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تُظهر هذه الصورة المقطعيَّة العرضية النتُّبات (تراكمات البكتيريا وجلطات الدَّم) على صمامات القلب الأربعة 8 مايو 2025 IDSA guidelines on Infective Endocarditis Care The Infectious Diseases Society of America (IDSA) has made a big step in helping doctors take care of infective endocarditis. They have put together idsa infective endocarditis guidelines that are based on the newest research. These guidelines are updated often these infectious diseases society of america endocarditis guidelines to make smart choices. They are key for the best care and prevention of endocarditis. It's important for doctors to know these guidelines well. Understanding Infective Endocarditis Infective endocarditis is a serious infection of the heart's inner lining. It mainly affects the heart valves. It needs quick medical help and a deep understanding for the best care. What is Infective Endocarditis? This infection hits the heart's inner lining and valves. It's often from bacteria, but can be from fungi too. Doctors stress the need for quick diagnosis and the right antibiotics to treat it. See also Gonorrhea vs Syphilis: Symptoms & Treatment DifferencesCauses and Risk Factors Many things can lead to infective endocarditis: Bacterial or fungal pathogens Prosthetic heart valves Previous endocarditis Congenital heart defects People with these risks should follow treatment guidelines to avoid getting this serious infection. Symptoms and Complications Infective endocarditis shows in many ways: Fever and chills Fatigue and malaise Heart murmur Shortness of breath Without quick and right treatment, it can lead to serious problems like heart failure or blood clots. Following treatment guidelines is key to avoiding these bad outcomes. IDSA Infective Endocarditis Guidelines The Infectious Diseases Society of America (IDSA) has guidelines for infective endocarditis. These guidelines help doctors and other health workers. They cover how to diagnose, manage, and treat this serious condition. These guidelines change over time to keep up with new research and practices. Overview of the Guidelines The IDSA guidelines are key for health workers. They give clear steps for finding infective endocarditis. They talk about how to use tests and what makes a diagnosis sure.They also stress working together to care for patients fully. Updates in the 2021 Revision The 2021 update to the IDSA guidelines brings big changes. It includes new advice on antibiotics, better ways to diagnose, and new ways to manage the condition. These changes make sure treatment is safe and works well. Important Changes and Additions The 2021 guidelines focus on three main areas: Antibiotic Stewardship: This means using antibiotics wisely to stop resistance and keep patients safe. Individualized Treatment Strategies: It's about making care plans that fit each patient's needs. Incorporation of New Evidence: It includes new info on blood thinners and their role in treating infective endocarditis. Looking at old and new guidelines shows how the IDSA's advice has evolved. Here's a table that points out some key changes: Aspect Previous Guidelines 2021 Guidelines Antibiotic Therapy Standard protocols Updated recommendations for dosing and duration Diagnostic Imaging Traditional methods Advanced imaging techniques Management Approach General practices Personalized treatment strategies Diagnosis and Evaluation of Infective Endocarditis Diagnosing infective endocarditis needs a detailed look at many things. This includes clinical signs, lab tests, and heart scans. Key signs are ongoing bacteria in the blood, heart damage seen on scans, and new heart valve problems. Tests like PET-CT and cardiac CT are key in seeing how bad the infection is and spotting problems. Getting the right treatment for endocarditis is very important. A careful check-up helps make a treatment plan that fits the patient. This careful check-up often includes: Clinical Evaluation: Doctors look at the patient's history and check for signs like fever, heart sounds, and blood clots. Microbiological Testing: Blood tests help find the bacteria causing the infection, which helps choose the right medicine. Echocardiography: Heart scans, like TTE and TEE, show if there are growths, abscesses, or if the heart valves are damaged. Advanced Imaging: Tests like PET-CT and cardiac CT are very useful in finding complex cases and spotting problems outside the heart. These steps are put together to help diagnose infective endocarditis quickly and correctly. By doing a thorough check-up, doctors can give the best treatment advice. This helps lower the risk of serious problems from the infection. Endocarditis Treatment Guidelines by IDSA The Infectious Diseases Society of America (IDSA) has made detailed guidelines for treating endocarditis. These guidelines cover antibiotic use, surgery, and handling complications. It's key to know these to manage infective endocarditis well. See also Beta Haemolytic Strep A InfectionsAntibiotic Therapy Recommendations Based on the idsa infective endocarditis guidelines, antibiotics are chosen based on the germ and how it reacts to antibiotics. Doctors look at the patient's kidney function, allergies, and past antibiotic use. Antibiotics like vancomycin and ceftriaxone are often used, but the choice depends on the germ type, like Staphylococcus aureus or Streptococcus viridans. Surgical Intervention