Methodist Health Services Corporation
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Department of Pathology
Peoria, IL 61636

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NEW

CRE Confirmation
(Carbapenem Resistant Enterobacteriaceae)

I. PRINCIPLE

Carbapenemases, or carbapenem-hydrolyzing enzymes, are produced by a variety of organisms, including *Enterobacteriaceae, Pseudomonas aeruginosa,* and *Acinetobacter* spp. They are classified into three molecular groups (Ambler Classes A, B, and D) and vary in prevalence by geographic location. The *Klebseilla pneumoniae* carbapenemase (KPC) enzymes encoded by the bla_{KPC} genes belong to Ambler Class A and are produced by *K. pneumoniae, Enterobacter Cloacae,* and *Escherichia coli,* among others. Other carbapenemases include metallo-beta-lactamases (MBLs) of Ambler Class B. *Serratia marcescens* enzymes (SMEs), imipenem-hydrolyzing beta-lactamases (IMIs), and "non metalloenzyme carbapenemases" (NMCs). These carbapenemases result in varying degrees of resistance to carbapenems as well as varying resistance to extended-spectrum cephalosporins and aztreonam.

II. CLINICAL SIGNIFICANCE

Carbapenems (Imipenem, Meropenem and Ertapenem) have the broadest antibacterial spectra of all b-lactams and are prescribed often to treat a variety of Enterobacteriaceae infections. CRE are usually resistant to all b-lactam agents as well as most other classes of antimicrobial agents. Patients colonized with CRE are thought to be the source of transmission in the health care setting. Carbapenem resistance in Enterobacteriaceae occurs when an isolate acquires a carbapenemase or when an isolate produces an extended-spectrum cephalosporinase in combination with porin loss. The most common mechanism of carbapenem resistance in the United States is the *Klebsiella pneumoniae* carbapenemase (KPC). CLSI has published guidelines for detection of isolates producing carbapenemases (CLSI document M100-S23 pages 53-59). The Modified Hodge Test is recommended when an Enterobacteriaceae demonstrates reduced susceptibility to carbapenems. Carbapenem resistance and carbapenemase-production in all species of Enterobacteriaeae is of critical concern for infection control. However, the vast majority of CRE encountered in the United States are represented by *E coli* and especially *Klebsiella* spp.

III. SPECIMEN

Isolated colonies of lactose-fermenting Enterobacteriaeae spp. (including non-lactose fermenting *E. coli)* with elevated resistance to the carbapenems as indicated by the Microscan Alert system or manually observed.

IV. PROCEDURE

Suspected CRE isolates will be flagged through the Microscan Alert system. Isolates will be repeated. If isolate still shows a non-susceptible result, it will be sent to OSF for Modified Hodge testing.

V. REPORTING RESULTS

E coli or *Klebsiella spp.* isolates testing positive with the Modified Hodge test and are intermediate or resistant to meropenem and/or doripenem **AND** are resistant to all tested 3rd generation cephalosporins (ceftriaxone, cefotaxime, ceftazidime) will be reported as CRE. The CRE will be reported with 7 days to the IDPH XDRO registry if the isolate is the first CRE-positive culture per patient stay. If the isolate is from Rock Island, Moline, Bettendorf, or Muscatine, their Infection Control Manager will report results to the IDPH XDRO registry. Results should also be phoned to the appropriate location.

While waiting for the Modified Hodge testing, the meropenem and doripenem results for the isolate should not be reported in LIS. If the Modified Hodge test is positive, the meropenem should then be reported as resistant. The actual doripenem MIC shoud also be reported. If the Modified Hodge test is negative, the meropenem and doripenem results should be resulted as reported by Microscan.

VI. PROCEDURAL NOTES/PROBLEM-SOLVING TIPS

A. The Modified Hodge focuses on the detection of carbapenemase-producing *Klebsiella spp* and *E coli.*
B. MHT provides for a high level of sensitivity and specificity (both >90%) in detecting KPC-type carbapenemases. The sensitivity and specificity of the test for detecting other carbapenemase production can vary.
C. The sensitivity of MHT for detecting New Dehli metallo-beta-lactamase (NDM-type) is low.
D. No data exist on the usefulness of these tests for detection of carbapenemase production in non-fermenting gram-negative bacilli such as *Proteus, Pseudomonas*, and *Acinetobacter spp*
E. If only the ertapenem result is non-susceptible, please report result from Microscan with no mention or testing for CRE.

VII. REFERENCES

A. CLSI document M100-S23 pages 53-59.
B. CDC 2012 CRE Toolkit documents
C. CDC protocol for detection of CRE from rectal swabs
D. Iranian Journal of Microbiology

MMCI Laboratory is a CAP accredited facility, as of 7/1/11 the responsibility of new and/or substantially revised policies and procedures will be restricted the Laboratory Director whose name appears on the CLIA certificate, whose signature appears below. The biennial review will be completed by the Administrative Director.

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Medical Director:

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DATE	NAME	SIGNATURE
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Lead	Date	Coordinator	Date	Manager	Date	Medical Director	Date
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