M031-5 Cerebrospinal Fluid: *Citrobacter koseri*—Antimicrobial Profile Reporting

KEY: COMPANION CULTURE TO GRAM SMEAR G-031 WAS SENT TO CATEGORY A LABORATORIES TO ISOLATE, IDENTIFY, AND PERFORM ANTIMICROBIALS SUSCEPTIBILITY TESTING FROM A CSF COLLECTED FROM A NEONATE. THE SAMPLE CONTAINTAINED *CITROBACTER KOSERI.* AN APPROPRIATE ANTIMICROBIAL REPORT FOR THIS ISOLATE AND SITE MUST BE REPORTED AND MUST INCLUDE A 3RD-GENERATION CEPHALOSPORIN RESULT.

HISTORY This sample was sent to category A laboratories as a simulated cerebrospinal fluid (CSF) from a neonate with a shunt who is febrile, vomiting, and lethargic. A Gram smear (G-031) was provided as a companion sample. The simulated sample contained a pure culture of *Citrobacter koseri*. Laboratories were requested to identify and perform antimicrobial susceptibility testing according to their laboratory protocol.

CMPT QA The sample contained a heavy growth of *C. koseri* that was viable for up to 19 days. As all 13 of the reference laboratories correctly identified *C. koseri*, the sample was considered acceptable for grading.

GRADING IDENTIFICATION All 74 category A laboratories correctly identified the isolate as *C. koseri* and received a grade of 4. Five laboratories parenthetically added *C. koseri (diversus)*, and one laboratory called the isolate *C. koseri (amalonaticus)*. There are three major human pathogens now identified in the genus *Citrobacte*r. These are *C. freundii* (biotypes a and b), *C. koseri* (formerly *diversus*) and *C. amalonaticus*[1]. This latter species as the name implies is malonate negative; it is also adonitol negative. The laboratory that identified the isolate as *C. koseri (amalonaticus)* should check their database to be sure that it is up to date. Shown in Table 1 are the methods used to identify the isolate. Most laboratories used a commercial system to correctly identify the organism

GRADING ANTIMICROBIAL SUSCEPTIBILITY PROFILE REPORTING As identified in a previous send-out from CSF (M022-2, August, 2002)[2] the grading of this type of sample will be based on Antimicrobial Profile Reporting only; individual antimicrobial susceptibility results will not be graded except as an incorrect result affects the overall report. Table 2 (on page 2) shows the antimicrobial profile results that were graded. The isolate was resistant to ampicillin and amoxicillin, and was susceptible to cefotaxime and ceftriaxone, gentamicin and meropenem. All 13 of the reference laboratories reported a result of susceptible ("S") for a 3rd-generation cephalosporin and none reported a 1st-generation cephalosporin result.

Various interpretive comments were included by a number of laboratories. Nineteen laboratories reported that this species may produce an inducible beta-lactamase. The comment noted "Aminoglycosides should not be used alone, and that 3rd-generation cephalosporins have been associated with treatment failure due to an inducible beta-lactamase. A microbiologist should be consulted for antibiotic treatment." One laboratory noted, "*C. koseri* strains that test susceptible to 1st-generation cephalosporins tend not to be cephalosporinase producers, but the possibility exists."

In past CMPT challenges of *Enterobacteriaceae* from CSF [3,4], participants were advised that the antimicrobial agents reported must be capable of adequately crossing the blood-brain barrier. First- and 2nd-generation cephalosporins do not cross this barrier in adequate concentration and must not be reported. In this challenge two laboratories did report a 1st-generation cephalosporin as resistant (one of these also reported the 3rd-generation cephalosporin resistant). The CMPT committee suspects that the 1st-generation report was a conscious effort to indicate to the physician that the result would be resistant despite the in vitro susceptibility result. However, despite the potential of an inducible beta-lactamase, the 3rd-generation cephalosporin should be reported as susceptible in this sample since there are so few options for therapy with agents that adequately cross the blood-brain barrier.

Third-generation cephalosporins (cefotaxime or ceftriaxone) are the treatments of choice for *Enterobacteriaceae* infections of the central nervous system and must be re-

(continued on page 2)

GRADING – Maximum grade = 8

Identification: 100% (74/74) of category A laboratories received a grade of 4/4.

Antimicrobial Profile Reporting:
80% (59/73) of category A laboratories received a grade of 4/4 or 3/4.

NOTES

- Third-generation cephalosporins (cefotaxime or ceftriaxone) are the treatments of choice for *Enterobacteriaceae* infections of the central nervous system and must be reported.

