3M Infection Prevention Solutions

CRE and friends: What's the problem and how to detect them?

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3M

House Keeping

Questions

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House Keeping

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Disclosure

I am employed part-time by Bioquell and received payment from 3M for this webinar.

1. Aug 19: CRE and friends: what's the problem and how to detect them?
2. Sept 16: Not all resistant Gram-negative bacteria are created equal: Enterobacteriaceae vs. non-fermenters
3. Oct 7: Filling the gaps in the guidelines to control resistant Gram-negative bacteria

Learner objectives

1. Understand the importance of the rising threat from multidrug-resistant Gram-negative rods.
2. Understanding the microbial challenge, by building on our knowledge of other pathogens.
3. Gain updates on global prevalence, clinical overview, risk factors and prevention and control measures.
4. Discuss the strengths and weaknesses of the various diagnostic approaches for resistant Gram-negative rods.

THE END OF ANTIBIOTICS IS NIGH

What's the problem?

"CRE are nightmare bacteria."
Dr Tom Frieden, CDC Director

"If we don't take action, then we may all be back in an almost 19th Century environment where infections kill us as a result of routine operations."
Dame Sally Davies, CMO

"If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine where treatable infections and injuries will kill once again."
David Cameron, Prime Minister

Rising threat from MDR-GNR

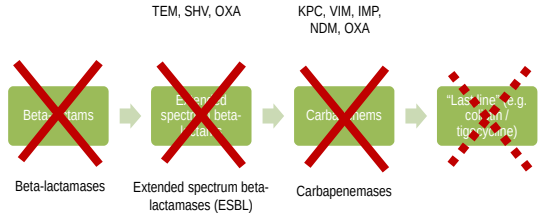
% of all HAI caused by GNRs.

% of ICU HAI caused by GNRs.

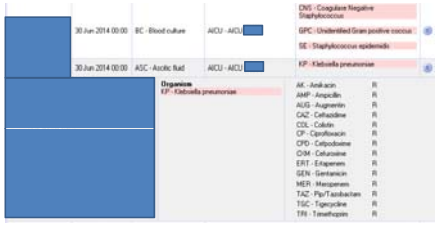
Non-fermenters	*Acinetobacter baumannii* *Pseudomonas aeruginosa* *Stenotrophomonas maltophilia*
Enterobacteriaceae	*Klebsiella pneumoniae* *Escherichia coli* *Enterobacter cloacae*

Hidron et al. *Infect Control Hosp Epidemiol* 2008;29:966-1011.
Peleg & Hooper. *N Engl J Med* 2010;362:1804-1813.

Beta-lactam resistance



What's the problem? Resistance



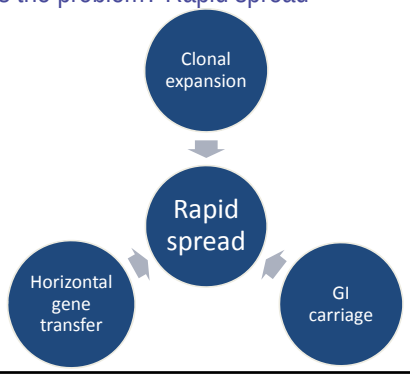
Courtesy of Pat Cattini

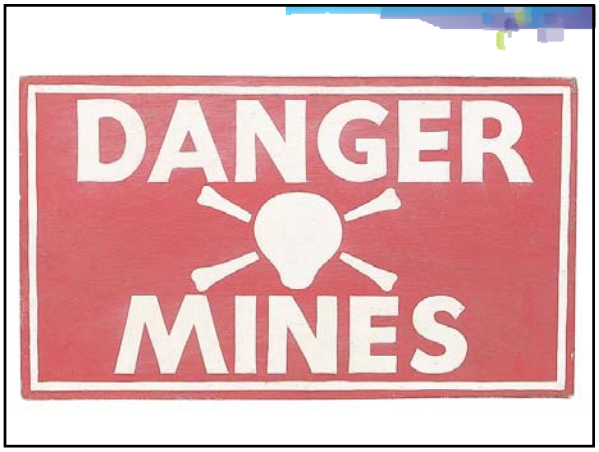
What's the problem? Mortality

	Enterobacteriaceae		Non fermenters
Organism	AmpC / ESBL	CPE	*A. baumannii*
Attributable mortality	Moderate	Massive (>50%)	Minimal

