

Panresistant nonfermenters

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Disclosure

- JPQ has \$ for his lab from MSD, ABT, Astra Zeneca, PFE, Cubist
- If you have any to spare please see me afterwards

Case report

- 71 yr old homeless man found unconscious
- In ER : acute abdomen: to OR for perforated duodenal ulcer
- Train wreck post-op : abdominal abscess drained, polypharmacy including one week piperacillin-tazobactam and 2 weeks imipenem
- pneumonia and sepsis on day 15

Case continued

- Endotracheal aspirate and blood : *P. aeruginosa*, only S to aztreonam
- Imipenem MIC > 256
- Imipenem-EDTA E strip positive for metalloenzyme (β -lactamase which destroys carbapenems): VIM-2 on an integron
- Rx : polymyxin : cleared cultures but died of sepsis syndrome
- first clonal outbreak in USA

P.aeruginosa VIM-2 Integron

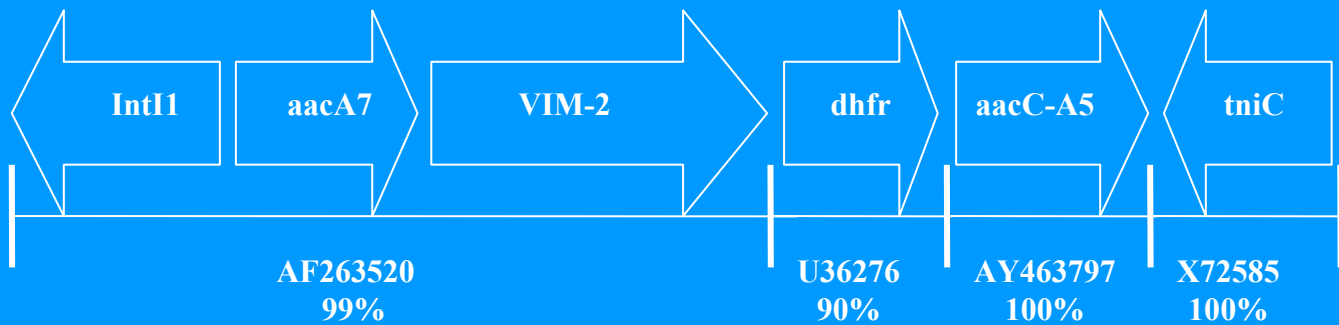


Fig 2. Genetic context of $\text{bla}_{\text{VIM-2}}$ containing integron fragment from *P.aeruginosa* 7052. Schematic structure (not to scale) of the 4.45 kB BamHI plasmid insert. Open reading frames of the various resistance genes and the transcriptional orientation are represented by arrows. Percent homologies are to the GenBank sequences listed.

VIM-2 outbreak in Chicago

- 2/3rds of cases in trauma unit
- 100 % exposed to beta-lactams
- 50 % exposed to carbapenems
- Environmental cultures negative
- Lolans AAC 2005; 49 : 3538-40

Key role of the micro lab

- First 8 cases missed
- Curious Infectious Disease fellow called JQ to bring this to light
- Now capturing bugs on the front end

A few kind words about Acinetobacter

- *P. aeruginosa*'s poor cousin
- Same type 1 beta-lactamase to nail extended-spectrum B-lactams
- Fewer virulence genes (see Stover, Nature 2000;46:959)
- Much less common
- About 7 % R to imi and rising slowly
- Often clonal see Landman, Arch Intern Med 2002;162:1515
- First carbapenemase in US ; Lolans et al in JQ lab AAC 2006;50:2941

