Clinical Impact and Current Epidemiology of Carbapenemase Producers

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Carbapenemase Producers: An Infection Control Failure

- Why?
- What are the consequences for
  - Individual patients?
  - Patient populations?
  - The Future?

Why Have Carbapenemase Producers Spread?

- Mostly ignored until recently
- Detection tests still evolving
- Lack of urgency is responsible for
  - Infection control failure
  - Gaps in understanding
  - Suboptimal detection tests
  - Imperfect understanding of epidemiology

Consequences: Individual Patients

- Incorrect therapy due to misleading lab reports
- Limited therapeutic options
- No therapeutic options

Consequences: Patient Populations

Uncontrolled spread and increasing resistance due to:

- Long-standing lack of testing recommendations or requirements
- Delayed infection control

Miami KPC Outbreak

- Admission file: XDR *K. pneumoniae*
- Pt isolated next day
- XDR *K. pneumoniae* transmitted to 10 more pts
- S to only colistin & gentamicin: PCR = KPC positive
- Clinical Impact:
  - 4/5 with bacteremia died
  - 1 other died
  - 2 had renal failure
  - Only 4/11 discharged no renal failure

Michelle Morris, Uni of Miami Hospital
ICAAC/IDSA 2008, K-902

KPC-positive *K. pneumoniae* Philadelphia Hospital

- > 30 cases before problem recognized
- Some reported as ESBL producers
- Ineffective Rx - carbapenems and cefepime
- Improved detection halted outbreak

Mishra et al. IDSA 2006, abstract 1010

Nursing Home Patient

Saint Vincent's Hospital, New York

- 2007, 70 yo woman NH pt – UTI, indwelling bladder catheter
- *K. pneumoniae* KPC-positive: tigecycline I, polymyxin B highly R
- Catheter removed, Rx tigecycline + rifampin
- Rash - rifampin discontinued
- Tigecycline R (> 8 µg/ml) – discontinued after 10 d
- Pt discharged, asymptomatic but panR *K. pneumoniae* >1 yr later

Elemam, A., J. Rahimian, and W. Mandell. 2009. Infection with panresistant *Klebsiella pneumoniae*: a report of 2 cases and a brief review of the literature. Clin Infect Dis 49:271-274.

Hepatic Abscess Patient

Saint Vincent's Hospital, New York

- 2008, 67 yo man – hepatic abscess
- *K. pneumoniae* & *E. cloacae* both KPC-positive:
  - carbapenem R, S to tigecycline & polymyxin B
- Rx initially tigecycline + daptomycin + caspofungin
- Changed to tigecycline + polymyxin B
- *E. cloacae* became intermediate to tigecycline and R to all other antibiotics
- Blood cultures positive - panR *K. pneumoniae*
- Patient died

Elemam, A., J. Rahimian, and W. Mandell. 2009. Infection with panresistant *Klebsiella pneumoniae*: a report of 2 cases and a brief review of the literature. Clin Infect Dis 49:271-274.

KPC-2 in *Enterobacteriaceae*: Is MIC Sufficiently Reliable?

Organism	Inoculum CFU/spot	Imipenem	Ertapenem
E. coli	10^4	8	4
	10^6	512	128
K. pneumoniae	10^4	8	4
	10^6	128	256
E. cloacae	10^4	2	2
	10^6	32	64

(A. Roth et al, ICAAC 2009)

5 Hodge +ve Kentucky Isolates

Organism	3GC* R	"Hodge"	Tris/EDTA	KPC PCR
K. pneumoniae	-	+	+	+
E. cloacae	+	+	+	+
E. cloacae	+	+	+	+
E. cloacae	+	+	-	-
P. vulgaris	+	+	-	-

* 3GC = 3rd generation cephalosporin

Surveillance Data

GOK!

17 Hospitals, Puerto Rico
Jan – June 2009

Organism	Isolates	"MDR"	KPC
E. coli	4,329	219	61/219 (28%)
K. pneumoniae	2,805	457	333/457 (73%)
P. aeruginosa	2,415	272	99/272 (36%)
Acinetobacter spp.	958	291	41/291 (14%)
TOTAL	10,507	1,239(12%)	534/1,239 (43%)

I.E. Robledo and G.J. Vázquez, Univ. Puerto Rico

More Epidemiology

- Class A (mainly *Enterobacteriaceae*)
  - KPCs – USA, Israel, some European and Asian countries
  - Others (SME, IMI, NMC-A, GES) infrequent
- MBLs – IMP and VIM – worldwide in many species
- OXAs – worldwide in *Acinetobacter*
- Recent discoveries
  - KPC-producing *P. aeruginosa* and *A. baumannii*
  - OXA-producing *Enterobacteriaceae*

Conclusion
Most Urgent Needs

- Improved detection
- Effective infection control
- Accurate guide to therapy
- Effective therapies