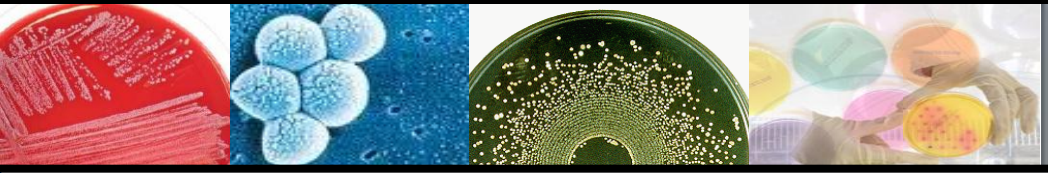

Global Antibiotic Resistance Partnership

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy

Private sector data and initiatives”

Adrian Brink

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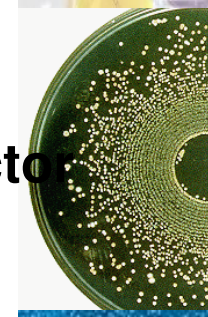
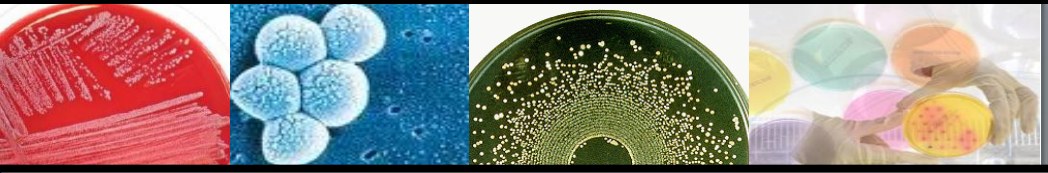
Scope

- Data presented of selected invasive pathogens only excluding fungi
- Published data for hospitals and not available for pvt primary care
- All private laboratories/hospitals in all major cities
- No data on economic impact of antibiotic-resistant infections in pvt sector
- CLSI breakpoints
- Shortcomings:
  - Repeat bloodculture specimens avoided
  - Laboratory surveillance without clinical info
  - Does not differentiate age
  - Neither whether community or hospital-acquired
  - Collated without defining type of service/hospital i.e level 1 trauma center vs oncology vs transplant units



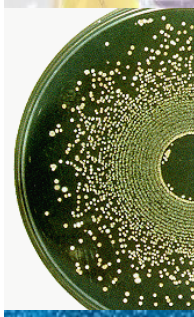
Gram-positive resistance patterns

% antibiotic resistance of bacteraemic strains of S. aureus private practice in South Africa: January - June 2006

Antibiotic	(n=629, all pvt hospitals in 5 major cities)		
	n	% Overall	Range
Cloxacillin	226	36	11-90
Trim/sulfa	182	29	21-70
Fusidic acid	19	3	21-61
Rifampicin	69	11	30-67
Gentamicin	75	12	21-67
Teicoplanin	0	0	11-67
Vancomycin	0	0	11-100
Linezolid	0	0	23-63

Brink et al. *South Afr Med J* 2007; **97:**630-636

Activities of vancomycin, teicoplanin and linezolid against bacteraemic MRSA strains in Gauteng, South Africa



- To determine
  ~ vancomycin "creep" of MRSA isolates from patients in the private sector in Gauteng, South Africa and to screen for
  ~ hetero-resistance to glycopeptides amongst these strains

- Fifty consecutive MRSA strains isolated from blood cultures in hospitalized patients were tested according to CLSI standards.

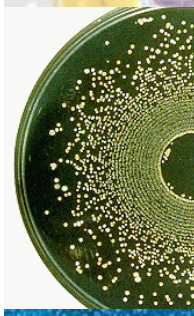
- The strains were screened for hGISA by using the Etest Macro method.

ME Botha, J Coetzee, AJ Brink, C Feldman, GA Richards (unpublished)

Results

Susceptibility patterns of MRSA isolated from bacteraemic patients (n=50).

mg/L	Vancomycin	Teicoplanin	Linezolid
MIC_{50}	1	2	1.5
MIC_{90}	2	3	2
Range	0.5-2	0.75-4	1-2
Breakpoint	S≤2	S≤8, R≥32	S≤4

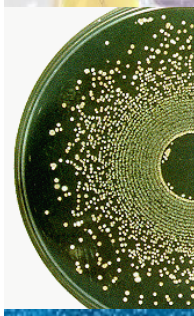
Results

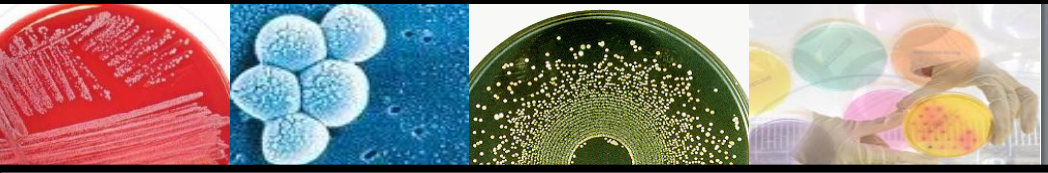
- The MIC_{90} of vancomycin was 2 mg/L which is at the breakpoint for susceptibility

