Challenging Gram-negative Infections

Perspectives from a Clinician and a Microbiologist

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KEYWORDS

• Gram-negative bacteria • Antimicrobial resistance • Enterobacterales
• *Pseudomonas* • Susceptibility testing

KEY POINTS

- Gram-negative infections in companion animals are common and increasingly impacted by antimicrobial resistance, particularly among Enterobacterales and *P aeruginosa*.
- Culture and susceptibility testing are essential for guiding therapy but must be interpreted alongside clinical findings to distinguish infection from colonization or contamination.
- Effective management requires appropriate antimicrobial selection, reassessment based on results, and attention to underlying disease and infection prevention to limit recurrence or spread.

INTRODUCTION

Gram-negative bacteria are ubiquitous pathogens that are considered a significant One Health and public health problem due to their increasing resistance to antimicrobials and prevalence across multiple species, including dogs and cats. Two of the most clinically relevant groups of gram-negative bacteria include Enterobacterales, previously known as Enterobacteriaceae, and the nonfermenters (eg, *Pseudomonas aeruginosa*, *Acinetobacter*, *Burkholderia*, and *Stenotrophomonas*). These bacteria have 2 membranes, outer and inner, where the outer membrane contains lipopolysaccharides (LPS) each composed of 3 units: core oligosaccharide, O antigen, and lipid A. While all components are immunogenic, lipid A is considered the biologically active portion and is also known as endotoxin due to its abilities to trigger the innate immune

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Abbreviations	
AST	antimicrobial susceptibility testing
CDC	Centers for Disease Control and Prevention
CLSI	Clinical & Laboratory Standards Institute
CRE	carbapenem-resistant Enterobacterales
ESBL	extended-spectrum β-lactamase
h	hours
IM	intramuscular
IV	intravenous
LPS	lipopolysaccharides
MALDI-TOF	matrix-assisted laser desorption/ionization time-of-flight
MDR	multidrug-resistant
MICs	minimum inhibitory concentrations
PK-PD	pharmacokinetic–pharmacodynamic
PO	per os (oral administration)
SC	subcutaneous
SDD	susceptible-dose dependent
UTI	urinary tract infection

system and cause massive cytokine release. The outer membrane also contains outer membrane proteins such as porins that allow passage of molecules in and out of the cell, including antimicrobials. While the outer membrane is one of the main reasons for resistance to a wide range of antimicrobials (eg, lincosamides such as clindamycin are too large to pass through), antimicrobial resistance in gram-negative bacteria arises from multiple mechanisms including antimicrobial modification or target alteration, porin loss or mutation, acquired resistance genes such as β-lactamases, or overexpression of efflux pumps.[1] Gram-negative bacteria are a major cause of nosocomial infections, and their rising antimicrobial resistance has increased morbidity and mortality for both humans and companion animals with recognition by the Centers for Disease Control and Prevention (CDC) as a public health risk. Appropriate treatment of these infections can be complicated by resistance to multiple first-tier and second-tier antimicrobials, and clinicians are now more frequently needing to utilize higher tier options.

Dogs and cats may present to clinicians with nonspecific and varied clinical signs and physical examination findings based on location and dissemination of the gram-negative bacterial infection. For example, overwhelming LPS release in dogs and cats can induce endotoxemia and secondary nephrogenic diabetes insipidus, where the gram-negative endotoxins impair renal response to antidiuretic hormone and result in polyuria and polydipsia.[2] Gram-negative bacterial infections should be suspected by clinicians when rod-shaped bacteria are identified on cytologic examination of tissue aspirates, lavage samples, blood and urine specimens, or purulent exudate. Isolation via culture to identify the organism and provide antimicrobial susceptibility results is important for appropriate therapeutic selection and antimicrobial stewardship.

A thorough antimicrobial history in dogs and cats is instrumental for identifying patients with possible multidrug-resistant (MDR) gram-negative infections. Previous antimicrobial use, especially repeated or prolonged courses of broad-spectrum drugs, can select for resistant bacteria. Knowing which drugs were used, how long they were given, and how the patient responded helps flag patterns like poor response or recurrence that suggest resistance. This is especially relevant in chronic or recurrent infections such as otitis or urinary tract infections (UTIs) or when indwelling devices are present. Taking a careful history supports better treatment choices and

encourages appropriate culture and susceptibility testing. Collaborating with the microbiology laboratory when complicated infections are present is particularly important.

