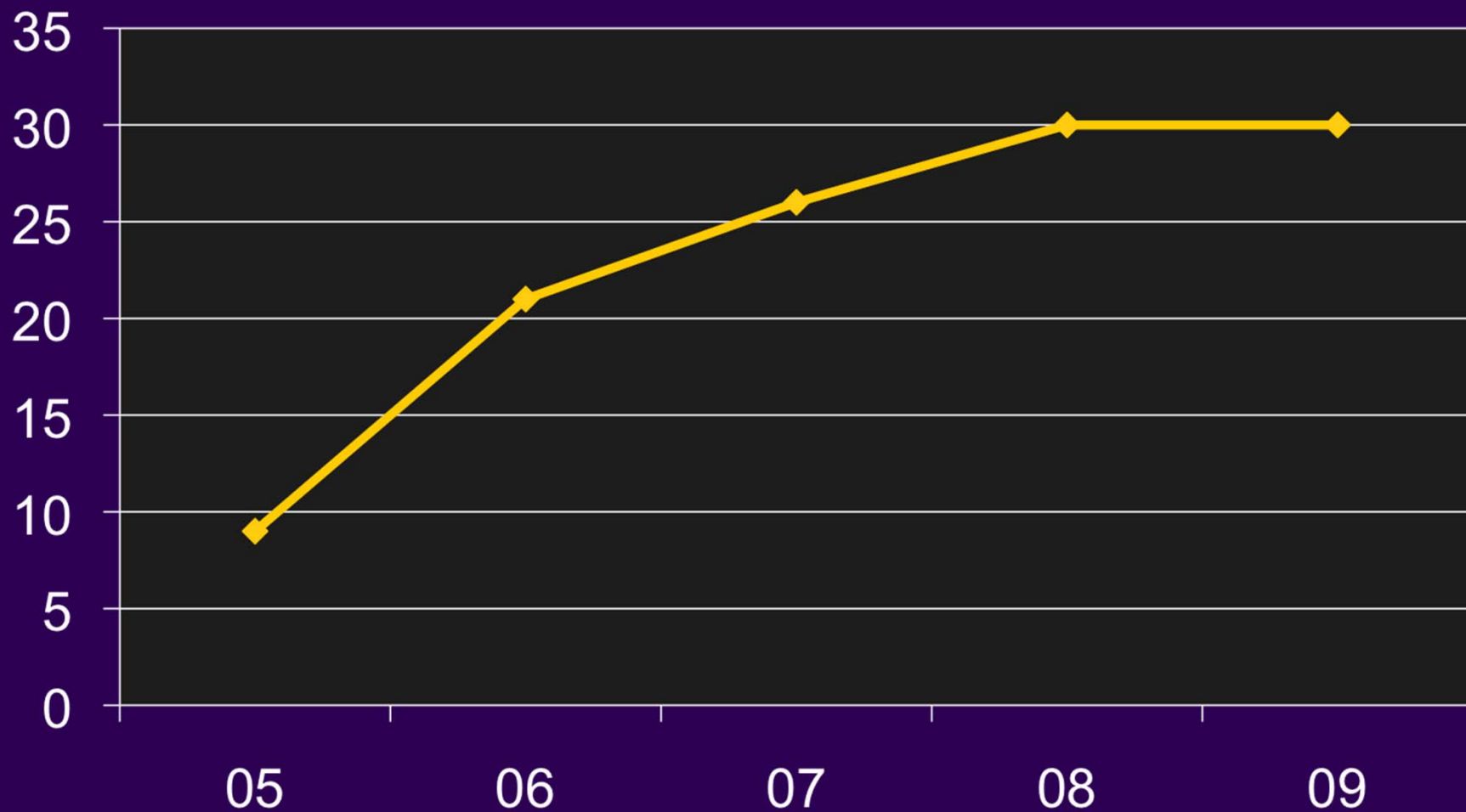


Detecting carbapenemases in non-fermenters

