Antibiotics: Potential Harms

Antibiotics are a valuable resource and judicious use is very important. For many serious infections (e.g. pneumonia, bacterial meningitis, sexually transmitted infections) the benefits of antibiotics clearly outweigh potential harms. However, for conditions that are primarily viral (e.g. pharyngitis, acute sinusitis, acute bronchitis), the benefits are minimal and likely outweighed by harms. Of note: antibiotic-related adverse drug events account for 1 out of every 5 visits to the Emergency Department.[1]

Common Adverse Events

Overall NNH = 8-12 **Yeast infection NNH = 23**

- In a meta-analysis (10 trials, 2450 patients) comparing antibiotics to placebo for acute rhinosinusitis, common adverse events (such as **nausea**, **vomiting**, **diarrhea**, or **abdominal pain**) occurred in 27% of patients on antibiotics versus 15% on placebo (NNH = 8-12).[2,5] The antibiotics used in this meta-analysis included **penicillins**, **macrolides**, and **tetracyclines**. Trials examining other populations have found similar numbers of adverse events.[3,4,5]
- A recent meta-analysis comparing amoxicillin or amox/clav to placebo found risk of **yeast infection** (candidiasis) ~ 8x higher in those on antibiotics (NNH = 23).[6]

Allergic Reactions

NNH from 20 (rash, hives) to 10,000 (anaphylaxis)

Allergic reactions can occur with any antibiotic; **penicillin** in particular is well studied. About 5-10% of patients will self-report a penicillin allergy;[7,8] however the vast majority of these reactions are delayed reactions, occurring days to weeks after initiating therapy, and do not typically indicate a true allergy.[9] Anaphylaxis occurs in about 0.01% of patients taking penicillin; about 10% of these reactions are fatal (i.e. 0.001% of all patients prescribed penicillin).[10,11,12]

Serious Adverse Events

NNH from 300 to 30,000

Rare but serious adverse events are associated with all antibiotics. Large, long-term randomized controlled trials are uncommon, and so it is difficult to put a precise estimate on how prevalent these events are. However, some adverse events include:

- ***Clostridium difficile* infection**: associated most often with **clindamycin** (RR≈4), cephalosporins, and fluoroquinolones; risk varies depending on patient factors.[13,14,15]
- **Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, & other severe skin reactions**: these events occur a few times per 100,000 antibiotic prescriptions.[16] Cotrimoxazole in particular has a higher association than most other antibiotics.[17]
- **QT prolongation**: associated most often with macrolides (esp. **clarithromycin** and **erythromycin**) and fluoroquinolones (esp. **levofloxacin** and **moxifloxacin**). Risk of QT prolongation is also dependent on other factors (e.g. cardiac, metabolic, other drugs, etc.). See RxFiles QT Prolongation page 32 (11th Ed).
- **Tendon rupture with fluoroquinolones**: one large cohort study found a risk of 3.5% for tendon rupture in adults over the age of 65.[18]
- **Hyperkalemia with cotrimoxazole**: in older adults taking medications which can raise potassium (such as **ACEIs**, **ARBs**, **spironolactone**, or **NSAIDs**), **cotrimoxazole** was associated with sudden death (NNH ≈ 300).[19,20]
- **Contraceptive failure/drug interaction?** Although this is thought to be unlikely, there is a small but real risk & a backup birth control method is always recommended.

Other

There are many other less common harms than can be covered here! e.g. serum sickness like reactions, pulmonary fibrosis with nitrofurantoin, tooth discoloration with tetracyclines

Antibiotic Resistance

NNH as low as 1??? Every course of antibiotic is likely to result in some emerging resistance which could affect the next choice of antibiotic regimen for that individual, especially if within 3 months of the previous antibiotic. Of course the NNH for catastrophic resistance would be much higher.

Resistance to an antibacterial can develop quickly. For example, strains of *Streptococcus pneumoniae* resistant to **levofloxacin** were documented in the same year levofloxacin was introduced to the market.[21] Rare, but worrisome, reports of bacteria resistant to every available antimicrobial can be found in the literature.[22] The good news is that when prescribing patterns change, resistance rates decline.[23,24]

Quotes from the team ☺: *Harms speak louder when there is little or no benefit to offset them!*

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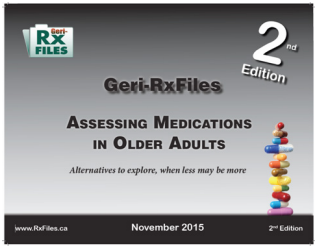

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