DISCUSSION

Multidrug-resistant Enterobacterales

The clinician's perspective

The most common (and therefore important) Enterobacterales associated with companion animal infections include *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae* complex. Other less common (but still important) species include *Serratia marcescens*, *Salmonella enterica*, and *Klebsiella aerogenes*. MDR Enterobacterales include extended-spectrum β-lactamase (ESBL) producing, AmpC-hyperproducing Enterobacterales, and carbapenem-resistant Enterobacterales (CRE). MDR Enterobacterales infections can have many different clinical manifestations in dogs and cats, including many types of opportunistic infections such as UTI, aspiration pneumonia, hepatobiliary infections such as cholangiohepatitis, sepsis, surgical site infections, and nosocomial infections such as those associated with esophagostomy and tracheostomy tubes and indwelling catheters.[3,4] When ongoing infection based on the clinical signs, examination findings, and initial workup is suspected by the clinician, obtaining appropriate samples to submit for culture and susceptibility is imperative. For example, urine samples via cystocentesis or sterile catheterization for suspected UTI, endotracheal or transtracheal wash or bronchoalveolar lavage samples for suspected aspiration pneumonia, liver aspirates and bile samples via cholecystocentesis for cholangiohepatitis, blood cultures for sepsis, and purulent exudate or tissue samples from infected sites.

In many of these cases, it may be clinically indicated to start empirical antimicrobial therapy while awaiting culture and susceptibility results. The clinician will need to consider the site of infection and tissue penetration of the antimicrobial, such as when the infection is within the lower urinary tract versus systemic, as well as the mode of administration and whether oral or parenteral formulations are more appropriate based on the patient's clinical status and other ongoing comorbidities. Based on available antimicrobial prescribing guidelines, empirical treatment of sporadic bacterial cystitis could be implemented with amoxicillin, amoxicillin-clavulanic acid, or a trimethoprim-sulfonamide.[5] For patients with suspected pyelonephritis or a systemic infection outside of the urinary tract, antimicrobials with efficacy against Enterobacterales such as fluoroquinolones or cefpodoxime could be initiated empirically.[5] Once culture and susceptibility results are available, antimicrobial therapy should be reevaluated to confirm an appropriate antimicrobial was selected and to adjust or deescalate as indicated, particularly if an ESBL-producing, AmpC-hyperproducing Enterobacterales, or CRE is ultimately identified.

Prevention of MDR Enterobacterales infections involves a complete systemic evaluation of the patient to assess for morbidities that could compromise systemic immunocompetence or impair local defense mechanisms. Management of underlying diseases such as lower urinary tract disease, endocrine disease, aerodigestive disorders, or gastrointestinal disease that could predispose to MDR Enterobacterales infections is an important component of prevention strategies along with proper care and handling of indwelling devices. Mitigation of risk factors that have been identified in companion animal acquisition of MDR Enterobacterales should also be considered such as antimicrobial administration and raw food diets.[6,7] Infection prevention strategies are valuable to consider as well and collaborative interventions may be

necessary in response to outbreaks to prevent further transmission within veterinary hospital settings such as environmental management, microbiologic sampling for active surveillance, hospital operations adjustments, workflow alterations, client and veterinary staff education, as well as expert consultation.[4,8]

The microbiologist's perspective

The Enterobacterales are readily cultured and isolated on nonselective (eg, blood agar and Luria-Bertani agar) and selective media (eg, MacConkey agar and Eosin Methylene Blue agar) in the microbiology laboratory. Their isolation from normally sterile sites (eg, blood, cerebrospinal fluid, deep tissues, or body cavities) or as a pure organism from a nonsterile infection site (eg, wounds and urine) often suggests a role in suspected infection. It is important to note that the Enterobacterales (as normal fecal and environmental flora) can represent both normal flora at some sites and contaminants. Isolation is not always clinically significant. These organisms amplify in enrichment culture easily and isolates recovered only from enrichment broth are clinically circumspect. Correlation with cytology findings is often important in interpreting cultures correctly. With the widespread adoption of matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) analysis for organism identification, less common Enterobacterales are increasingly reported, including genera such as *Pantoea*, *Kluyvera*, and *Raoultella*, whose clinical relevance in companion animal infections may be uncertain.

