



There's a new kid on the block KPC



We have had β -lactamases, extended spectrum β -lactamases (ESBLs) and now there are *Klebsiella pneumoniae* carbapenamases (KPCs)



Have you noticed how bacteria are always able to stay or get one step ahead of us pretty quickly? This time it is inactivating the carbapenems. The carbapenems now available in the United States are imipenem/cilastatin (Primaxin[®]), ertapenem (Invanz[®]), meropenem (Merrem) and doripenem (Doribax[®]).

What makes this group of antibiotics different and what is the significance of KPC in this equation? Members of the carbapenem class of beta-lactam antibiotics are among the most broadly active antibiotics available for systemic use in humans. They are active against streptococci, methicillin-sensitive staphylococci, *Neisseria*, *Haemophilus*, anaerobes, and the common aerobic Gram-negative hospital-acquired pathogens. Resistance to imipenem and meropenem may emerge during treatment of *P. aeruginosa* infections, as has occurred with other beta-lactam agents; *Stenotrophomonas maltophilia* is typically resistant to both imipenem and meropenem. Like the penicillins, the carbapenems have inhibitory activity against enterococci. In general, the *in vitro* activity of imipenem against aerobic Gram-positive cocci is somewhat greater than that of meropenem, whereas the *in vitro* activity of meropenem against aerobic Gram-negative bacilli is somewhat greater than that of imipenem.

The carbapenems should be considered for treatment of mixed bacterial infections and aerobic Gram-negative bacteria that are not susceptible to other beta-lactam agents. Indiscriminate use of these drugs will promote resistance to them. The *Klebsiella pneumoniae* carbapenamases (KPC) occur in *Enterobacteriaceae* and can confer resistance to all β -lactam agents including carbapenems, as well as aztreonam. These enzymes may confer low-level carbapenem resistance, and the failure of susceptibility methods to identify this resistance has been reported (see below).

As of January 1, 2008 KPC-positive Gram-negative bacilli have been identified in the area in Pennsylvania, Maryland and Virginia. KPC-positive *K. pneumoniae* and *Salmonella enterica* were first reported in Maryland in 1998-1999. Isolates in our area *per se* are still very infrequent if they have, in fact, been seen here at all.

At the present time there is no straightforward, clear cut method available for detecting KPC-positive organisms in the clinical laboratory. A "marker" such as high MIC values, e.g., to ertapenem, may suggest the presence of such isolates but it is not definitive. Polymerase Chain Reaction is presently the gold standard for detecting the presence of KPC. The DNA coding for the specific protein mutation in the β -lactamase gene is used as the basis for this assay. However, the microbiology laboratory is investigating approaches that will aid in identifying KPC-positive isolates when present in patient specimens.

Of great concern is that KPC-resistance is carried on a bacterial plasmid, a small piece of DNA that is separate from the bacterial chromosome. Such plasmids are transmissible from one organism to another. It is recognized that *K. pneumoniae* is a species that can transfer such plasmids readily. Additionally, these pieces of DNA often contain resistance genes to other antimicrobial agents, including aminoglycosides, quinolones and trimethoprim/sulfamethoxazole (Bactrim[®]). Owing to this broad spectrum of resistance mortality in patients infected with organisms containing KPC plasmids is high.

The patients most vulnerable to KPC-positive infections and mortality include transplant recipients, neutropenic patients and those on ventilators. As with other infectious agents, ICU, nursing home and patients with long hospitalizations are most prone to such exposure and infection.

Tigecycline (Tygacil[®]), a glycylicycline derivative, is one of the few alternatives for the treatment of Gram negative bacilli harboring extended-spectrum β -lactamases and its role against carbapenemase-producing strains is advocated. In addition to its Gram negative coverage it is active against some anaerobes as well as enterococci including vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium*. Colistin comprises another option in these cases.

Addendum to [The Clinical Newsletter](#) of January 2008. According to a study in *Lancet* 371:621 (2008) using probiotic therapy to reduce infectious complications in severe pancreatitis increases mortality, Researchers randomized ~300 patients with first episodes of acute pancreatitis judged to be at risk for severe disease. In a double-blind study patients received a 28-day course of either placebo or a combination of *Lactobacillus*, *Lactococcus*, and *Bifidobacterium* species via feeding tube or ingested orally. By follow-up at 90 days, rates of infectious complications between the groups did not differ. However, those on probiotic therapy had mortality rates twice as high as those on placebo, and nine suffered bowel ischemia. It is speculated that increased oxygen demands of the infused bacteria may have led to the ischemia. The authors conclude that "probiotics can no longer be considered to be harmless adjuncts to enteral nutrition, especially in critically ill patients."

A second article [Brit J Sports Med, February 2008] referenced in an accompanying editorial states: "Prophylactic administration of PCC (*Lactobacillus fermentum* VRI 003) was associated with a substantial reduction in the number of days and severity of respiratory illness in a cohort of highly trained distance runners. Maintenance of IFN- γ levels may be one mechanism underpinning the positive clinical outcomes."