Guidelines Surgery is needed when antibiotics alone can't clear the infection. The endocarditis treatment recommendations suggest surgery for uncontrolled infections, heart failure, or to prevent blood clots. Doctors, heart specialists, and surgeons work together to decide on surgery. Management of Complications Handling complications is key in treating endocarditis, as the idsa infective endocarditis guidelines state. This includes managing blood clots, kidney problems from certain drugs, and heart failure from valve damage. Quick action is vital to lessen these issues. Complication Management Strategy Embolic Events Early surgical intervention; anticoagulation therapy if indicated Renal Impairment Adjustment of antibiotic dosing; supportive renal care Heart Failure Medical management with diuretics; surgical valve repair or replacement IDSA Endocarditis Prophylaxis Endocarditis is a serious heart infection. It can be prevented with the right steps. The Infectious Diseases Society of America (IDSA) has guidelines for this. They help keep high-risk patients safe during certain medical procedures. When is Prophylaxis Recommended? Patients with heart conditions are at higher risk for endocarditis. They need extra protection during dental, GI, or urological procedures. This includes things like getting teeth pulled, some surgeries, and certain tests. Prophylactic Antibiotics Guidelines Guidelines say which antibiotics to use based on the patient and the procedure. For dental work, amoxicillin is often the first choice. But, if you're allergic to penicillin, other antibiotics like cephalexin or azithromycin might be used. For other procedures, the antibiotic choice can change. It depends on the infection and the patient's needs. Here's a table with some common recommendations: Procedure Type First-line Antibiotic Alternative Antibiotics Dental (e.g., extractions, periodontal surgery) Amoxicillin Cephalexin, Clindamycin, Azithromycin, Clarithromycin Gastrointestinal (e.g., GI endoscopy with biopsy) Ampicillin Vancomycin, Gentamicin Genitourinary (e.g., urological procedures) Amoxicillin Cephalexin, Ciprofloxacin Following IDSA guidelines and choosing the right antibiotics is key to preventing endocarditis. Doctors must look at the patient's history and the procedure to make sure antibiotics are used correctly. Endocarditis Management in Acibadem Healthcare Group The Acibadem Healthcare Group is leading the way in treating endocarditis. They follow the idsa infective endocarditis guidelines closely. This ensures patients get the best care for this serious condition. We'll look at how they use these guidelines and share success stories that prove their effectiveness. Adoption of IDSA Guidelines Acibadem Healthcare Group is committed to top-notch care. They use the idsa infective endocarditis guidelines in their treatments. This means they focus on precise diagnosis and the best treatments for patients. Case Studies and Success Stories Many case studies show how the idsa infective endocarditis guidelines help. They show how even tough cases of endocarditis can be handled well. From start to finish, patients get the right care. Patients are very happy with their treatment. They say the strict following of guidelines by doctors made a big difference. This makes Acibadem Healthcare Group a top choice for endocarditis care. Component Description Guideline Adoption Full integration of idsa infective endocarditis guidelines into clinical practice. Case Study Detailed analysis of complex endocarditis scenarios managed successfully. Patient Success Stories Notification of patient outcomes showcasing the effectiveness of guideline-based care. See also Doxycycline Hyclate Effectiveness for GonorrheaIDS Guidelines on Infective Endocarditis Care: Challenges in Endocarditis Therapy Endocarditis treatment has big challenges, especially with new drug-resistant germs. These germs make treatment harder and longer. It's tough for patients with other health problems too. Patients with high risks, like those with fake heart valves or ongoing health issues, face special challenges. They need to follow idsa guidelines for infective endocarditis closely. Doctors, specialists, and surgeons must work together to help them. Success in treating endocarditis means overcoming these challenges. It's key to make the right diagnosis, act fast, and care for each patient as an individual. This helps beat the hurdles in treating endocarditis. Knowing about these challenges and keeping up with new research is crucial. It helps make endocarditis treatments better. Working together as a team and following guidelines is key to tackling endocarditis treatment challenges. Future Directions in Endocarditis Care Medical research is moving forward fast. It's now focusing on using genes and precision medicine to help patients. By looking at each patient's genes, doctors can make treatments that work better for them. This means treatments will be more effective and safer. Researchers are also working on making antibiotics work better. They want to use them in a smarter way. This will help stop bacteria from becoming resistant and help patients get better faster. It's important to find new ways to spot endocarditis early and accurately. Scientists are looking into new imaging and testing methods. These will help doctors catch infections sooner and treat them right.IDS Guidelines on Infective Endocarditis Care Creating