A relatively wide array of antimicrobials are effective against wildtype (bacteria without acquired resistance mechanisms) Enterobacterales. This means that a relatively large number of clinical breakpoints have been established for interpretation of antimicrobial susceptibility testing (AST) results for Enterobacterales infections in dogs (**Table 1**). Fewer interpretive criteria have been established for cats, but canine interpretive criteria are often extrapolated. AST is, therefore, an incredibly useful tool for refining antimicrobial therapy in companion animals. More recently, the establishment of susceptible-dose dependent (SDD) breakpoints for fluoroquinolones has further refined interpretation of AST results for Enterobacterales in dogs. SDD breakpoints have also been proposed for cats but are not yet published.[9] These breakpoints acknowledge that clinical efficacy may be achieved with higher dosing regimens, providing clinicians with additional guidance on dosing while emphasizing the importance of pharmacokinetic–pharmacodynamic (PK-PD) considerations in antimicrobial selection.

According to the Clinical & Laboratory Standards Institute (CLSI) guidelines, *E coli* and other Enterobacterales should be reported as resistant to ampicillin, amoxicillin, and amoxicillin-clavulanic acid because of inadequate drug concentrations achieved to reach the therapeutic target when following the dosage regimen used to establish veterinary breakpoints.[10] However, the European Committee on Antimicrobial Susceptibility Testing is now recommending optimal treatment of wild-type Enterobacterales using a high exposure intravenous (IV) dosing regimen of injectable amoxicillin-clavulanic acid with either extended infusions (20 mg/kg IV q8h given over 3 hours) or intermittent boluses (40 mg/kg IV q8h or 20 mg/kg IV q6h given over 30 minutes) based on PK-PD studies.[11] As injectable amoxicillin-clavulanic acid is not available in the United States, this dosing could potentially be extrapolated for use with injectable ampicillin or ampicillin-sulbactam but research is needed to confirm this. Cefovecin (except for lower UTI) and doxycycline also are ineffective against Enterobacterales in companion animals due to pharmacokinetic limitations.

A major driver of antimicrobial resistance in Enterobacterales is the production of β-lactamases, which are categorized into 4 main classes. Class A enzymes (eg,

Table 1
Clinical breakpoints established for Enterobacterales

	Dog	Cat	Associated Dosage	Other Notes
Amikacin	X		15 mg/kg SC, IM, or IV q24h	—
Amoxicillin-clavulanate	X	X	11 mg/kg PO q12h (amoxicillin)	Urinary breakpoint distinct from systemic. All wildtype isolates will test resistant using systemic breakpoints. For cats, 12.5 mg/kg PO q12h (amoxicillin) is used.
Ampicillin	X	X	11 mg/kg PO q12h (amoxicillin)	See amoxicillin-clavulanate. For cats, 10 mg/kg PO q12h (amoxicillin) is used.
Cefazolin	X		25 mg/kg IV q6h	Urinary breakpoint distinct from systemic.
Cefovecin	X	X	8 mg/kg SC once	Only urinary breakpoints set.
Cefpodoxime	X		5–10 mg/kg PO q24h	—
Ceftazidime	X		25 mg/kg SC, IM, or IV q8h	—
Cephalexin	X		25 mg/kg PO q12h	—
Chloramphenicol	X		50 mg/kg PO q8h	—
Difloxacin	X		5 mg/kg PO q24h	—
Doxycycline	X		5 mg/kg PO q12h	All wildtype isolates will test resistant using these breakpoints.
Enrofloxacin	X	X	5 mg/kg PO q24h	SDD breakpoints also set for 10 and 20 mg/kg dosages for dogs. Enrofloxacin should not be dosed above 5 mg/kg in cats.
Gentamicin	X		10 mg/kg IM q24h	—
Levofloxacin	X		25 mg/kg PO q24h	—
Marbofloxacin	X	X	2.75 mg/kg PO q24h	SDD breakpoints also set for 5.5 mg/kg dosage for dogs.
Orbifloxacin	X	X	2.5 mg/kg PO q24h	—
Piperacillin-tazobactam	X		350 mg/kg IV q6h or 3.2 mg/kg/h constant rate IV infusion	—
Pradofloxacin	X	X	3 mg/kg PO q24h	—

Abbreviations: h, hours; IM, intramuscular; IV, intravenous; PO, per os (oral administration); SC, subcutaneous; SDD, susceptible-dose dependent.

