

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 do not include formal grading of evidence, and they are made available and updated at least annually online.

In the present document, guidance is provided on the treatment of infections caused by extended-spectrum β -lactamase-producing Enterobacterales (ESBL-E), carbapenem-resistant Enterobacterales (CRE), and *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-*P. aeruginosa*) [3]. These pathogens have been designated urgent or serious threats by the CDC [1]. Each pathogen causes a wide range of infections that are encountered in US 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 susceptibility testing methods are included, this document does not provide a comprehensive review of these topics. Due to differences in the molecular epidemiology of resistance and availability of specific anti-infectives internationally, treatment recommendations are geared toward antimicrobial-resistant infections in the United States. The content of this document is current as of 24 October 2021; updates will be provided annually.

METHODS

IDSA convened a panel of 6 actively practicing infectious diseases specialists with clinical and research expertise in the treatment of antimicrobial-resistant bacterial infections. Through a series of virtual meetings, the panel developed commonly encountered treatment questions and corresponding answers for each pathogen group. Answers include a brief discussion of the rationale supporting the recommendations. This guidance document applies to both adult and pediatric populations. Suggested antibiotic dosing for adults with antimicrobial-resistant infections, assuming normal renal and hepatic function, is provided in Table 1.

GENERAL MANAGEMENT RECOMMENDATIONS

Treatment recommendations in this guidance document assume that the causative organism has been identified and that in vitro activity of antibiotics is demonstrated. Assuming 2 antibiotics are equally effective, safety, cost, convenience, and local formulary availability are important considerations in selecting a specific agent. The panel recommends that infectious diseases specialists and physician or pharmacist members of the local antibiotic stewardship program are involved in the management of patients with infections caused by antimicrobial-resistant organisms.

In this document, the term complicated urinary tract infection (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 (eg, 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 uncomplicated cystitis.

Empiric Therapy

Empiric treatment decisions should be guided by the most likely pathogens, severity of illness of the patient, the likely source of the infection, and any additional patient-specific factors (eg, severe penicillin allergy, chronic kidney disease). When determining empiric treatment for a given patient, clinicians should also consider: (1) previous organisms identified from the patient and associated antibiotic susceptibility data in the last 6 months, (2) antibiotic exposures within the past 30 days, and (3) local susceptibility patterns for the most likely pathogens. Empiric decisions should be refined based on the identity and susceptibility profile of the pathogen.

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 phenotypes. After antibiotic susceptibility results are available, it may become apparent that inactive antibiotic therapy was initiated empirically. This may impact the duration of therapy. For example, cystitis is typically a mild infection [4]. If an antibiotic not active against the causative organism was administered empirically for cystitis, but clinical improvement nonetheless occurred, the panelists agree that 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 antibiotic susceptibility data 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 recommended. 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 antimicrobial-resistant infections, as with the treatment of any bacterial infection. Finally, whenever possible, oral step-down therapy should be considered, 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