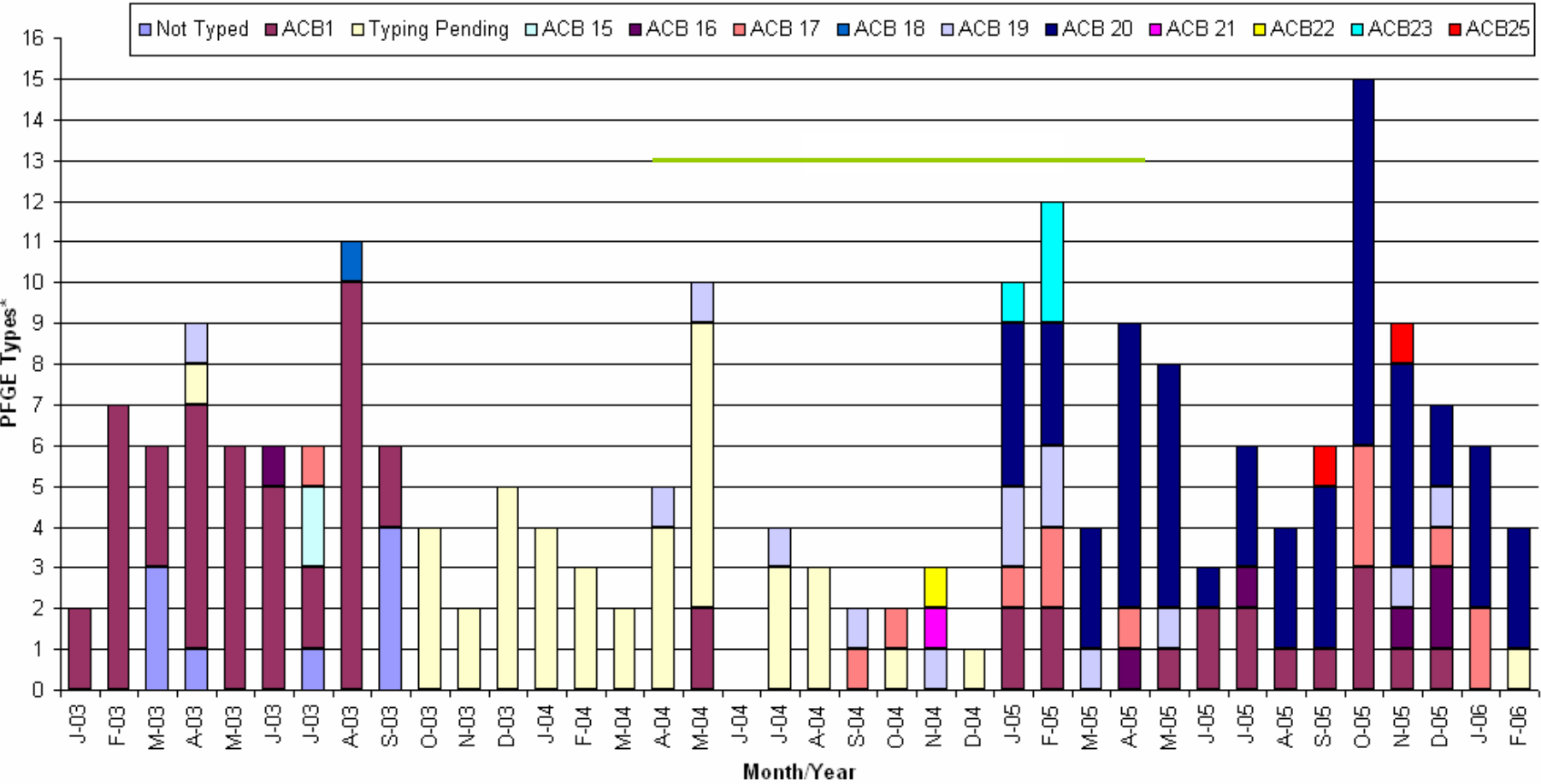
NNIS 2003

- **Gaynes CID 2005; 41:848**
- **Acinetobacter stands out**
- **Only bug to increase in prevalence (esp pneumonia)**
- **Carbapenem resistance creeping up to 10 %**

Genomics of MDR A b

- PLOS Genetics 2006;2:e7
- Forniere et al
- Compare endemic MDR strain from France w a saprophytic strain
- 45 R genes on a R “ island “
- Many borrowed from *P aeruginosa*

John H. Stroger Jr. Hospital of Cook County
Acinetobacter baumannii
Onset by PFGE Type January 2003 - February 2006*



City wide outbreak of MDR A b

- 100 isolates/6 centers over 30 miles
- Most only S to colistin
- Environmental contamination
- 2 clones
- Major clone tige R
- OXA 40 carbapenemase detected

Outbreak Background

- Began in January 2005
- Unusual high level imipenem resistance in *A.baumannii* (MIC 64-128 μ g/ml); ~50% of IMI-R isolates are ceftazidime susceptible/intermediate.
- Occurring in 3 cities (Chicago, IL; East Chicago, IN; Merrillville, IN)
- Spanning 7 acute care hospitals and 2 extended care facilities
- Analysis of first 40 isolates identified recovery from various sites: respiratory (10), wound (8), catheter tip (5), patient environment (6), blood (4), urine (3) and other (4).