TEM, SHV, and CTX-M) are serine β-lactamases, class B enzymes are metallo-β--lactamases that require zinc (eg, NDM, VIM, and IMP), class C includes AmpC enzymes (eg, CMY, FOX, and DHA), and class D consists of OXA-type enzymes such as OXA-48.[12]

ESBLs, typically class A enzymes, are among the most clinically significant resistance mechanisms. They are inhibited by clavulanic acid and generally lack activity against cephamycins. CTX-M enzymes (particularly CTX-M-15 and CTX-M-27) are now the most prevalent ESBLs in both veterinary and human medicine.[13] Detection often relies on screening with cefpodoxime, with cefotaxime and ceftazidime helping differentiate enzyme types.[10] However, interpretation can be complicated because ESBLs frequently coexist with other β-lactamases, and isolates may appear resistant to amoxicillin-clavulanate despite the enzyme being clavulanate-inhibitable. AmpC β--lactamases (class C) differ from ESBLs in that they are not inhibited by clavulanic acid and confer resistance to penicillins, monobactams, and most cephalosporins, including cephamycins, while cefepime may retain activity.[12] A key clinical concern is derepression, where certain Enterobacterales (such as *Enterobacter*, *Citrobacter*, and *Serratia*) can upregulate AmpC expression during therapy.[10] This can result in isolates that initially test susceptible becoming resistant within a few days of treatment, emphasizing the importance of repeat susceptibility testing in some cases.

Carbapenemases represent a more advanced resistance mechanism and include enzymes such as KPC, OXA-48-like, and NDM. Enterobacterales producing carbapenemases are considered the most urgent antimicrobial resistance threats by the World Health Organization and the CDC. These enzymes can hydrolyze carbapenems and are divided into serine carbapenemases and metallo-β-lactamases.[12] Treatment options are limited but may (in humans) include newer β-lactam/β-lactamase inhibitor combinations (eg, ceftazidime-avibactam and meropenem-vaborbactam) or agents such as cefiderocol. Use of these novel agents in veterinary medicine has not been studied, and it presents an ethical (and potentially legal) dilemma given that these drugs should be reserved for use in high-risk human populations. Detection methods include phenotypic assays like the modified carbapenem inactivation method, CarbaNP testing, and lateral flow assays that are currently performed in very few veterinary diagnostic laboratories.[14]

Resistance to many other antimicrobial classes can also occur in Enterobacterales from dogs and cats. Resistance to fluoroquinolones, trimethoprim-sulfamethoxazole and chloramphenicol are relatively common in isolates demonstrating ESBL, AmpC, or carbapenemase activity. Rates of susceptibility to aminoglycosides (specifically amikacin) and nitrofurantoin (using human breakpoints) remain high in the authors' laboratory.

Pseudomonas aeruginosa

The clinician's perspective

P aeruginosa is an opportunistic pathogen that can be isolated in dogs and cats with acquired pneumonia, chronic rhinitis, otitis, postgrooming furunculosis, soft tissue wounds, bacterial keratitis, nosocomial infections, and less commonly UTIs.[15–19] As with suspected MDR Enterobacterales infections, when concern for ongoing infection is determined by the clinician through initial evaluation and workup, obtaining appropriate samples to submit for culture and susceptibility will provide additional guidance regarding organism identification and selecting antimicrobials. For instance, clinicians can consider submitting ear canal swabs for otitis, purulent exudate or tissue samples from skin, wounds, and infected sites, and corneal or conjunctival swabs for suspected bacterial keratitis.

P aeruginosa isolates can have both intrinsic and acquired antimicrobial resistance and may develop resistance rapidly within 3 to 4 days after initiation of therapy with all antimicrobial agents.[10] Because of the degree of intrinsic antimicrobial resistance to many classes of antimicrobials including penicillins, first-generation and second-

generation cephalosporins, chloramphenicol, tetracyclines, and sulfonamides, clinicians should consider selection of antimicrobials with antipseudomonal β-lactams such as piperacillin-tazobactam, ceftazidime, or carbapanems alone or in combination with an aminoglycoside or fluoroquinolone. Fluoroquinolones are frequently used empirically or as a first-choice drug to treat infections with *P aeruginosa* and many other gram-negative organisms; however, this has resulted in progressively increasing fluoroquinolone-resistant strains.[20] Clinicians can consider discussing susceptibility testing for levofloxacin with their microbiology laboratory, as *P aeruginosa* isolates may not have developed resistance and PK-PD studies have demonstrated adequate absorption following oral administration in dogs.[21] Due to the nature of *P aeruginosa*, higher and more aggressive dosing regimens are generally recommended for many antimicrobials in concordance with established CLSI veterinary-specific breakpoints (**Table 2**). When possible and clinically indicated, topical therapy should be considered over systemic antimicrobial administration such as in cases of otitis externa, soft tissue wounds, or bacterial keratitis.