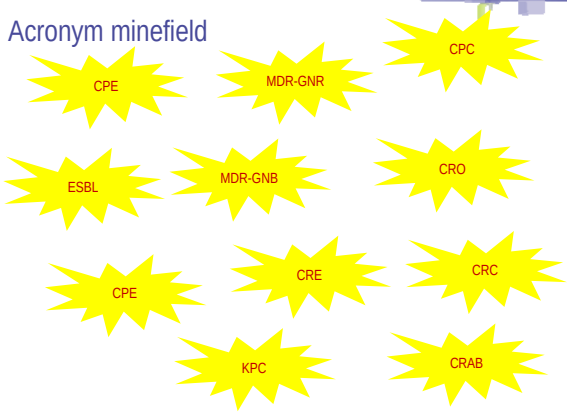
Shorr *et al. Crit Care Med* 2009;37:1463-1469.
Patel *et al. Iinfect Control Hosp Epidemiol* 2008;29:1099-1106.

What's the problem? Rapid spread





Acronym minefield



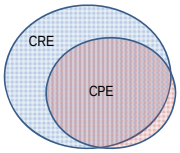
Poll: would you be comfortable explaining the difference between 'carbapenem-resistant Enterobacteriaceae (CRE)' and 'carbapenemase producing Enterobacteriaceae (CPE)' to a colleague?

A) Yes
B) No

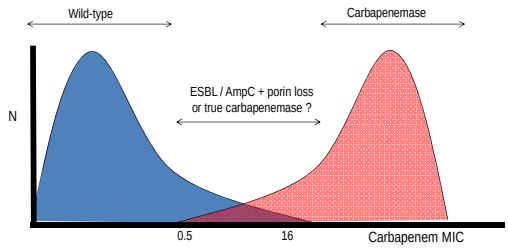
What are CRE?

Carbapenem-resistant Enterobacteriaceae (CRE) – Enterobacteriaceae that are resistant to carbapenems by any mechanism.

Carbapenemase-producing Enterobacteriaceae (CPE) – Enterobacteriaceae that are resistant to carbapenems by means of an acquired carbapenemase.

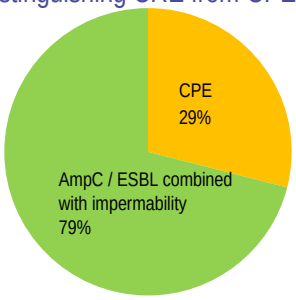


When CRE is not CPE



Courtesy of Dr Katie Hopkins, PHE.

Distinguishing CRE from CPE



Breakdown of 24 CRE isolates identified at Alder Hey, Sept 2011 – Aug 2012

Drew *et al.* *J Hosp Infect* 2013;84:300-304.

Understanding the enemy

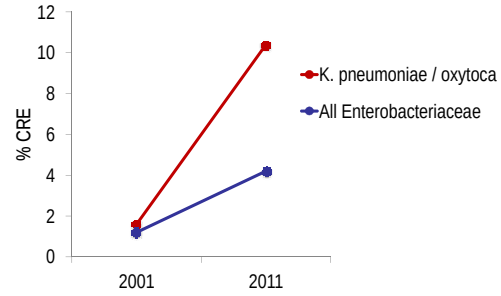
Pathogen	CRE[1]	CRAB[2]	MRSA	VRE	*C. difficile*
Resistance	+++	+++	+	+	+/-
Resistance genes	Multiple	Multiple	Single	Single	n/a
Species	Multiple	Single	Single	Single	Single
HA vs CA	HA & CA	HA (ICU)	HA	HA	HA
At-risk pts	All	ICU	Unwell	Unwell	Old
Virulence	+++	+/-	++	+/-	+
Environment	+/-	+++	+	++	+++

1. Carbapenem-resistant Enterobacteriaceae.
2. Carbapenem-resistant *Acinetobacter baumannii*.

Poll: How much CRE have you seen in your hospital?