vaccines is a big goal too. Scientists are trying to make vaccines that stop infections before they start. This could make endocarditis much less common and save a lot of money on healthcare. Innovative Strategies Expected Outcomes Current Status Genomic and Precision Medicine Personalized therapy, reduced adverse effects Ongoing research, preliminary success Antibiotic Optimization Effective use, reduced resistance Active development Advanced Diagnostics Early detection, accurate identification Research and implementation Vaccination Development Reduced incidence, lower healthcare costs In progress Importance of Adherence to IDSA Endocarditis Guidelines Following IDSA endocarditis guidelines is key to better patient care. These guidelines help doctors give the best care possible. They lead to more lives saved, fewer complications, and lower costs. The IDSA guidelines are made with lots of research and evidence. They cover how to diagnose, treat, and prevent endocarditis. Doctors must follow these guidelines to give the best care and keep up with medical standards. It's important to keep doctors updated on these guidelines. Medical places should offer training and resources. This keeps care high and helps patients with endocarditis get better. Infective endocarditis is a serious heart infection. It's often caused by bacteria or fungi. People with certain heart conditions or implants are at higher risk. The IDSA guidelines give advice on diagnosing and treating endocarditis. They use the latest research and clinical findings. This helps doctors make the best treatment plans. The 2021 updates suggest new ways to treat infections. They talk about better imaging and personalized treatment plans. The focus is on using antibiotics wisely and new findings on blood thinners. *The information on our website is not intended to direct people to diagnosis and treatment. Do not carry out all your diagnosis and treatment procedures without consulting your doctor. The contents do not contain information about the therapeutic health services of Acıbadem Health Group. IDSA is committed to providing up-to-date guidance on the treatment of antimicrobial-resistant (AMR) infections. This fourth updated guidance document focuses on infections caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E), AmpC β- lactamase-producing Enterobacterales (AmpC-E), carbapenem-resistant Enterobacterales (CRE), Pseudomonas aeruginosa with difficult-to-treat resistance (DTR P. aeruginosa), carbapenem-resistant Acinetobacter baumannii (CRAB), and Stenotrophomonas maltophilia. This updated document replaces previous versions of the guidance document. Please submit your feedback and comments on the AMR Guidance by emailing us at PracticeGuidelines@idsociety.org. Published by CID, August 7, 2024 | Clinical Infectious Diseases, ciae403, Pranita D. Tamma*, Emily L. Heil, Julie Ann Justo, Amy J. Mathers, Michael J. Satlin, & Robert A. Bonomo, *Corresponding Author: Pranita D. Tamma, MD, MHS, Johns Hopkins University School of Medicine, Department of Pediatrics, Baltimore, Maryland, USA; ptamma1@jhmi.edu Keywords: ESBL; AmpC; carbapenem-resistant Enterobacterales; Pseudomonas aeruginosa; CRAB; Stenotrophomonas maltophilia July 18, 2023 Version 3.0 of the guidance has been released. The reader is encouraged to review the entire AMR Guidance document as edits and updated pre-clinical and clinical data have been made to virtually all questions. The following represent some key changes to the 2023 IDSA AMR Guidance Document. ESBL-E Fosfomycin continues to not be suggested for pyelonephritis and complicated urinary tract infections (cUTI); however, the uncertainty of the additive benefit of additional doses of oral fosfomycin for these indications was highlighted in light of recent clinical data. Amoxicillin-clavulanic acid continues to not be a preferred agent for uncomplicated ESBL-producing cystitis; however, it was acknowledged that there may be occasions where it is prescribed if resistance or toxicities preclude the use of alternative oral antibiotics and there is a preference to avoid IV antibiotics. It is advised that caution be given to patients about the potential increased risk of recurrent infection if amoxicillin-clavulanic acid is administered for this indication. Additional details on the mechanistic reasons why piperacillin-tazobactam is not anticipated to be effective for ESBL-E infections are provided. Piperacillin-tazobactam continues to not be preferred for the treatment of pyelonephritis and cUTI; however, it was acknowledged that if piperacillin-tazobactam was initiated for pyelonephritis or cUTI caused and clinical improvement occurs, the decision to continue piperacillin-tazobactam should be made with the understanding that theoretically there may be an increased risk for microbiological failure with this approach. A re-review of available data and newer data indicate that ceftolozane-tazobactam is likely to be effective against ESBL-E; however, it suggested that this agent be preserved for the treatment of DTR aeruginosa or polymicrobial infections (e.g., both DTR P. aeruginosa and ESBL-E). AmpC-E The term "moderate to high risk" clinically significant AmpC production was replaced with "moderate risk" throughout. It was clarified that even without upregulation of AmpC production, basal production of AmpC β-lactamases by organisms with inducible ampC expression leads to intrinsic resistance