ESSAY

The Prime Directive: Choosing an Appropriate Antibiotic Duration

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The toddler hospitalized early yesterday morning with periorbital cellulitis looks much better on today's morning rounds. There's been no fever overnight, and the eye redness is significantly diminished after just 24 hours of an intravenous, antistaphlococcal antibiotic. It's time for discharge, and the housestaff decides amoxicillin-clavulanic acid is a good choice to complete the antibiotic course as an outpatient. The team turns to you, the experienced clinician, and asks, "How long should we treat?"

Consulting your memory bank and weighing factors such as today's relative humidity and the vibe you're getting from the collective consciousness of pediatricians everywhere, you make the following authoritative declaration: 7 days. Boom! That was easy. On to the next case.

"Wait a minute," the senior resident says, "I think Harriet Lane says 10 days."[1] "Right," the junior resident says, "and that's what the infectious disease fellow said when I curbsided her last night about this kid."

The debate is joined. Should it be 7 days, 10 days, or something else? Honest answers like, "It probably doesn't matter much," or "who knows," just don't cut it. No one appreciates the weary cynicism, and in the end, you have to give definitive direction to the team, the pharmacist, and the parents.

You know the pocket references provide consensus rules of thumb, which are more eminence-based than evidence-based. You also know that for generations US infectious disease experts have taught that antibiotic durations should be based on scores likely found in an American football game (eg, 7, 10, 14, and 21).

Over the past 11 years, I have used the following elegant solution to the antibiotic duration conundrum: the prime directive. With a nod to Star Trek, the method offers a rigorous, mathematical approach that is more scientifically satisfying and internationally applicable than American football scores. Except for infections treated by a single dose of antibiotics, I recommend choosing a total antibiotic duration that is a prime number >2 (3, 5, 7, 11, 13, 17, 19, 23, 29, and so on). Table 1 shows how the prime directive complements expert recommendations. When more than 1 prime number exists within a duration range, I typically choose the smaller prime (a shorter duration) unless I get push back, in which case I turn to advanced decision tools, such as the Magic 8 Ball.[2,3]

I have used the method for inpatients and outpatients with any infectious disease. Although a multicenter, double-blind trial of the prime directive has not yet begun, there have been 0 bad outcomes so far. The housestaff, nurses, and pharmacy adopted the scheme with great enthusiasm. Parents are generally unsurprised by durations of 3, 5, or 7 days; the longer, unfamiliar courses provide opportunities to teach parents or children about prime numbers and dispel myths about the number 13.

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TABLE 1 Total Antibiotic Duration (Parenteral Alone, Parenteral Plus Oral, or Oral Alone)

Reference and/or Consultant Recommendations	Prime to Prescribe
3 d	3 d
3–7 d	3, 5, or 7 d[a]
7 d or 1 wk	7 d
7–10 d	7 or 11 d[b]
10 d	11 d
10–14 d	11 d
1–2 wk	11 d
14 d or 2 wk	13 d[c]
2–3 wk	17, 19, or 23 d[a]
4 wk	29 d
4–6 wk	29, 31, 37, or 41 d[a]
6 wk	41 or 43 d[b]

[a] Whereas shorter durations are preferentially chosen when multiple primes meet the directive, longer durations may be selected when the illness is deemed bad. Otherwise, determine by using the Magic 8 Ball.
[b] Coin flip or Magic 8 Ball recommended.
[c] Triskaidekaphobia aside, this duration has proven to be safe and effective.

Buoyed by the unmitigated success of using prime numbers for antibiotic management, the next research question is whether the prime directive or an equally stylish approach can guide weaning regimens for patients on steroids, opiates, benzodiazepines, and other medications. Published guidance can be reduced to the Goldilocks principle: not too fast and not too slow. Early work suggests that some combination of primes, perfect squares (4, 9, 16, 25, etc), and the Fibonacci sequence (1, 1, 2, 3, 5, 8, 13, etc) might provide welcome mathematical underpinning to medication tapering decisions that are otherwise ad hoc and whimsical.[4–7]

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