A) None
B) One or two cases
C) One or two outbreaks
D) Regularly (not related to known outbreaks)

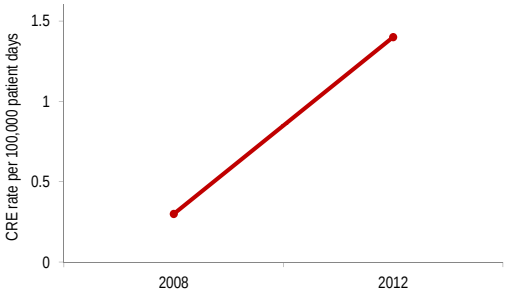
CRE in the USA



NHSN / NNIS data; *MMWR* 2013;62:165-170.

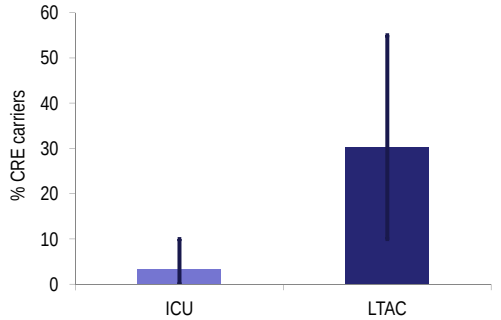
CRE in the USA

25 community hospitals in Southwestern USA

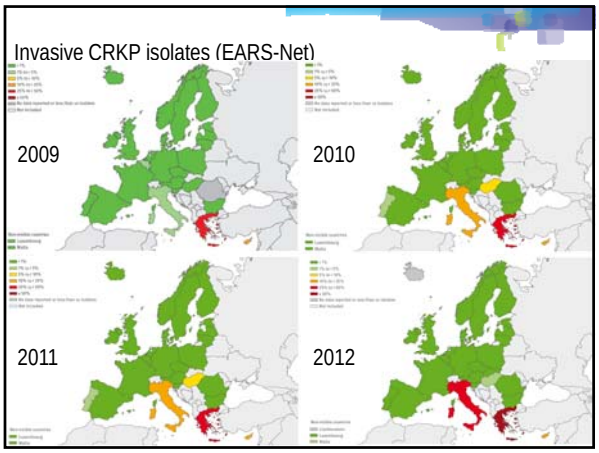


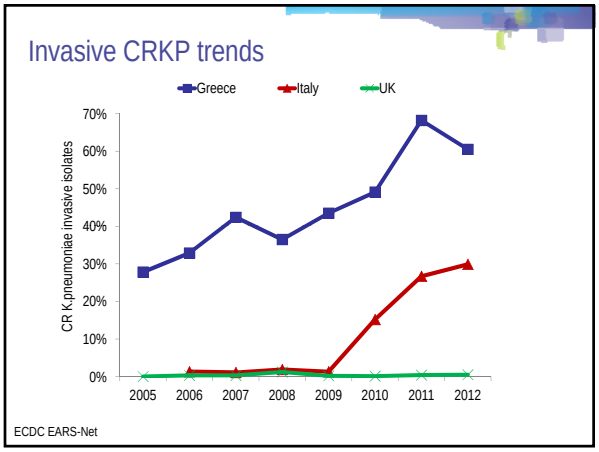
Thaden *et al. Infect Control Hosp Epidemiol* 2014;35:978-983.