to ampicillin, amoxicillin-clavulanate, ampicillin-sulbactam, and first- and second-generation cephalosporins. The suggestion that cefepime is not advised for Enterobacter cloacae, Citrobacter freundii, and Klebsiella aerogenes with cefepime MICs of 4-8 µg/mL because of concerns for an increased risk of ESBL production in this cefepime MIC range was removed in light of newer data and a rereview of existing data. CRE An increase in the prevalence of CRE isolates producing metallo-beta-lactamases (MBL) in the United States (e.g., NDM, VIM, IMP) is acknowledged. A description of a Clinical and Laboratory Standards Institute (CLSI) endorsed method (i.e., broth disk elution method) to test for activity of the combination of ceftazidime-avibactam and aztreonam for MBL-producing Enterobacterales is discussed. Dosing suggestions for ceftazidime-avibactam in combination with aztreonam are updated in Table 1 and Supplemental Material. Both agents are suggested to be administered every 8 hours to facilitate simultaneous administration in clinical practice. DTR P. aeruginosa For infections caused by P. aeruginosa isolates not susceptible to any carbapenem agent but susceptible to traditional β-lactams (e.g., cefepime), administration of a traditional agent as high-dose extended-infusion therapy continues to be suggested, although the panel no longer emphasizes the importance of repeating AST on the initial isolate before administration of the traditional agent given the frequency with which this susceptibility profile occurs. A new question (i.e., Question 4.2) has been added "Are there differences in percent activity against DTR aeruginosa across available β-lactam agents?" Differences in DTR P. aeruginosa susceptibility percentages to the newer β-lactams are described along with regional differences in enzymatic mechanisms of resistance that contribute to some of these differences. Once-daily tobramycin or amikacin were added as alternative treatment options for pyelonephritis or cUTI caused by DTR aeruginosa given the prolonged duration of activity of these agents in the renal cortex and the convenience of once daily dosing. CRAB Sulbactam-durlobactam, in combination with meropenem or imipenem-cilastatin, was added as the preferred agent for the treatment of CRAB infections. High-dose ampicillin-sulbactam in combination with at least one other agent has been changed from a preferred to an alternative regimen if sulbactam-durlobactam is not available. The suggested dosing of high-dose ampicillin-sulbactam has been adjusted to be 27 grams of ampicillin-sulbactam (18 grams ampicillin, 9 grams sulbactam) daily. S. maltophilia Questions have been adjusted to list agents in order of preference (i.e., cefiderocol [with a second agent at least initially], ceftazidime-avibactam and aztreonam, minocycline [with a second agent], TMP-SMX [with a second agent], or levofloxacin [with a second agent]. A description of a CLSI endorsed method (i.e., broth disk elution method) to test for activity of the combination of ceftazidime-avibactam and aztreonam for maltophilia activity is discussed. Tigecycline has been removed as a component of combination therapy. Updated guidance from the CLSI advising against the testing of ceftazidime for maltophilia infections has been added. Background: The Infectious Diseases Society of America (IDSA) is committed to providing up-to-date guidance on the treatment of antimicrobial-resistant (AMR) infections. This guidance document focuses on infections caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E), AmpC β- lactamase-producing Enterobacterales (AmpC-E), carbapenem-resistant Enterobacterales (CRE), Pseudomonas aeruginosa with difficult-to-treat resistance (DTR P. aeruginosa), carbapenem-resistant Acinetobacter baumannii (CRAB), and Stenotrophomonas maltophilia. This updated document replaces previous versions of the guidance document. Methods: A panel of six infectious diseases specialists with expertise in managing antimicrobial- resistant infections formulated questions about the treatment of infections caused by ESBL-E, AmpC-E, CRE, DTR P. aeruginosa, CRAB, and S. maltophilia. Because of differences in the epidemiology of AMR and availability of specific anti-infectives internationally, this document focuses on the treatment of AMR infections in the United States. Results: Preferred and alternative suggested treatment approaches are provided with accompanying rationales, assuming the causative organism has been identified and antibiotic susceptibility results are known. Approaches to empiric treatment, transitioning to oral therapy, duration of therapy, and other management considerations are discussed briefly. Suggested approaches apply for both adult and pediatric populations, although suggested antibiotic dosages are provided only for adults. Conclusions: The field of AMR is highly dynamic. Consultation with an infectious diseases specialist is recommended for the treatment of AMR infections. This document is current as of December 31, 2023 and will be updated periodically. The most current version of this document, including date of publication, is available at www.idsociety.org/practice-guideline/amr-guidance/. Antimicrobial-resistant (AMR) infections are a global crisis. Internationally, approximately 1.3 million deaths were estimated to be directly attributable to AMR pathogens in 20191. In the United States, AMR pathogens caused more