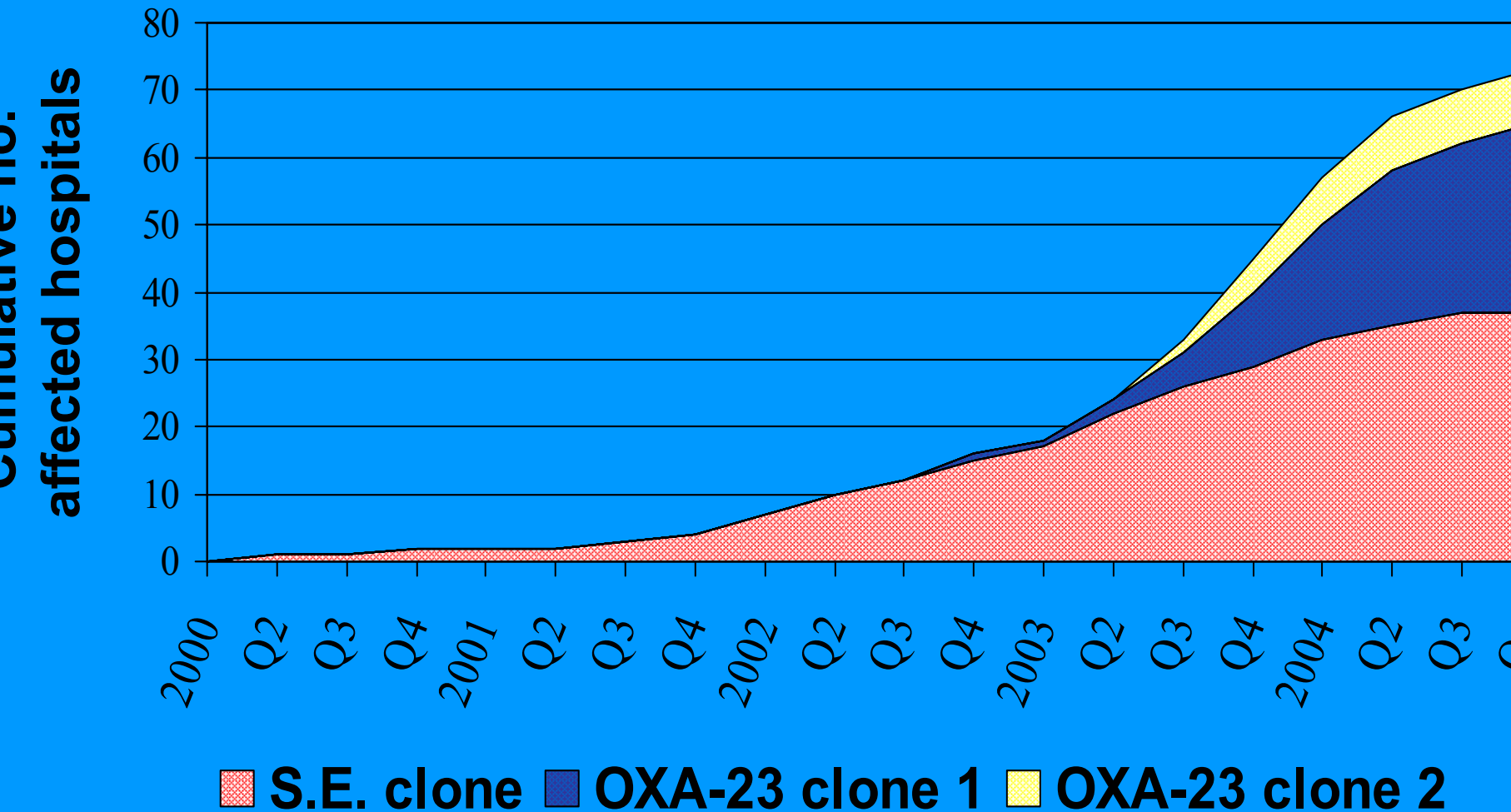
Center A: ACB Epidemiology

Admit date period	# patients	mean (range) hospital length of stay	All cultures			Bacteremias		
			Mean (range) days to 1st pos culture	# (%) single pos	>1pos: mean (range) days pos	# (%) total	# (%) single pos	>1 pos: mean (range) days pos
1/1/05 - 4/13/05	18	34.3 (6 - 118)	18.7 (1 - 55)	12 (66.6)	18.5 (6 - 62)	3 (15)	3 (100)	-
4/18/05 - 9/29/05	19	41.0 (17 - 98)	23.2 (1 - 65)	10 (52.6)	13.6 (2 - 34)	6 (31.5)	5 (83)	11 (11)
9/17/05 - 11/29/05	18	39.22 (1 - 133)	16 (0 - 44)	5 (27.8)	23 (3 - 107)	10 (55.6)	7 (70)	59 (37-85)
Total	55	38.3 (1 - 133)	19.4 (0 - 65)	27 (49)	19.7 (2 - 107)	19 (34.5)	15 (78)	47 (11-85)

Treatment of pan R

- Colistin is mainstay
- Success in bacteremia around 60 %, less in VAP
- Tigecycline effective vs some *A. baumannii* (not Chicago clone)
- In catheter sepsis, removal of device may suffice (Munoz-Price & JPQ mafia ICAAC 2006)

OXA Carbapenemases in *Acinetobacter* UK



OXAs in So America

- Villegas et al ICAAC 06
- 30 % prevalence of carb R in Acinetobacter in many Latin countries including Colombia
- OXA-23 detected in all 10 teaching hospitals tested in 6 cities

Conclusions

- Carbapenemases are here to stay
- E test is a reasonable screen for MBLs altho 50 % false positives
- OXAs are an emerging threat in Acinetobacter
- Detection is an issue with all of the above