Table 1. M031-5. Methods used by category A laboratories to identify *C. koseri.*

Method	Number (%) of Laboratories
Vitek	38 (51%)
MicroScan	28 (38%)
API 20E	4 (5%)
BBL Crystal	1 (1%)
Replicator	1 (1%)
BD Phoenix	1 (1%)
Classical	1 (1%)
TOTAL	74

ported[5]. Laboratories that reported a 3rd-generation cephalosporin as susceptible and ampicillin as resistant with or without reporting gentamicin as susceptible were given a grade of 4. Laboratories that substituted meropenem for the 3rd-generation cephalosporin were given a grade of 3 because, as of the writing of this critique, the U.S. FDA does not consider there to be sufficient information to fully approve the use of meropenem in infants under 3-months of age. Laboratories that reported co-trimoxazole (SXT) in place of the 3rd-generation cephalosporin were given a grade of 0 (one laboratory reported imipenem as well as SXT). SXT is not indicated for the treatment of meningitis and *Citrobacter* species are not included in the product monograph[6]. Laboratories that reported SXT should consult with their pharmacists to ensure that appropriate antimicrobial agents are reported for the infections indicated. Laboratories that reported the 1st-generation cephalosporins were graded as 0.

CLINICAL SIGNIFICANCE Meningitis is an important cause of illness and death in the neonatal period. The most frequently isolated organisms are *Escherichia coli* and *Streptococcus agalactiae* (group B streptococcus). The choice of antimicrobial therapy for neonates who are considered septic is slowly changing. In the past most neonates received ampicillin and gentamicin as standard antimicrobial treatment. While these agents will also achieve reasonable concentrations in the inflamed meninges of the newborn, observations of other pathogens, such as *C. koseri* in this case, with altered antimicrobial susceptibilities or inducible enzymes, may affect treatment practices[7]. Clearly 3rd-generation cephalosporins are the agents of choice for susceptible isolates[5]. Occasionally, infections with strains of *C. koseri* having inducible beta-lactamases may not respond adequately. Meropenem, a newer carbapenem, has activity in the CSF[8]. Imipenem has also been reported to have efficacy in the treatment of *C. koseri* meningitis. It is critical that laboratories keep their antibiotic susceptibility profiling up to date to support appropriate treatment practices in these types of infectious processes.

REFERENCES

1. Farmer JJ III. 2003. p. 636-652. *In* PR Murray et al. (eds.) *Manual of Clinical Microbiology*, 8th ed. ASM Press Washington, DC.
2. CMPT critique M022-2 CSF: *Escherichia coli*. August 2002.
3. CMPT critique M21-3 CSF: *Proteus mirabilis*. May 2000.
4. CMPT Critique M011-2 CSF: *Klebsiella pneumoniae*. May 2001.
5. NCCLS 2003. Performance standards for antimicrobial susceptibility testing; Thirteenth Informational Supplement. M100 – S13. NCCLS, Wayne, PA.
6. CPS. 2003 Compendium of Pharmaceuticals and Specialties. Canadian Pharmacists Association.
7. Doran TI. 1999. The role of *Citrobacter* in clinical disease of children: review. Clin Infect Dis. 28:384-394.
8. Straussberg R, Harel L, Amir J. 2001. Long term outcome of neonatal *Citrobacter koseri (diversus)* meningitis treated with imipenem/meropenem and surgical drainage. Infection. 29:280-282.

Table 2. Antimicrobial profile results received from category A laboratories for M031-5 and grades assigned.

Antimicrobial Profile Results	No. (%) of Labs	Grade
Reported ampicillin (or amoxicillin) resistant, 3rd -generation cephalosporin (cefotaxime or ceftriaxone) susceptible, +/- gentamicin-susceptible. No result for 1st -generation cephalosporin or reported as resistant.	55 (75%)	4
Reported ampicillin (or amoxicillin) resistant, no report for 3rd -generation cephalosporin, +/- gentamicin susceptible, no report for 1st generation cephalosporin, but reported meropenem or imipenem susceptible, no report for co-trimoxazole (SXT).	3 (4%)	3
Reported 3rd -generation cephalosporin susceptible, gentamicin susceptible, No report for ampicillin or 1st -generation cephalosporin.	1 (1%)	3
Reported ampicillin (or amoxicillin) resistant, no report for 3rd -generation cephalosporin, +/- gentamicin susceptible, no report for 1st -generation cephalosporin.	6 (8%)	0
Reported ampicillin (or amoxicillin) resistant, no report for 3rd -generation cephalosporin, +/- gentamicin susceptible, no report for 1st -generation cephalosporin, but reported co-trimoxazole (SXT) susceptible.	2 (3%)	0
Reported 1st-generation cephalosporin susceptible with any other combination of results.	5 (7%)	0
Reported 3rd-generation cephalosporin as resistant, ampicillin resistant, and 1st-generation cephalosporin resistant with no other choices.	1 (1%)	0
Referred for susceptibility testing.	1 (1%)	Ungraded