than 2.8 million infections and over 35,000 deaths annually from 2012 through 2017, according to the Centers for Disease Control and Prevention (CDC) Antibiotic Resistance Threats in the United States Report2. As an alternative to practice guidelines, the Infectious Diseases Society of America (IDSA) has endorsed developing more narrowly focused guidance documents for the treatment of infections where data may not be very robust and continue to rapidly evolve – such as with AMR. Guidance documents are prepared by a small team of experts, who answer questions about treatment based on a comprehensive (but not necessarily systematic) review of the literature, clinical experience, and expert opinion. Documents are made available online and updated annually. In the present document, guidance is provided on the treatment of infections caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E), AmpC β-lactamase-producing Enterobacterales (AmpC-E), carbapenem-resistant Enterobacterales (CRE), Pseudomonas aeruginosa with difficult-to-treat resistance (DTR P. aeruginosa), carbapenem-resistant Acinetobacter baumannii (CRAB), and Stenotrophomonas maltophilia. Many of these pathogens have been designated urgent or serious threats by the CDC2. Each pathogen causes a wide range of infections that are encountered in United States hospitals of all sizes, and that carry with them significant morbidity and mortality. Guidance is presented in the form of answers to a series of clinical questions for each pathogen. Although brief descriptions of notable clinical trials, resistance mechanisms, and antimicrobial susceptibility testing (AST) methods are included, the document does not provide a comprehensive review of these topics. GRADE methodology (i.e., Grading of Recommendations, Assessment, Development, and Evaluations) are not employed. Due to differences in the molecular epidemiology of resistance and availability of specific antibiotics internationally, treatment suggestions are geared toward AMR infections in the United States. This guidance document applies to both adult and pediatric populations. Suggested antibiotic dosing for adults with AMR infections, assuming normal renal and hepatic function, are provided in Table 1. Pediatric dosing is not provided. The content of this document is current as of December 31, 2023. The most current version of this IDSA guidance document and corresponding date of publication is available at: www.idsociety.org/practice-guideline/amr-guidance. Suggested treatment approaches in this guidance document assume that the causative organism has been identified and that in vitro activity of antibiotics is demonstrated. If two antibiotics are equally effective, important considerations in selecting a specific agent include safety, cost, convenience, and local formulary availability. Complicated Urinary Tract Infection Definition In this document, the term cUTI refers to UTIs occurring in association with a structural or functional abnormality of the genitourinary tract, or any UTI in an adolescent or adult male. In general, the panel suggests cUTI be treated with similar agents and for similar treatment durations as pyelonephritis. For cUTI where the source has been controlled (e.g., removal of a Foley catheter) and ongoing concerns for urinary stasis or indwelling urinary hardware are no longer present, it is reasonable to select antibiotic agents and treatment durations similar to those that would be selected for uncomplicated cystitis, with day 1 of therapy being the day source control occurred. Empiric Therapy Empiric treatment decisions are outside the scope of this guidance document. However, in general, empiric therapy should be informed by the most likely pathogens, severity of illness of the patient, the likely source of the infection, and any additional patient-specific factors (e.g., severe penicillin allergy, severe immune compromise, chronic kidney disease). When determining empiric treatment for a given patient, clinicians should also consider: (1) previous organisms identified from the patient and associated antimicrobial susceptibility testing (AST) data in the last 12 months3, (2) antibiotic exposure within the past 3 months3, and (3) local AST patterns for the most likely pathogens. Treatment decisions should be refined based on the identity and the AST profile of the pathogen, as well as on the identification of any prominent β-lactamase genes that have been identified. For all organisms, but for DTR P. aeruginosa, CRAB, and S. maltophilia in particular, a distinction between bacterial colonization and infection is important because unnecessary antibiotic therapy will only further the development of resistance and may cause unnecessary antibiotic related harm to patients. Commonly selected empiric antibiotic regimens are generally not active against CRAB and S. maltophilia infections. The decision to target treatment for CRAB and/or S. maltophilia in empiric antibiotic regimens should involve a careful risk-benefit analysis after reviewing previous culture results, clinical presentation, individual host risk factors, and antibiotic-specific adverse event profiles. Duration of Therapy and Transitioning to Oral Therapy Recommendations on durations of therapy are not provided, but clinicians are advised that the duration of therapy should not differ for infections caused by organisms with resistant phenotypes compared to infections