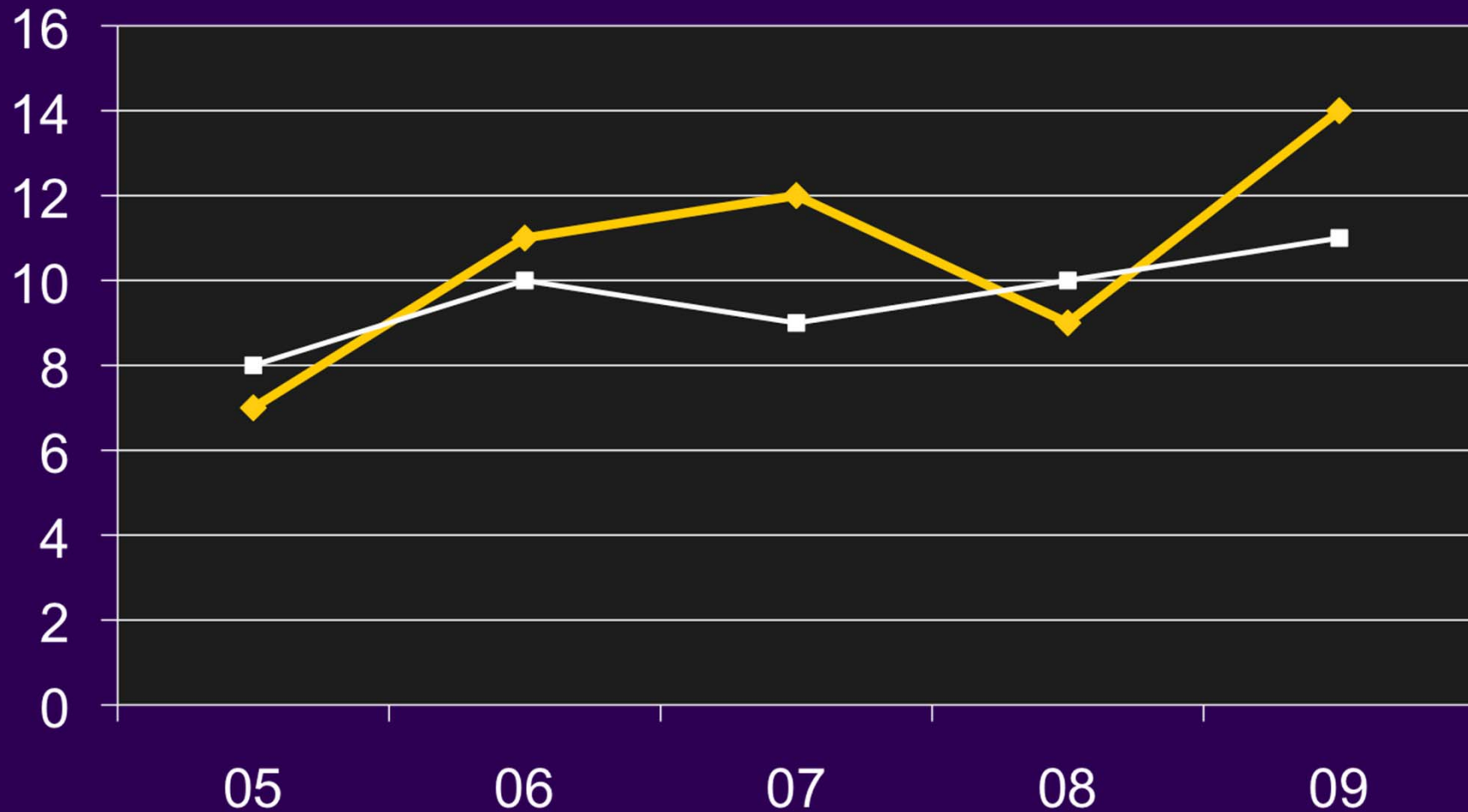
David Livermore

*Health Protection Agency,
Colindale, London*

