

VIEWPOINT

Rethinking How Antibiotics Are Prescribed

Incorporating the 4 Moments of Antibiotic Decision Making Into Clinical Practice

Pranita D. Tamma, MD, MHS

Department of Pediatrics, School of Medicine, Johns Hopkins University, Baltimore, Maryland.

Melissa A. Miller, MD, MS

Center for Quality Improvement and Patient Safety, Agency for Healthcare Research and Quality, Rockville, Maryland.

Sara E. Cosgrove, MD, MS

Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, Maryland.

Antibiotics save countless lives, but can also cause significant harm including antibiotic-associated adverse events, *Clostridium difficile* (also known as *Clostridioides difficile*) infections, increasing antibiotic resistance, and changes to the microbiome (the implications of changes to the microbiome are only beginning to be understood).¹ Antibiotic stewardship programs have become increasingly commonplace in hospitals in the United States and around the world, but these programs almost always rely heavily on restrictive practices (eg, requiring approval before prescribing certain antibiotics) or persuasive practices (eg, discussions with clinicians regarding the continued need for antibiotics).² Although these approaches have had success in improving antibiotic use,² they depend on external motivators, and their ability to influence how clinicians will prescribe antibiotics in the absence of an antibiotic stewardship program-driven intervention is questionable.

Some conceptual frameworks have been shown to assist clinicians with recognizing problems and guiding them through a logical sequence of questions and potential solutions (eg, patient care handoffs between clinicians).³ Similar low-cost, straightforward approaches have been successfully used to improve adherence with hand hygiene guidelines⁴ and central line insertion practices.⁵ A structured approach emphasizing the 4 critical time points of antibiotic prescribing may improve antibiotic decision making by clinicians and communication surrounding antibiotic decisions among health care practitioners (eg, nurses, pharmacists).

The Agency for Healthcare Research and Quality (AHRQ) Safety Program for Improving Antibiotic Use aims to improve antibiotic prescribing practices by combining adaptive change theories and evidence-based diagnostic and treatment practices to accomplish meaningful and sustained change.⁶ A core feature of the AHRQ safety program is training clinicians to incorporate the 4 moments of antibiotic decision making into their thought process when prescribing antibiotics. The 4 moments framework provides an easy-to-remember, structured approach to improve antibiotic prescribing that could be used in the acute care setting (Table).

Moment 1

Moment 1 asks: "Does this patient have an infection that requires antibiotics?" Prescribing antibiotics to hospitalized patients can be habitual in response to an abnormal vital sign (eg, an isolated fever) or an isolated clinical change is observed (eg, delirium in patients >65 years of age). Moment 1 asks prescribers to pause and consider if a non-infectious process is more likely. For example, several con-

ditions may account for dyspnea with chest imaging changes, including aspiration pneumonia, atelectasis, congestive heart failure, pulmonary embolism, or viral infection for which antibiotics are unlikely to be of benefit.

A common scenario for which antibiotics are generally not indicated is asymptomatic bacteriuria (the isolation of significant bacterial colony counts in urine in the absence of relevant urinary symptoms). Numerous studies have shown that both bacteriuria and pyuria are common and that antibiotic treatment of patients with asymptomatic bacteriuria increases the likelihood of subsequent urinary tract infections that are resistant to common antibiotics.⁷ Moment 1 reminds the clinician to synthesize all relevant patient information to determine the likelihood of an infection that requires antibiotic therapy.

Moment 2

Moment 2 asks: "Have I ordered appropriate cultures before starting antibiotics? What empirical antibiotic therapy should I initiate?" Before administering antibiotics, it is critical that cultures be obtained when appropriate. Lack of appropriate cultures can lead to prolonged antibiotic therapy when no bacterial process exists or continuation of broad-spectrum antibiotics when narrower-spectrum agents with a more favorable adverse event profile could be used. The second component of moment 2 is to ensure timely administration of appropriate empirical antibiotic therapy. It reminds the prescriber to think carefully about specific patient risk factors and severity of illness in association with the likely source of infection.

For example, most patients with community-acquired pneumonia, intra-abdominal infections, urinary tract infections, and nonpurulent cellulitis are not at high risk for methicillin-resistant *Staphylococcus aureus* and do not benefit from empirical vancomycin. Similarly, double coverage of potential gram-negative infections or initiation of broad-spectrum agents such as piperacillin-tazobactam, cefepime, or meropenem are not routinely necessary for patients who lack specific risk factors. To ensure that appropriate knowledge is available to enact moment 2, local antibiotic guidelines should be developed and available at the point of care for common inpatient infectious conditions.

Moment 3

Moment 3 asks: "A day or more has passed. Can I stop antibiotics? Can I narrow therapy? Can I change from intravenous to oral therapy?" Too often, the decision to continue antibiotic therapy is not revisited as more clinical and microbiological data become available. Moment 3

Corresponding Author: Pranita D. Tamma, MD, MHS, Division of Pediatric Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, 200 N Wolfe St, Ste 315, Baltimore, MD 21287 (ptamma1@jhmi.edu).