caused by more susceptible phenotypes4. After AST results are available, it may become apparent that inactive antibiotic therapy was initiated empirically. This may impact the duration of therapy. For example, uncomplicated cystitis is typically a mild infection 5. If an antibiotic not active against the causative organism was administered empirically for uncomplicated cystitis, but clinical improvement nonetheless occurred, it is generally not necessary to repeat a urine culture, change the antibiotic regimen, or extend the planned treatment course. However, for all other infections, if AST results indicate a potentially inactive agent was initiated empirically, a change to an active regimen for a full treatment course (dated from the start of active therapy) is suggested. Additionally, important host factors related to immune status, ability to attain source control, and general response to therapy should be considered when determining treatment durations for AMR infections, as with the treatment of any bacterial infection. Finally, whenever possible, transitioning to oral therapy should be considered (assuming IV therapy was initially prescribed), particularly if the following criteria are met: (1) susceptibility to an appropriate oral agent is demonstrated, (2) the patient is hemodynamically stable (3) reasonable source control measures have occurred, and (4) concerns about insufficient intestinal absorption are not present 6. Table 1. Suggested dosing of antibiotics for the treatment of antimicrobial-resistant infections in adults, assuming normal renal and hepatic function1,2 Table 2. 2024 Clinical and Laboratory Standards Institute Breakpoints for Select Gram-Negative Organisms and Antibiotic Combinations as Suggested in the IDSA AMR Guidance Document1 ESBLs are enzymes that inactivate most penicillins, cephalosporins, and aztreonam. EBSL-E generally remain susceptible to carbapenems. ESBLs do not inactivate non-β-lactam agents (e.g., ciprofloxacin, trimethoprim-sulfamethoxazole [TMP-SMX], gentamicin). However, organisms carrying ESBL genes often harbor additional genes or mutations in genes expanding their resistance to a broad range of antibiotics. Any gram-negative organism has the potential to harbor ESBL genes; however, they are most prevalent in Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, and Proteus mirabilis7-9. CTX-M enzymes, particularly CTX-M-15, are the most common ESBLs in the United States9. ESBLs other than CTX-M with unique hydrolyzing abilities are also present, including variants of TEM and SHV β- lactamases with amino acid substitutions, but they have undergone less rigorous clinical investigation than CTX-M enzymes10-14. Routine EBSL testing is not performed by most clinical microbiology laboratories15,16. Rather, non-susceptibility to ceftriaxone (i.e., ceftriaxone minimum inhibitory concentrations [MICs] ≥2 µg/mL), is often used as a proxy for ESBL production, although this threshold has limitations with specificity as organisms not susceptible to ceftriaxone for reasons other than ESBL production may be falsely presumed to be ESBL-producers17,18. For this guidance document, ESBL-E refers to presumed or confirmed ESBL-producing E. coli, K. pneumoniae, K. oxytoca, or P. mirabilis. Treatment suggestions for ESBL-E infections assume that in vitro activity of preferred and alternative antibiotics has been demonstrated. Question 1.1: What are preferred antibiotics for the treatment of uncomplicated cystitis caused by ESBL-E? Suggested approach: Nitrofurantoin and TMP-SMX are preferred treatment options for uncomplicated cystitis caused by ESBL-E. Ciprofloxacin, levofloxacin, and carbapenems are alternative agents for uncomplicated cystitis caused by ESBL-E. Although effective, their use is discouraged when nitrofurantoin or TMP-SMX are active. An aminoglycoside (as a single dose) and oral fosfomycin (for E. coli only) are also alternative treatments for uncomplicated cystitis caused by ESBL-E. Rationale Nitrofurantoin and TMP-SMX have been shown to be effective options for uncomplicated cystitis, including uncomplicated ESBL-E cystitis5,19,20 21. Although carbapenems and the fluoroquinolones ciprofloxacin or levofloxacin are effective agents against ESBL-E cystitis22,23, their use for uncomplicated cystitis is discouraged when other effective options are available. Limiting use of these agents preserves their activity for future infections when treatment options may be more restricted. Moreover, limiting their use reduces the risk of associated toxicities, particularly with the fluoroquinolones, which have been associated with an increased risk for prolonged QTc intervals, tendinitis and tendon rupture, aortic dissections, seizures, peripheral neuropathy, and Clostridioides difficile infections24-27. Treatment with a single intravenous (IV) dose of an aminoglycoside is an alternative treatment option for uncomplicated ESBL-E cystitis. Aminoglycosides are nearly exclusively eliminated by the renal route. A single IV dose is generally effective for uncomplicated cystitis, with minimal toxicity, but robust clinical trial data are lacking28. Oral fosfomycin is an alternative treatment option exclusively for uncomplicated ESBL-E cystitis caused by E. coli. Susceptibility of E. coli to fosfomycin is not routinely tested by most clinical microbiology laboratories but E. coli resistance to fosfomycin remains rare in the United States29,30. CLSI