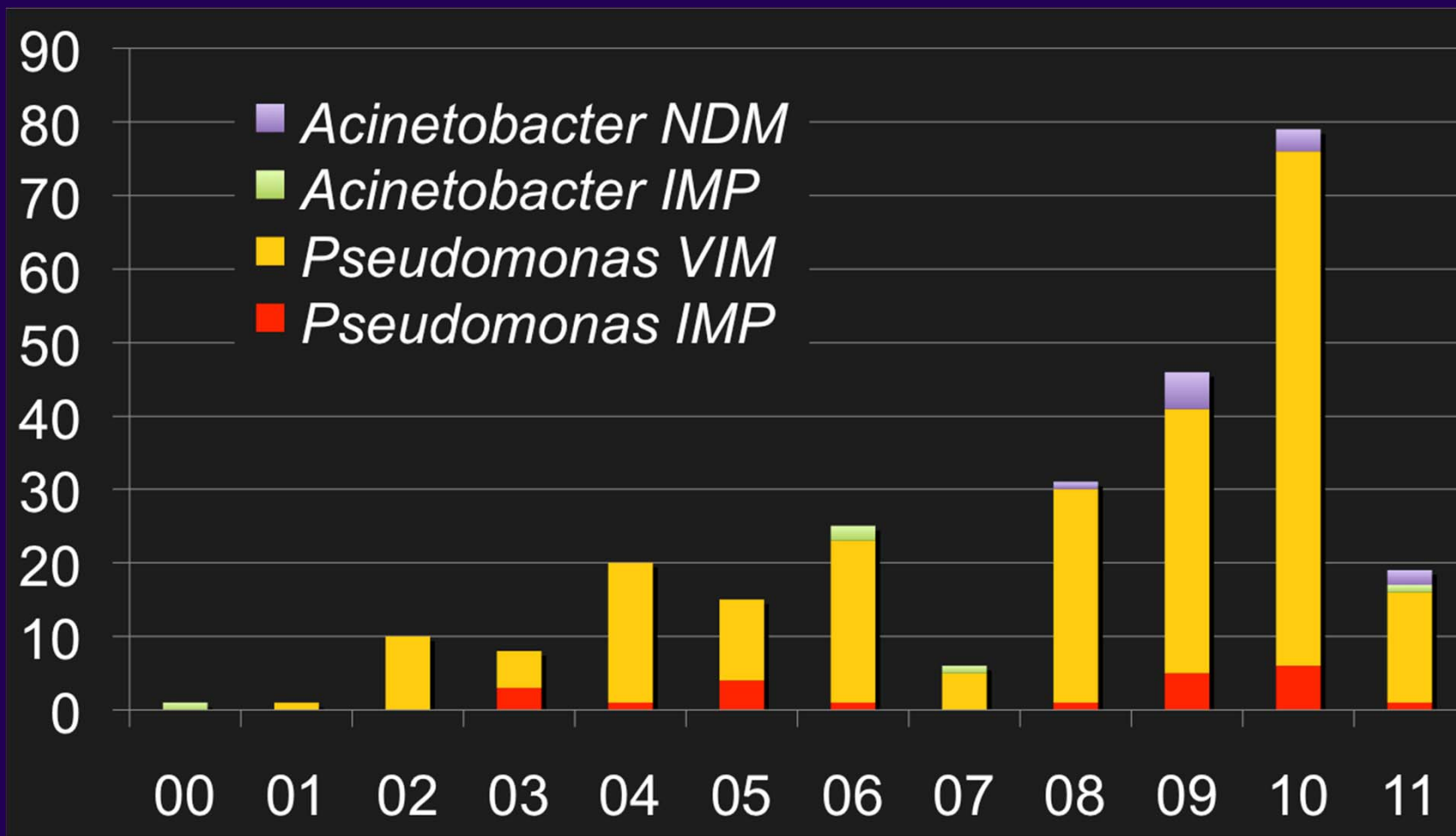
Rising imipenem resistance in *Acinetobacter* from bacteraemias



