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NEWS

Resistance of enterobacteria to carbapenem antibiotics is a global crisis

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A large family of Gram negative bacteria, the enterobacteriaceae, are developing resistance to carbapenem antibiotics, a class of β lactam antibiotics that are often antibiotics of last resort, speakers at a New York Academy of Sciences symposium have said. They called it a global crisis.

The problem was greater than that posed by the New Delhi metallo-β-lactamase-1 plasmid (NDM-1), which confers resistance to nearly all the β lactam antibiotics (*BMJ* 2010;341:c5124, doi:10.1136/bmj.c5124), said the microbiologist Barry Kreiswirth of the Public Health Research Institute at the University of Medicine and Dentistry of New Jersey. "We just don't have many treatment options: colistin, polymyxin B, tigecycline, and rifampicin," he said.

David Perlin, executive director of the Public Health Research Institute, said that carbapenemase producing *Klebsiella pneumoniae* is the most common drug resistant pathogen in the mid-Atlantic region of the US east coast. It has spread elsewhere in North America and to Europe, South America, and Asia. Salmonella, *Escherichia coli*, enterobacter, *Yersinia pestis*, and the pseudomonas are among other bacteria that have also shown resistance to carbapenems.

Carbapenemase producing *Klebsiella* first appeared in the mid-Atlantic region and then spread to the New York city area, where it is now endemic in hospitals in New York and in the adjoining state of New Jersey. It is also widespread in the community. Dr Perlin called it "a major clinical challenge" because of its high transmissibility via plasmids.

Dr Kreiswirth explained that there were three classes of carbapenemases, all located on plasmids. Resistant infections are highly pathogenic and easy to transmit by hand and in contaminated food and water.

Death rates from *Klebsiella pneumoniae* pneumonia are higher than 50%, Dr Kreiswirth said.

Robert Bonomo of the Louis Stokes Cleveland Veterans Affairs Medical Center and Case Western Reserve University in Cleveland, Ohio, said, "The dependability of our last line antibiotics is shattered" and that resistance to colistin was rapidly appearing.

He said that 50% to 70% of clinical isolates of *Acinetobacter baumannii* are extensively drug resistant and that bloodstream infections with these highly drug resistant pathogens result in 50% to 60% mortality. He said he feared that resistant *A baumanni* "will be as big a threat worldwide as TB."

Dr Bonomo said that carbapenem resistant *Pseudomonas aeruginosa* was another problem, because half of hospitalised patients were colonised with *P aeruginosa*, especially immunocompromised and burn patients.

Thomas Walsh, director of the transplantation and oncology infectious diseases programme at New York Presbyterian Hospital/Weill-Cornell, called the situation "a global emergency," with a quarter of all healthcare infections with *K pneumoniae* and *E coli* showing antibiotic resistance and 21% showing complete carbapenem resistance. He said that they were caused "by profligate antibiotic use and poor infection control. A local problem can become a worldwide problem."

Patients typically affected were men aged about 60 with catheter associated bacteraemia. Other patients had intra-abdominal infections (especially in patients with cancer), urosepsis, ventriculitis, osteomyelitis, empyema, and deep sinusitis.

"In patients with renal impairment who are infected with carbapenem resistant enterobacteriaceae, what do you do when you can't give an aminoglycoside?" he asked. "The options are minimal."

He cited a study from the 1171 bed Mount Sinai Medical Center in New York of patients who had received organ or stem cell transplants, were on mechanical ventilation, had long stays because of infections, and had exposure to cephalosporins (*Infection Control and Hospital Epidemiology* 2008;29:1099-106, doi:10.1086/592412). The death rate during hospitalisation was 48% among those with carbapenem resistant infections, more than double the 20% rate among patients who did not have resistant infections. Surgical removal of the focus of infection improved survival.

Dr Walsh called for increased surveillance of high risk patients, more rapid culture and treatment with an active agent, augmentation of host response, use of corticosteroid sparing agents, and nutritional support—as well as considering drugs approved for other uses.

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