Table. Hypothetical Scenario Incorporating the 4 Moments of Antibiotic Decision Making Into Daily Practice

Moment	Scenario	Patient and Symptom Description	Decision
1	Does this patient have an infection that requires antibiotics?	Patient is a 34-year-old previously healthy woman with dysuria, fever, hypotension, and flank pain	Patient has signs and symptoms concerning for pyelonephritis
2	Have I ordered appropriate cultures before starting antibiotics? What empirical antibiotic therapy should I initiate?	Urine dipstick indicates pyuria and bacteriuria	<ul style="list-style-type: none"> Urine and blood cultures are obtained prior to administering antibiotic therapy Ceftriaxone is prescribed as empirical therapy for pyelonephritis Broader therapy is not indicated because the patient has no risk factors for pseudomonal or antibiotic-resistant infection Vancomycin is not administered because methicillin-resistant <i>Staphylococcus aureus</i> is not a common cause of pyelonephritis
3	A day or more has passed. Can I stop antibiotics? Can I narrow therapy? Can I change from intravenous to oral therapy?	<ul style="list-style-type: none"> Patient has an appropriate response to therapy Urine cultures grow <i>Escherichia coli</i> resistant to trimethoprim and sulfamethoxazole but susceptible to ciprofloxacin 	<ul style="list-style-type: none"> Because <i>E coli</i> recovered in the urine has oral treatment options available, ceftriaxone is stopped and ciprofloxacin is initiated The patient is able to tolerate oral therapy and shows clinical improvement; thus, patient is switched from intravenous to oral therapy
4	What duration of antibiotic therapy is needed for this patient's diagnosis?	Patient is on day 3 of therapy and is ready to be discharged home	<ul style="list-style-type: none"> Treatment with ciprofloxacin for 7 d has been shown to be effective for pyelonephritis The patient is discharged home to complete additional 4 d of antibiotic therapy

reminds the prescriber to perform a daily antibiotic time-out for every patient receiving antibiotics. This might include use of a form that is completed or a routine verbal discussion on a daily basis by the clinical care team during rounds.

For patients who are hospitalized, a nurse or pharmacist can be an excellent resource to prompt clinicians to verbalize plans for antibiotics.⁸ Prescribers should document decisions that result from the daily review in progress notes, including the indication for continued antibiotic therapy, the day of therapy, plans to narrow therapy or switch to oral therapy, and the expected duration of therapy. Ensuring effective changes are occurring because of the time-out underscores the importance of a stewardship team for backup support in complex cases and encouragement for changing long-standing practices.

Moment 4

Moment 4 asks: "What duration of antibiotic therapy is needed for this patient's diagnosis?" Traditionally recommended durations of therapy have lacked scientific evidence, leading to excessively long

courses. Increasing numbers of studies support shorter durations of therapy than previously administered for infections including community-acquired pneumonia, ventilator-associated pneumonia, intra-abdominal infections, urinary tract infections, cellulitis, and gram-negative bacteremia.⁹ These infections constitute more than half of inpatient antibiotic use regardless of hospital size.¹⁰ The duration of therapy should be based on the literature and an assessment of whether patients have had appropriate clinical responses.

Conclusions

Optimizing antibiotic use is essential to reduce antibiotic-associated harm and the spread of antibiotic resistance. Acute care clinicians must take active responsibility as stewards of antibiotic use. An organized approach such as the 4 moments of antibiotic decision making could be helpful if used every time antibiotic therapy is considered. Antibiotic stewardship programs can then help ensure that clinicians and prescribers are equipped with the necessary information to guide appropriate, evidence-based decisions during each moment of care.

ARTICLE INFORMATION

Published Online: December 27, 2018.
doi:10.1001/jama.2018.19509

Conflict of Interest Disclosures: None reported.

Funding/Support: This work was supported by contract HHSP2332015000201/HHSP23337003T from the Agency for Healthcare Research and Quality (AHRQ).

Role of the Funder/Sponsor: The AHRQ had no role in preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The findings and conclusions are those of the authors and do not necessarily represent the views of the AHRQ. No statement in this report should be construed as an official position of the AHRQ or of the US Department of Health and Human Services.

REFERENCES

- Marston HD, Dixon DM, Knisely JM, Palmore TN, Fauci AS. Antimicrobial resistance. *JAMA*. 2016; 316(11):1193-1204.
- Tamma PD, Avdic E, Keenan JF, et al. What is the more effective antibiotic stewardship intervention: preprescription authorization or postprescription review with feedback? *Clin Infect Dis*. 2017;64(5): 537-543.
- Mohorek M, Webb TP. Establishing a conceptual framework for handoffs using communication theory. *J Surg Educ*. 2015;72(3):402-409.
- World Health Organization. WHO Guidelines on Hand Hygiene in Health Care. http://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf;jsessionid=07476D4B3781C4672FD20AED6DD6536D?sequence=1. Accessed July 10, 2018.
- Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;355(26):2725-2732.
- Agency for Healthcare Research and Quality. AHRQ Safety Program for Improving Antibiotic Use. <https://www.ahrq.gov/professionals/quality-patient-safety/hais/tools/antibiotic-stewardship/index.html>. Accessed November 13, 2018.
- Cai T, Nesi G, Mazzoli S, et al. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. *Clin Infect Dis*. 2015;61(11):1655-1661.
- Olans RN, Olans RD, DeMaria A Jr. The critical role of the staff nurse in antimicrobial stewardship—unrecognized, but already there. *Clin Infect Dis*. 2016;62(1):84-89.
- Spellberg B. The new antibiotic mantra. *JAMA Intern Med*. 2016;176(9):1254-1255.
- Magill SS, Edwards JR, Beldavs ZG, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Prevalence of antimicrobial use in US acute care hospitals, May-September 2011. *JAMA*. 2014;312(14):1438-1446.