breakpoints are only available for E. coli for fosfomycin. Fosfomycin is not suggested for the treatment of infections caused by K. pneumoniae and several other gram-negative organisms which frequently carry fosA hydrolase genes that may lead to clinical failure31,32. A randomized open-label trial indicated that a single dose of oral fosfomycin is associated with higher clinical failure than a five-day course of nitrofurantoin for uncomplicated cystitis 19. Although this trial was not limited to E. coli cystitis, in a subgroup analysis exclusively of E. coli infections, outcomes remained poor in the fosfomycin group with day 14 clinical failure of 50% in the fosfomycin group versus 22% in the nitrofurantoin group19. The additive benefit of additional doses of oral fosfomycin for uncomplicated cystitis is not known but may be a reasonable option as has been suggested for cUTI33 (Question 1.2). Amoxicillin-clavulanic is not suggested for the treatment of ESBL-E cystitis. A randomized clinical trial compared a three-day regimen of amoxicillin-clavulanic acid (500 mg/125 mg twice daily) to a three-day course of ciprofloxacin (250 mg twice daily) for 370 women with uncomplicated E. coli cystitis22. Clinical cure was observed in 58% and 77% of the women randomized to the amoxicillin- clavulanic and ciprofloxacin arms, respectively. The higher failure rates with amoxicillin-clavulanic acid appear to be associated with persistent vaginal bacterial colonization, which occurred in 45% and 10% of patients in the amoxicillin-clavulanic acid and ciprofloxacin arms, respectively22. The proportion of women in the trial infected with ESBL-E strains is not available. Of note, both agents were administered at dosages lower than generally suggested (Table 1). Even though data indicate that clavulanic acid is effective against ESBLs in vitro34,35, this may not translate to clinical efficacy36. Robust data indicating that oral amoxicillin-clavulanic acid is effective for ESBL-E uncomplicated cystitis are lacking. While amoxicillin-clavulanic acid is not a preferred agent for uncomplicated ESBL-producing cystitis, if it is prescribed because resistance or toxicities preclude use of alternative oral antibiotics and there is a preference to avoid IV antibiotics, caution should be given to patients about the potential increased risk of recurrent infection if amoxicillin-clavulanic acid is administered. The panel suggests avoiding doxycycline for the treatment of ESBL-E uncomplicated cystitis. Two clinical outcomes studies, published nearly 50 years ago, demonstrated that oral tetracyclines may be effective for the treatment of UTIs37,38. Both of these studies, however, primarily focused on P. aeruginosa, an organism not susceptible to oral tetracyclines, questioning the impact that antibiotic therapy had on clinical cure. Doxycycline is primarily eliminated through the intestinal tract39 with limited urinary excretion (35-60%)39. Until more convincing data demonstrating the clinical effectiveness of oral doxycycline for the treatment of ESBL-E cystitis are available, the panel suggests against the use of doxycycline for this indication. The roles of piperacillin-tazobactam, cefepime, and the cephamycins for the treatment of uncomplicated cystitis are discussed in Question 1.4, Question 1.5, and Question1.6, respectively. Question 1.2: What are preferred antibiotics for the treatment of pyelonephritis or cUTI caused by ESBL-E? Suggested approach: TMP-SMX, ciprofloxacin, or levofloxacin are preferred treatment options for pyelonephritis or cUTIs caused by ESBL-E. Ertapenem, meropenem, and imipenem-cilastatin are preferred agents when resistance or toxicities preclude the use of TMP-SMX or fluoroquinolones. Aminoglycosides are alternative options for the treatment of ESBL-E pyelonephritis or cUTI. Rationale TMP-SMX, ciprofloxacin, and levofloxacin are preferred treatment options for patients with ESBL-E pyelonephritis or cUTIs, assuming in vitro susceptibility has been demonstrated, based on the ability of these agents to achieve adequate and sustained concentrations in the urine, clinical trial results, and clinical experience40-42. Carbapenems are also preferred agents, when resistance or toxicities prevent the use of TMP-SMX or fluoroquinolones, or early in the treatment course if a patient is critically ill (Question 1.3). If a carbapenem is initiated and susceptibility to TMP-SMX, ciprofloxacin, or levofloxacin is demonstrated, transitioning to oral formulations of these agents is preferred over completing a treatment course with a carbapenem. Limiting use of carbapenem exposure will preserve their activity for future AMR infections, which frequently often arise in patients with cUTIs43. Aminoglycosides are alternative options for pyelonephritis and cUTI. Although expected to be effective, they are considered alternative agents because of their associated nephrotoxicity risk. Animal models suggest aminoglycosides concentrate in the renal parenchyma44. In a clinical trial of 609 adults receiving plazomicin for cUTI infections, clinical relapse occurred in 2% versus 7% and increases in serum creatinine levels of ≥0.5 mg above baseline occurred in 7% versus 4% of patients in the plazomicin and meropenem groups, respectively45. In general, higher percentages of Enterobacterales clinical isolates are susceptible to plazomicin compared to other aminoglycosides46. Other aminoglycosides