and the incomparability with food make fluoroquinolones a poor choice for oral antibiotic therapy in pediatric patients unless absolutely necessary based on documented resistant infections.**

6. **Also watch out for azithromycin with long QTc and for poor treatment for most infections.** Also in 2016, the FDA published a safety alert regarding arrhythmias (most notably long QTc) that can be worsened with azithromycin (7). Although one of the most widely prescribed antibiotics, azithromycin provides poor coverage for many causative organisms for pneumonia, sinusitis, and AOM, and is especially poor for pneumococcal coverage (8). Azithromycin can be used for *Mycoplasma*, but clinical benefit of its use for “walking pneumonia” is debatable. **Bottom line: Given arrhythmia risks and emerging resistance patterns, azithromycin is a poor choice for AOM as well as most upper and lower respiratory infections, and risk vs. benefit should be carefully weighed.**

7. **Amoxicillin and ampicillin do not cover MSSA.** *Staphylococcus aureus* produces a narrow spectrum penicillinase, rendering both ampicillin and amoxicillin inactive. MSSA can be treated with ampicillin-sulbactam (Unasyn®) or amoxicillin-clavulanate (Augmentin®) given the added β-lactamase inhibitor; however, these are usually broader than necessary as they also cover anaerobes and gram-negative organisms. MSSA is best treated by cefazolin (IV) or cephalxin (PO, see above). Other options include nafcillin (though difficult to use IV, so reserved for endocarditis or CNS infection), and multiple other choices that treat both MSSA and MRSA (9). Notably, about 20% of MSSA (and MRSA) at CHCO is resistant to clindamycin, so providers must follow up with sensitivities to ensure clindamycin will cover their patient’s infection. **Bottom line: If you intend to treat MSSA, don’t use ampicillin or amoxicillin!**

8. **Not all medications cost the same:** Cost-conscious medicine is an emphasis at all hospitals. Keep in mind that some antibiotic choices are much more expensive than others. A few surprising examples include clindamycin (IV and PO), nafcillin, and cefuroxime. This can be especially important for our patients without insurance to cover costs (out of pocket clindamycin can be hundreds of dollars)! **Bottom line: Try to consider both cost and coverage when choosing your antibiotics.**

9. **Vancomycin has some special considerations.** Remember vancomycin’s nephrotoxic effects, especially with prolonged use. All patients should get a baseline creatinine and a vancomycin trough prior to the 4th dose or earlier with underlying renal dysfunction. With continued use, you should repeat a creatinine every 1-3 days in critically ill patients and every 5-7 days in those who are less ill. Make sure you are watching hydration status and urine output closely along with limiting other nephrotoxic medication use if possible. **Bottom line: Remember to watch for signs of acute kidney injury (AKI) and check labs as needed for prolonged vancomycin use.**

10. **Vancomycin isn’t the only medication that’s hard on the kidneys.** Other nephrotoxic antimicrobials that may surprise you include piperacillin-tazobactam (Zosyn®), gentamicin, and acyclovir. Be especially careful when you use these medications with NSAIDs, furosemide, immunosuppressant medications, and IV contrast. **Bottom line: Several different classes of drugs are nephrotoxic – make sure to watch for signs of AKI and check creatinine when these medications are being used.**

11. **IV extravasation risk varies by antibiotic.** Extravasations of medications intended for intravenous administration can be harmful to the patient and can lead to tissue damage and need for surgical intervention. However, there are some medications that are particularly harmful when they extravasate usually due to direct tissue injury of the medication. Antimicrobials particularly implicated in risk of phlebitis or local tissue injury following extravasation include acyclovir, nafcillin, and rifampin. **Bottom line: Make sure to check the Children’s website for the IV extravasation policy.**
12. Since IV extravasation and central line complications can be dangerous, consider oral antibiotics whenever possible. Several medications are equally bioavailable in PO and IV forms. Some examples include clindamycin, sulfamethoxazole-trimethoprim, metronidazole, fluconazole, levofloxacin, doxycycline, ciprofloxacin, and rifampin. Don’t forget about changing from IV penicillins and cephalosporins to PO versions as soon as you are able. **Bottom line:** Change from IV to PO antibiotics as often and as early as clinically indicated.

13. **Enterococcus sensitivities can be confusing.** Enterococcus has several different strains with different sensitivities. *Enterococcus faecalis* is 100% ampicillin sensitive at CHCO, so you don’t have to wait for sensitivities to narrow your coverage! *Enterococcus faecium* is only 65% sensitive to ampicillin, so vancomycin is the best choice until sensitivities return. Note there are several *Enterococcus* species that are intrinsically resistant to vancomycin but still sensitive to ampicillin – this is NOT the same thing as VRE. These species include *Enterococcus gallinarum* and *Enterococcus cassiloflavus*. **Bottom line:** Don’t forget to refer to Bugs and Drugs when approaching *Enterococcus* treatment.

14. **Swabs are not good for sample collection.** Swabs tend to absorb purulence, bacteria, and cells that can be helpful in deciphering treatment after abscess incision and drainage. Because swabs are so absorbent, the lab is not able to perform a gram stain and often the bacteria cannot grow on culture. Whenever possible, an aspirate of fluid (even a small amount aspirated into a syringe) is much more helpful to the lab. **Bottom line:** If at all possible, send an aspirate instead of a swab.

15. **True penicillin allergies are rare.** Patients often get labeled as having a penicillin allergy for rash or other nonspecific symptoms while taking a medication when in reality approximately 90% of these patients are able to tolerate penicillins (9). These patients are at risk for antibiotic mistreatment for the rest of their lives (10). Therefore, especially in pediatrics, it is important to get advice from an allergist for patients with a suspected penicillin allergy to see if referral or oral challenges are in order. **Bottom line:** Most penicillin allergies are not true allergies. Get advice from an allergist regarding referral or oral challenge to avoid a life-long label that leads to inferior treatment of future infections.

REFERENCES:

7. FDA.gov (2016). FDA Drug Safety Communication: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms. Last updated: 02/26/2016
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