Carbapenem resistance in *Pseudomonas* from bacteraemias



Metallo carbapenemase in referred non-fermenters 2000-May 2011



HPR June 24th 2011

Carbapenem resistance in *Acinetobacter*



- Almost all due to OXA carbapenemases
- Rarely due to metallo-carbapenemases
- Suspect MBL if:
 - STRONG imipenem EDTA synergy (>8 fold)
 - Carbapenem MICs >64 mg/L
- Strains with OXA carbapenemases often give weak imipenem EDTA synergy: maybe stabilised by zinc

OXA Carbapenemases in *Acinetobacter*



- OXA-51-like chromosomal—all *A. baumannii*
 - In strains from 1950s; can use to identify *A. baumannii*
 - Resistance needs up-regulation by ISAba-1
- OXA-23, OXA-40 (-24) & OXA-58-like
 - Widespread acquired types; associated with clones
 - OXA-23 acquired from *A. radioresistens*
- Feeble carbapenemases when extracted
 - But loss reverses resistance...

Multiplex distinguishing *bla*_{OXA} carbapenemase alleles



OXA-58-like : 599-bp



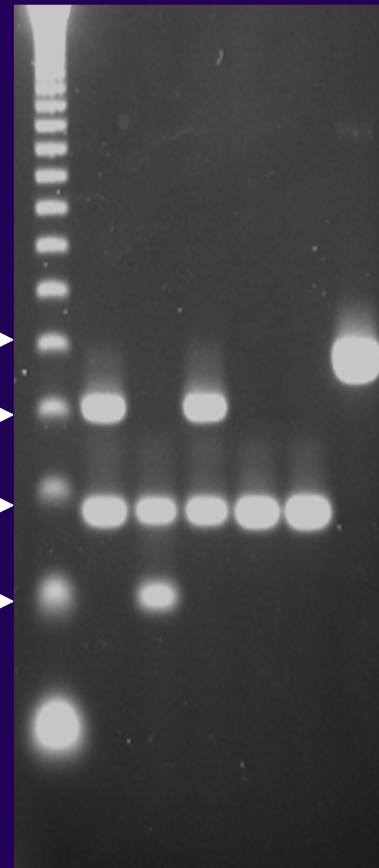
OXA-23-like : 501-bp



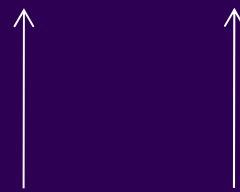
OXA-51-like : 353-bp



OXA-24-like : 246-bp



Activation of *bla*_{OXA-51-like} in *A baumannii*



PCR product
demonstrates linkage

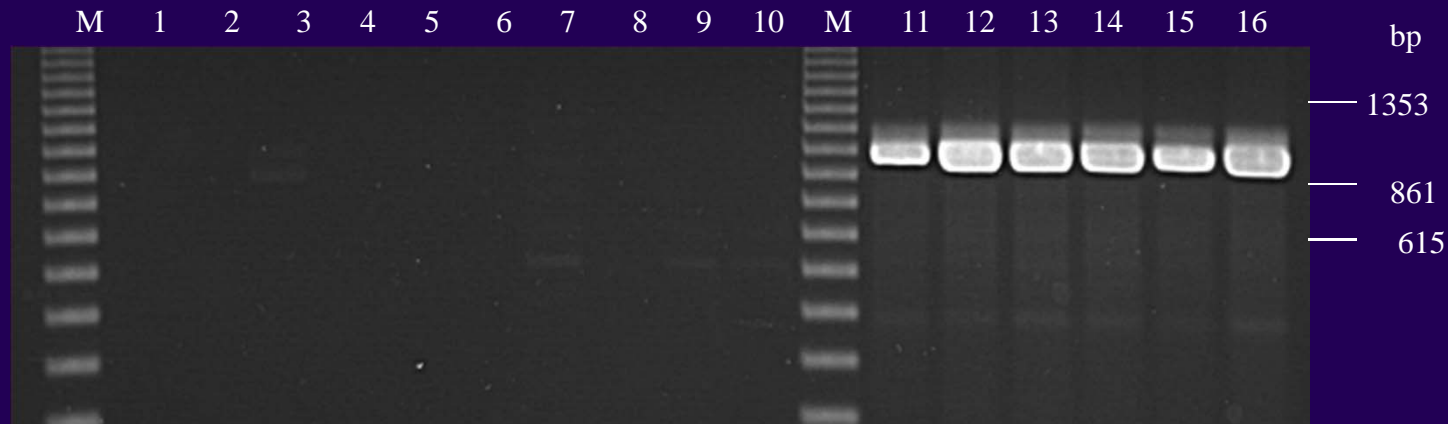
*bla*_{OXA-51-like} alone

- Imipenem MIC, 0.12-0.5 mg/L

ISAbal-1- *bla*_{OXA-51-like}

- Imipenem MIC >2 mg/L

IS_{ABA-1} F/ OXA-51-like PCR



**Susceptible
isolates**

Meropenem 0.06-2 mg/L

Imipenem 0.06-2 mg/L

**Resistant
isolates**

Meropenem 8-32 mg/L

Imipenem 1-8 mg/L

Carbapenem resistance in *P. aeruginosa*



- Gradually increasing both in prevalence & level
- Mostly (>95%) due to loss of OprD porin & (meropenem) up-regulation of efflux
