

Educational Pearl

Gram-Negative Bacteremia: Shorter is Better

Each day of additional antibiotics is associated with an increased risk for new resistance development, adverse drug event, and *C. difficile* infection (<u>see KASIC Pearl: Every Dose Matters</u>).¹⁻³ Therefore, the shortest effective duration should be used whenever possible. When it comes to uncomplicated gram-negative bacteremia, what is the shortest, effective duration?

Is 7 days enough for gram-negative bacteremia?

Yes! Several randomized controlled trials have compared 7 days to 14 days for uncomplicated gram-negative bacteremia. Collectively, these studies have found non-inferior rates of mortality, clinical failure, readmissions, and duration of hospitalization with 7 days of therapy compared with 14 days of therapy.⁴⁻⁶

Should duration start from the first day of antibiotics or first day of negative blood cultures?

Day 1 of therapy was defined as the first day of microbiologically active therapy and NOT the first day of negative blood cultures in all studies comparing 7 days to 14 days.⁴⁻⁶ Routinely repeating blood cultures in uncomplicated gram-negative bacteremia is not necessary.⁷

<u>Key Takeaway</u>: Treat uncomplicated gram-negative bacteremia for 7 days. Count duration of therapy from first day of active antibiotics, NOT first day of negative blood cultures.

References:

- 1. Teshome BF, Vouri SM, Hampton N, Kollef MH, Micek ST. Duration of Exposure to Antipseudomonal β-Lactam Antibiotics in the Critically III and Development of New Resistance. *Pharmacotherapy*. 2019;39(3):261-270.
- 2. Vaughn VM, Flanders SA, Snyder A, et al. Excess Antibiotic Treatment Duration and Adverse Events in Patients Hospitalized With Pneumonia: A Multihospital Cohort Study. Ann Intern Med. 2019;171(3):153-163. doi:10.7326/M18-3640
- 3. Branch-Elliman W, O'Brien W, Strymish J, Itani K, Wyatt C, Gupta K. Association of Duration and Type of Surgical Prophylaxis With Antimicrobial-Associated Adverse Events. *JAMA Surg*. 2019 Jul 1;154(7):590-598.
- 4. Yahav D, Franceschini E, Koppel F, Turjeman A, Babich T, Bitterman R, Neuberger A, Ghanem-Zoubi N, Santoro A, Eliakim-Raz N, Pertzov B, Steinmetz T, Stern A, Dickstein Y, Maroun E, Zayyad H, Bishara J, Alon D, Edel Y, Goldberg E, Venturelli C, Mussini C, Leibovici L, Paul M; Bacteremia Duration Study Group. Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial. *Clin Infect Dis*. 2019 Sep 13;69(7):1091-1098. doi: 10.1093/cid/ciy1054. PMID: 30535100.
- 5. Von Dach E, Albrich WC, Brunel AS, et al. Effect of C-Reactive Protein-Guided Antibiotic Treatment Duration, 7-Day Treatment, or 14-Day Treatment on 30-Day Clinical Failure Rate in Patients With Uncomplicated Gram-Negative Bacteremia: A Randomized Clinical Trial. *JAMA*. 2020. 323:2160-9.
- 6. Molina J, Montero-Matos E, Praena-Segovia J, et al. Seven versus 14-days course of antibiotics for the treatment of bloodstream infections by Enterobacterales. A randomized, controlled trial. *Clin Microbiol Infect*. 2022. 28(4):550-557.
- 7. Heil EL, Bork JT, Abbo LM, et al. Optimizing the Management of Uncomplicated Gram-Negative Bloodstream Infections: Consensus Guidance Using a Modified Delphi Process. *Open Forum Infect Dis*. 2021;8(10):ofab434. Published 2021 Oct 11. doi:10.1093/ofid/ofab434