Similar to prevention of MDR Enterobacterales infections, reducing risk of infection with *P aeruginosa* involves a complete systemic evaluation of the patient as well as management of underlying diseases and predisposing factors. For example, successful treatment and prevention of recurrent canine otitis involves managing any underlying cause such as atopy, proper and routine ear cleaning, and reducing inflammation in the ear canal along with selecting appropriate antimicrobial therapy.[15] Dogs and cats with wounds infected with *P aeruginosa* benefit greatly from surgical debridement

Table 2
Current clinical breakpoints established for *Pseudomonas aeruginosa*

	Dog	Cat	Associated Dosage	Other Notes
Amikacin	X		15 mg/kg SC, IM, or IV q24h	—
Ceftazidime	X		25 mg/kg SC, IM, or IV q6h	—
Enrofloxacin	X	X	5 mg/kg PO q24h	SDD breakpoints also set for 10 and 20 mg/kg dosages for dogs. Enrofloxacin should not be dosed above 5 mg/kg in cats and a revision to this breakpoint has been proposed.
Gentamicin	X		10 mg/kg IM q24h	—
Levofloxacin	X		25 mg/kg PO q24h	—
Marbofloxacin	X		2.75 mg/kg PO q24h	SDD breakpoints also set for 5.5 mg/kg dosage for dogs. An SDD breakpoint for only a 5.5 mg/kg dose in cats has been proposed.
Piperacillin-tazobactam	X		350 mg/kg IV q6h or 3.2 mg/kg/h constant rate IV infusion	—

Abbreviations: h, hours; IM, intramuscular; IV, intravenous; PO, per os (oral administration); SC, subcutaneous; SDD, susceptible-dose dependent.

and removal of any necrotic tissue or foreign material. Gaps in infection prevention control (eg, hand hygiene, personal protective equipment use, equipment and environmental cleaning and disinfection) should also be identified and addressed to prevent companion animals from becoming reservoirs for further potential animal-to-human or animal-to-animal transmission.[22]

The microbiologist's perspective

P aeruginosa is readily cultured on routine media (eg, blood agar and MacConkey agar), often producing a characteristic blue-green pigment and a distinctive, sweet odor that can aid presumptive identification in the microbiology laboratory. Its isolation from normally sterile sites or as a predominant organism from infected tissues (eg, wounds, otitis, and urinary tract) is typically clinically significant, although it may also be recovered as an environmental contaminant or colonizer, particularly in chronic or previously treated sites. As with other organisms, correlation with cytology and clinical findings is essential for appropriate interpretation of culture results.

Compared to Enterobacterales, *P aeruginosa* has a more limited range of effective antimicrobials due to intrinsic resistance mechanisms, and AST is therefore critical to guide therapy. Fewer veterinary-specific breakpoints (see **Table 2**) are available, particularly for cats, and interpretation often relies on extrapolation from canine or human data. SDD breakpoints have also been introduced for fluoroquinolones against *P aeruginosa*, emphasizing the importance of achieving adequate drug exposure for clinical efficacy.[9,10,23]

Intrinsic resistance in *P aeruginosa* is driven by multiple mechanisms, including low outer membrane permeability, efflux pumps, and production of chromosomal AmpC β-lactamase. Acquired resistance may further arise through mutations affecting porins (eg, OprD), mutation to DNA synthesis genes and acquisition of genes encoding carbapenemases such as VIM, IMP, or NDM. These mechanisms often coexist, leading to MDR phenotypes and limiting therapeutic options. Consequently, treatment commonly relies on agents such as antipseudomonal β-lactams, fluoroquinolones, or aminoglycosides, guided by AST and informed by PK-PD considerations.