- Rarely due to carbapenemases
 - IMP & VIM seen in UK
 - NDM, SPM & KPC recorded internationally

When to suspect a carbapenemase



- High level resistance, esp. if aztreonam relatively spared
 - e.g. growth up to ceftazidime & carbapenem discs
 - or MIC meropenem >64 mg/L; ceftazidime >128 mg/L
- If EDTA–imipenem synergy ≥ 32 fold and NOT from CF
 - Beware: EDTA disrupts outer membrane of *P. aeruginosa*, or interferes with OprD expression
 - Weak false +ves common... IMP: IMP+EDTA ratios of 8-16 rarely indicate a carbapenemase

When NOT to suspect a carbapenemase



- Isolate broadly S to other β -lactams except carbapenems
 - If ceftazidime MIC ≤ 16 mg/L
 - If carbenicillin MIC ≤ 512 mg/L
- If antibiogram fits other common phenotypes
 - Efflux: carbenicillin MIC $>$ cefotaxime $>$ piperacillin $>$ ceftazidime
 - AmpC: cefotaxime $>$ piperacillin / carbenicillin $>$ ceftazidime
- CF isolates
 - But KPC recently found in Brazil- Leao *et al. J Cyst Fibros* 2011;**10**:140

Quiz time



	<i>A. baum</i>	<i>A. baum</i>	<i>P. aerug.</i>	<i>P. aerug.</i>	<i>P. aerug.</i>
Imipenem	32	128	64	64	128
+EDTA	8	4	8	1	64
Meropenem	64	128	32	128	64
Carbenicillin	>1024	>1024	256	>1024	>1024
Cefotaxime	>64	>64	128	>256	>64
Pip/taz	>64	>64	32	>64	>64
Ceftazidime	>64	>64	4	256	256
Aztreonam	>64	>64	8	32	>64
Gent/Tob/Ak	R,R,R	R,R,R	S,S,S	S,R,R	R,R,R

OXA

MBL

Efflux
OprD -ve

MBL

???
Clover leaf
& PCR

Other non-fermenters



S. maltophilia & *Chryseobacterium (Elizabethkingella) spp.*

- chromosomal carbapenemases

Burkholderia spp.

- mechanisms unclear
- carbapenemases claimed by distribution among species and regulation of expression wholly unclear