are likely equally effective for the treatment of ESBL-E pyelonephritis or cUTI if susceptibility is demonstrated45,47,48. Of note, in 2023 the CLSI revised gentamicin, tobramycin, and amikacin breakpoints for the Enterobacterales16 (Table 2). Aminoglycosides may be reasonable to consider for completing treatment courses (e.g., transitioning from another agent for terminal doses) given their prolonged duration of activity in the renal cortex and the convenience of once daily dosing47,48 (Table 1, Supplemental Material). Duration-dependent risks of nephrotoxicity should be considered with all aminoglycosides49,50. Fosfomycin is not suggested for the treatment of pyelonephritis or cUTI given its limited renal parenchymal concentrations. More data are needed to evaluate the role of oral fosfomycin for patients with pyelonephritis or cUTI, particularly when administered as a multidose regimen and after several days of preferred therapy. In a clinical trial of 97 women with E. coli pyelonephritis (approximately half of patients had associated bacteremia) who received up to 5 days of IV therapy, participants were subsequently transitioned to either once-daily 3 g doses of oral fosfomycin or twice daily 500 mg doses of oral ciprofloxacin for 10 days of total antibiotic therapy51. Similar clinical cure percentages were identified in both groups (75% versus 65%, respectively). However, only approximately 6% of isolates were ESBL-producing, limiting generalizability to pyelonephritis caused by drug-resistant phenotypes51. Moreover, as 7 days is generally sufficient for the treatment of pyelonephritis, the attributable benefit of the additional days of oral fosfomycin or ciprofloxacin is unclear. Another clinical trial randomized 51 patients with cUTI to 3 g of fosfomycin daily or 750 mg of levofloxacin daily for 5-7 days, after up to two days of IV therapy33. Clinical cure at the end of therapy was similar in both treatment groups (69% versus 68%). In this study, 63% of infections were caused by E. coli but only one isolate in each arm was caused by an ESBL-producing isolate. IV fosfomycin is not clinically available in the United States. Although some data suggest IV fosfomycin may have activity against organisms beyond E. coli, it is difficult to translate data from IV fosfomycin to oral fosfomycin given the limited oral bioavailability and lower daily dosages with oral fosfomycin52. Transitioning to daily oral fosfomycin needs further investigation before suggesting for or against this practice for the treatment of ESBL-E pyelonephritis or cUTI; however, it may be a reasonable option when other preferred or alternative oral options are not available. Fosfomycin is an alternative option for the treatment of prostatitis caused by ESBL-producing E. coli when preferred options (i.e., carbapenems, TMP-SMX, or fluoroquinolones) cannot be tolerated or do not test susceptible53-59. In an observational study, fosfomycin, dosed at 3 g orally daily for one week, followed by 3 g orally every 48 hours for 6 to 12 weeks, was associated with clinical cure in 36 (82%) of 44 males with chronic bacterial prostatitis53. Fosfomycin is not suggested for prostatitis caused by gram- negative organisms other than E. coli due to the likely presence of the fosA gene and its ability to inactive this agent (Question 1.1). Nitrofurantoin does not achieve adequate concentrations in the renal parenchyma and is not advised for the treatment of pyelonephritis or cUTI. Doxycycline is also not advised for the treatment of ESBL-E pyelonephritis or cUTIs due to its limited urinary excretion (Question 1.1)39. The roles of piperacillin-tazobactam, cefepime, and the cephamycins for the treatment of pyelonephritis or cUTIs are discussed in Question 1.4, Question 1.5, and Question 1.6, respectively. Question 1.3: What are preferred antibiotics for the treatment of infections outside of the urinary tract caused by ESBL-E? Suggested approach: Meropenem, imipenem-cilastatin, or ertapenem are preferred for the treatment of infections outside of the urinary tract caused by ESBL-E. For patients who are critically ill and/or experiencing hypoalbuminemia, meropenem or imipenem-cilastatin are the preferred carbapenems. After appropriate clinical response is achieved, transitioning to oral TMP-SMX, ciprofloxacin, or levofloxacin should be considered, if susceptibility is demonstrated. Rationale A carbapenem is recommended as first-line treatment of ESBL-E infections outside of the urinary tract, based primarily on data from a large clinical trial, as described below60. Meropenem, imipenem-cilastatin, or ertapenem are preferred agents; ertapenem offers a more convenient option for patients needing to continue carbapenem therapy in the outpatient setting when oral treatment options are not available. For patients who are critically ill and/or experiencing hypoalbuminemia, meropenem or imipenem-cilastatin are the preferred carbapenems. Ertapenem, in contrast to meropenem and imipenem, is highly protein bound leading to a relatively prolonged serum half-life61. In patients with hypoalbuminemia, the free fraction of ertapenem increases, leading to increased ertapenem clearance and a significant decrease in the serum half-life of this agent, which may not be optimal with daily dosing of this agent62-64. An observational study of 279 patients with Enterobacterales infections found that hypoalbuminemia (defined as serum albumin