Acinetobacter, Burkholderia, and Stenotrophomonas

The clinician's perspective

Acinetobacter, *Burkholderia*, and *Stenotrophomonas* are ubiquitous organisms in the environment that can cause opportunistic infections, particularly nosocomial ones. *Acinetobacter baumanii* has been isolated from the urogenital tract, respiratory tract, wounds, blood cultures, and central venous catheters in hospitalized companion animals as well as from healthy canine skin.[24–26] *Burkholderia gladioli* and *Burkholderia cepacia* complex have been described to cause deep pyoderma in dogs receiving immunomodulatory medications such as cyclosporine and oclacitinib as well as dogs not receiving immunomodulatory medications.[27,28] *Stenotrophomonas maltophilia* has been isolated from airway samples of animals with chronic respiratory disease and bronchiectasis, although the significance of this isolation and distinguishing between infection versus colonization has not been clearly delineated.[29,30]

Guidelines in terms of empirical antimicrobial therapy for *Acinetobacter* and *Burkholderia* have not been published for veterinary medicine, and clinicians may need to extrapolate recommendations from human medicine and available literature when encountering these specific opportunistic infections. As mentioned earlier, isolation of *S maltophilia* from normally sterile sites should be considered significant; however, in other samples such as from the lower airways, clinicians should consider

whether the bacteria is contributing to infection or acting as a colonizer. If considered representative of ongoing infection, a first-line antimicrobial for *S maltophilia* is trimethoprim-sulfamethoxazole. Clinicians should be aware that concerns regarding dosing adequacy and resistance development have been raised for using trimethoprim-sulfamethoxazole as a single agent, and fluoroquinolones (eg, levofloxacin) or minocycline may be appropriate alternatives in cases of trimethoprim-sulfamethoxazole intolerance or elevated minimum inhibitory concentrations (MICs), although no monotherapy regimen has been shown to be superior in people.[31]

Prevention of infections with *Acinetobacter*, *Burkholderia*, and *Stenotrophomonas* includes the management of underlying conditions such as bronchiectasis and chronic respiratory disease that may predispose to secondary infections, as well as appropriate care and handling of indwelling devices that may increase the risk for nosocomial infections. Infection prevention strategies addressing patient handling, proper use of personal protective equipment, and environmental management are also instrumental in preventing nosocomial infections in hospitalized patients.

The microbiologist's perspective

Isolation of *Acinetobacter*, *Burkholderia*, and *Stenotrophomonas* is rare in the clinical veterinary microbiology laboratory. These organisms can be difficult to identify biochemically but are more reliably identified using MALDI-TOF MS in many laboratories. As environmental organisms they can theoretically contaminate cultures and isolation in mixed cultures should be interpreted with caution. No clinical breakpoints have been established for these organisms in veterinary medicine; however, they are all known to have extensive antimicrobial resistance. Breakpoints (human only) have been established for a limited number of drugs for *Acinetobacter* and *Stenotrophomonas.* Recent CLSI updates have removed clinical breakpoints for *B cepacia* complex due to poor reliability of AST methods and a lack of correlation between MIC results and clinical outcomes in people.[31] Given these complexities, treatment (especially of severe or chronic infections) should be done in consultation with a clinical microbiologist, pharmacologist, or infectious disease clinician.

SUMMARY

Gram-negative infections in dogs and cats are common but often complicated by antimicrobial resistance and the diversity of organisms involved. Both Enterobacterales and nonfermenters such as *P aeruginosa*, *Acinetobacter*, *Burkholderia*, and *Stenotrophomonas* require careful interpretation of culture and susceptibility results, particularly given their ability to act as pathogens, colonizers, or contaminants depending on the clinical context. While antimicrobial susceptibility testing is a critical tool, it is not a perfect tool and recent changes in breakpoints and reporting further highlight the need for thoughtful interpretation.

Successful management depends on integrating laboratory data with clinical findings, selecting antimicrobials based on site of infection and expected drug exposure, and reassessing therapy as new information becomes available. Attention to underlying disease, appropriate sample collection, and infection prevention practices are equally important in reducing recurrence and limiting the spread of resistant organisms. Ultimately, a practical, case-by-case approach, often involving collaboration with microbiology or infectious disease experts, remains essential for optimizing outcomes in these challenging infections.

CLINICS CARE POINTS

- Always obtain appropriate samples for culture and susceptibility testing as this is critical for guiding targeted therapy and antimicrobial stewardship.
- Interpret culture results in clinical context, recognizing that gram-negative organisms may represent contamination or colonization rather than true infection, especially in nonsterile sites or mixed cultures.
- Reassess antimicrobial therapy once susceptibility results are available and de-escalate when appropriate, particularly in cases involving suspected or confirmed MDR organisms.
- Select empiric antimicrobials based on site of infection and expected drug exposure, ensuring adequate tissue penetration.
- Address underlying diseases and implement infection prevention practices to reduce recurrence and limit spread of resistant organisms.

DISCLOSURE

The authors have nothing to disclose.

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