- The MIC_{90} of teicoplanin and linezolid was 3 and 2 mg/L, respectively, both well below the breakpoint, suggesting that these agents are more active against bacteraemic strains of MRSA

- More importantly, 50% (25/50) of the strains demonstrated hetero-resistance to vancomycin

- Study on-going and awaiting PAP analysis for confirmation of hVISA

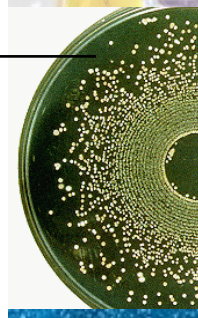




Non-fermentative Gram-negative resistance patterns

% antibiotic resistance of bacteraemic strains of non-fermentative Gram-negative pathogens in private practice in South Africa: January - June 2006

Antibiotic	*P.aeruginosa* (n=382, all pvt hospitals in 5 major cities)		
	n	% Overall	Range
Ceftazidime	172	45	11-90
Cefepime	202	53	21-70
Piperacillin-tazobactam	183	48	21-61
Ciprofloxacin	176	46	30-67
Levofloxacin	176	46	21-67
Amikacin	183	48	11-67
Tobramycin	202	53	11-100
Imipenem	172	45	23-63
Meropenem	160	42	15-64

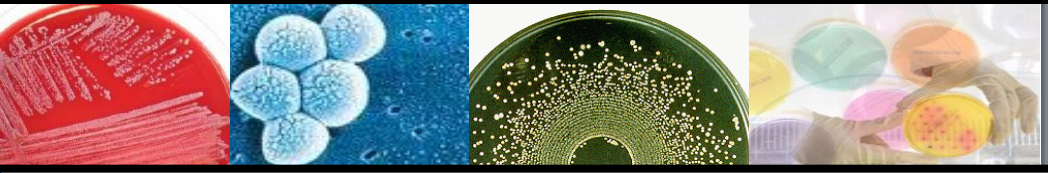



Brink et al. *South Afr Med J* 2007; **97:**630-636

% antibiotic resistance of bacteraemic strains of non-fermentative Gram-negative pathogens in private practice in South Africa: January - June 2006

Antibiotic	*A. baumannii* (**n=190,** all pvt hospitals in 5 major cities)		
	n	**% Overall**	**Range**
Ceftazidime	**82**	**43**	**11-90**
Cefepime	**82**	**43**	**21-70**
Piperacillin-tazobactam	**80**	**42**	**21-61**
Ciprofloxacin	**68**	**36**	**30-67**
Levofloxacin	**59**	**31**	**21-67**
Amikacin	**55**	**29**	**11-67**
Tobramycin	**36**	**19**	**11-100**
Imipenem	**63**	**33**	**23-63**
Meropenem	**63**	**32**	**15-64**

Brink et al. *South Afr Med J* 2007; **97:**630-636



Emergence of extensive drug-resistance (XDR) among Gram-negative bacilli in South Africa
“moving a step closer”

Brink et al. *SAMJ* 2008;8:586-592

Susceptibilities of selected invasive strains of the fermentative Gram-negatives

- **Isolated from patients in all private institutions in 7 major centers in South Africa**
- **The study was conducted from 1st July 2007 to 31st December 2007.**
- **Over this period a total of 1241 blood culture isolates were tested;**
  E.coli **(n=503)**
  K.pneumoniae **(n=548)**
  Enterobacter **spp (n=190)**

% resistance

Antibiotic	*E.coli* (n=503) Overall (Range)	*K.pneumoniae* (n=548) Overall (Range)	*Enterobacter* spp (n=190) Overall (Range)
Ampicillin	82 (65-90)	100 (-)	100 (-)
Co-amoxiclav	39 (0-57)	62 (31-73)	99 (91-100)
Cefuroxime	18 (0-33)	62 (31-72)	83 (0-96)
Ceftriaxone/Cefotaxime	7 (0-15)	57 (43-66)	62 (44-91)
Cefepime	5 (0-14)	54 (50-64)	26 (10-46)
Piperacillin-tazobactam	9 (0-23)	49 (26-67)	38 (17-66)
Ciprofloxacin	16 (0-36)	39 (18-64)	16 (0-40)
Levofloxacin	16 (0-36)	39 (28-64)	16 (0-40)
Gentamicin	14 (0-32)	31 (0-43)	25 (10-52)
Amikacin	6 (0-15)	25 (8-50)	6 (0-16)
Ertapenem	2 (0-8)	2 (0-8)	5 (0-17)
Imipenem	1 (0-6)	1 (0-1)	1 (0-5)
Meropenem	1 (0-6)	1 (0-1)	1 (0-5)
% ESBL production	5 (0-11)	50 (33-59)	23 (9-37)

