



Clinical Laboratory Guidance for the Detection of KPC-producing Organisms

9/27/07

Currently hospitals in New Jersey are combating the problem of carbapenem resistance in species of *Enterobacteriaceae*, most commonly in *Klebsiella pneumoniae*. Clinical microbiologists are finding Gram-negatives with this newly identified mechanism of resistance throughout the state and across the country (data from the Centers for Disease Control and Prevention).

This new mechanism of resistance is a plasmid-mediated carbapenemase called the *Klebsiella pneumoniae* carbapenemase or KPC. KPC is a β -lactamase enzyme that hydrolyzes all β -lactam agents including extended spectrum cephalosporins and the carbapenems: imipenem, meropenem, and ertapenem,

KPC is not equally active against all carbapenems. In general, ertapenem susceptibility is a more sensitive indicator of KPC-mediated resistance than either meropenem or imipenem.

It is important to note that nonsusceptibility* to carbapenems, can be mediated by mechanisms other than KPC, e.g., the combination of an AmpC-type β -lactamase and porin loss. These other mechanisms are clinically important, but as of today, no documented outbreaks have been attributed to them.

As of September 27, 2007, KPC-producing *Klebsiella pneumoniae* isolates have been confirmed by molecular testing in 22 healthcare institutions in New Jersey and it is likely that many more laboratories will encounter these organisms in the near future. Below are recommendations to help clinical microbiologists recognize the KPC mechanism of resistance in their laboratories.

Microbiologists should look for evidence of carbapenemase-mediated resistance in *Enterobacteriaceae* using the following criteria, paying particular attention to isolates of *Klebsiella* spp. and *E. coli* that.

- **Are resistant to carbapenems by any standardized testing method. These are very likely KPC-producers.** Confirmation of the resistance mechanism in these organisms is not currently a clinical or public health necessity, since KPC-producers are already known to exist widely throughout the state..
- **Test susceptible to carbapenems, but with elevated MICs. These isolates may also possess the enzyme..** A rule of thumb is to "flag" isolates with carbapenem MICs of 2 or 4 μ g/ml. Hospitals are evaluating their reporting protocols for these organisms.
- **Produce a nonsusceptible ertapenem disk diffusion result (I or R).** This is a sensitive indicator of KPC-production.

*nonsusceptibility in this instance refers to carbapenem disc diffusion results of Intermediate or Resistant or carbapenem MIC results of 2 μ g/ml or greater.

Clinical Laboratory Guidance for the Detection of KPC-producing Organisms

9/27/07

If you identify an isolate with these characteristics and KPC-producing bacteria have not previously been recognized at your institution, then confirmation of KPC-production may be appropriate.

Confirmatory Testing

A method for confirming the KPC-mechanism of resistance is PCR for the *bla_{KPC}* gene. This testing is available at CDC and can be coordinated through the New Jersey Public Health and Environmental Laboratories' Special Bacteriology Laboratory.

Clinical laboratories may alternatively consider implementing a phenotypic assay for carbapenemase detection, such as the Modified Hodge Test [Lee K, Chog Y, Shin HB, Kim YA, Yong D, Yum JH. 2001. *Clinical Microbiology and Infection* 7(2):88-91.]. This test is highly sensitive for detection of the enzyme.

Report to Physicians

When laboratories either suspect or confirm carbapenemase-mediated resistance in *Enterobacteriaceae*, it is recommended that the treating physician and the infection control practitioner be notified of the presence of this enzyme either through written or verbal communication with the laboratory. Currently, there are no CLSI guidelines requiring reporting of the presence of this enzyme, however, guidance should be available shortly.

Sample report:

“The carbapenemase enzyme (KPC), which confers Gram negative resistance against carbapenem antimicrobials, in addition to all beta-lactam drugs (including extended spectrum cephalosporins), has been determined by our laboratory to have occurred in at least one inpatient within our facility. Our laboratory will continue to screen for this enzyme using currently established methods.”

Clinical Laboratory Guidance for the Detection of KPC-producing Organisms
9/27/07

NJDHSS Criteria for Submission of Isolates for *bla*_{KPC} testing

- All laboratories that have not previously identified KPC-producing bacteria should *limit* molecular detection testing to
 - 1) isolates with carbapenem MICs of 2 or 4 µg/ml or
 - 2) isolates that test nonsusceptible to ertapenem by disk diffusion.
- If your isolate is determined to carry the carbapenemase gene, as indicated by a Positive *bla*PCR, you will be notified by NJDHSS, and no further testing will be currently necessary..

NJDHSS Submission Procedure for *bla*_{KPC} Testing.

- 1) Select the first *Klebsiella pneumoniae* inpatient isolate you obtain which meets the criteria for submission described in the previous paragraph.
- 2) Make sure you have a PURE culture
- 3) Prepare a slant of 24-hour growth of the isolate on TSA or other nutrient agar.
- 4) Enclose a copy of the identification profile and susceptibility results for the isolate in the package.
- 5) Package and ship the sample as an Infectious substance, affecting humans according to Hazardous Materials Transport regulations 49 CFR 171-178 or Dangerous Goods Regulations PI 602 (depending on the carrier utilized).
- 6) Send to:

New Jersey Public Health and Environmental Laboratories
Special Bacteriology Laboratory
John Fitch Plaza
Market and S. Warren Sts.
Trenton, NJ 08625
Attn: Maria Orsini (609) 984-2514

- 7) If your laboratory is applying the ertapenem screening procedure above for other Gram negative organisms and a pattern of nonsusceptibility is detected, contact Maria Orsini to discuss confirmatory testing options.

Note: Please send isolates for receipt during regular business hours. Do not ship anything on Friday, unless it is handcarried for receipt before 4 PM.