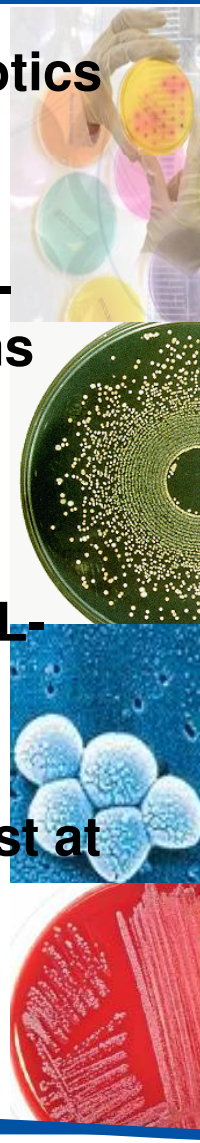
The study highlights the following.....

- **The high levels of resistance to "key workhorse" Gram-negative antibiotics used in the hospitals studied.**

- The *significant prevalence* of broad spectrum antibiotic-inactivating ß-lactamases (ESBLs)] in some centers, and other resistance mechanisms affecting fluoroquinolones and aminoglycosides in strains of invasive Enterobacteriaceae.

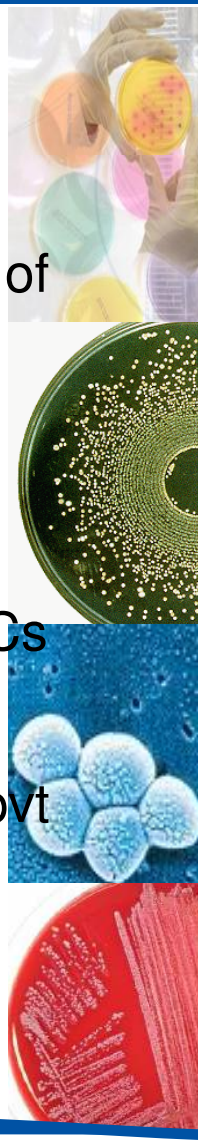
- The *considerable differences* in the prevalence of resistance and ESBL-production between the various centers in *K.pneumoniae* (33-59%).

- This emphasizes the need for routine antimicrobial surveillance at least at regional level, and preferably at each hospital or even each unit.



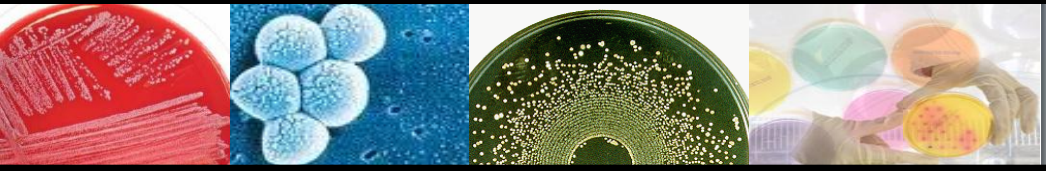
XDR *K. pneumoniae*

- The recent case report of a patient with pneumonia from a private hospital in Cape Town, South Africa is cause for great concern[1]
- For the first time, the *in vivo* development of ertapenem resistance in a strain of ESBL-producing *K.pneumoniae* (CTX-M in conjunction with porin-deficiency) which elevated imipenem and meropenem MICs 4- and 7-fold respectively compared to pre-treatment strains, was described
- Two recent case reports by Segal *et al* described a similar phenomenon at Groote Schuur Hospital, in which increases in imipenem and meropenem MICs of 4 and 8-fold respectively occurred during meropenem therapy[2]
- ? Emergence of carbapenemases (14 carbapenem resistant isolates from 4 pvt hospitals in JHB - positive Hodge test – awaiting PCR confirmation of KPC)



[1]Elliott E, *et al. Clin Infect Dis* 2006; 42: e95-8

[2]Segal H, Elisha BG. *South Afr J Epidemiol Infect* 2006;21:41-44



Initiatives

Ethical dilemma

- As private institutions in South Africa do not employ the doctors who provide services in their hospitals, they are not able to influence prescribing habits.
- The fact that the antibiotic prescribing fraternity has not yet accepted "stewardship" of the emerging problem of XDR Gram-negative bacilli, has given rise to an ethical dilemma both here and internationally
- In order to delay the imminent end of the antibiotic era, it may be time to challenge the right of doctors to prescribe whichever antibiotic they wish, which dose and for how long
- But restriction of established prescribing habits is controversial
- Punitive measures ?
- Impact on on going education/Adequate training ?

Pilot study

- **Recording duration of IVI antibiotic use in ICU's > 7 days**
- **Recording of inappropriate combinations i.e piperacillin/tazobactam + carbapenem**
- **New clinical pharmacologist daily rounds leaving note for prescriber**
- **Response has been encouraging**

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