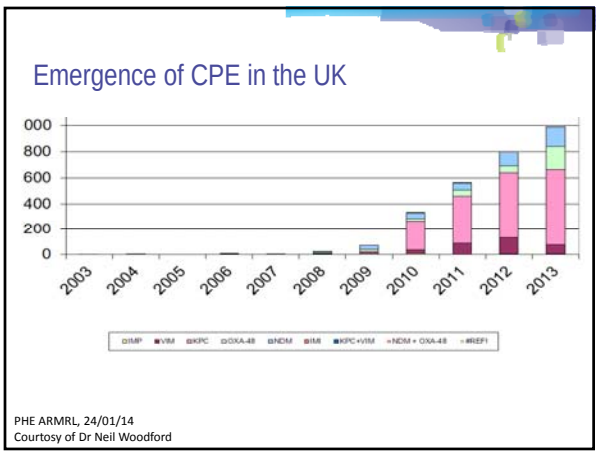
CRE in LTACs, USA



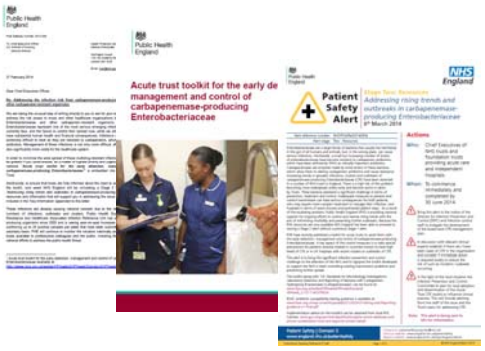
Lin *et al. Clin Infect Dis* 2013;57:1246-1252.


Invasive CRKP isolates (EARS-Net)
2009
2010
2011
2012


Invasive CRKP trends
Greece
Italy
UK
CR K.pneumoniae invasive isolates
70%
60%
50%
40%
30%
20%
10%
0%
2005
2006
2007
2008
2009
2010
2011
2012
ECDC EARS-Net


Emergence of CPE in the UK
000
800
600
400
200
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
PHE ARMRL, 24/01/14
Courtesy of Dr Neil Woodford

CPE in the UK



Risk factors & at-risk population

	Enterobacteriaceae	Non-fermenters
Risk factors	LOS ICU stay Catheters / devices Ventilation Prior antibiotics Travel	LOS ICU stay Catheters / devices Ventilation Prior antibiotics Trauma (esp. burns)
At-risk population	Patients in acute settings, particularly those with recent travel to areas of high prevalence. Potential for community spread.	High-risk patients in the ICU and burns units; rare cause of community-acquired infection.

ECDC CPE risk assessment, 2011.
Peleg *et al. Clin Microbiol Rev* 2008;21:538-582.

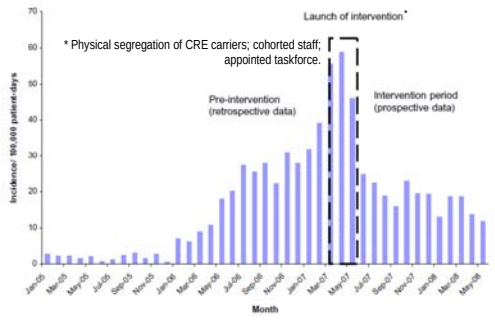
What can be done? NIH

Also consider:

- Daily chlorhexidine baths
- 'Enforcers' for hand hygiene compliance
- Communication with all staff
- Characterisation of outbreak strains (WGS)

Palmore. *Clin Infect Dis* 2013;57:1593-9.

Prevention and control



Schwaber *et al. Clin Infect Dis* 2011;52:848-855.

Who do I screen?

PHE CPE Toolkit screening triggers:

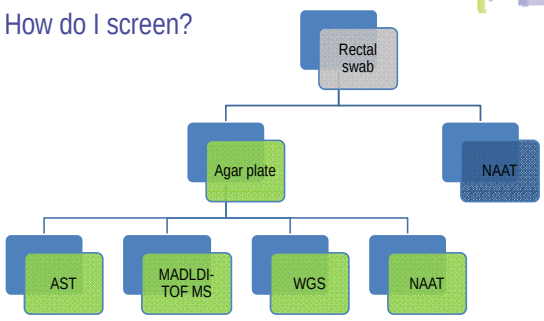
a) an inpatient in a hospital abroad, or

b) an inpatient in a UK hospital which has problems with spread of CPE (if known), or

c) a 'previously' positive case.

Also consider screening admissions to high-risk units such as ICU, and patients who live overseas.

How do I screen?



NAAT = nucleic acid amplification techniques
AST = antimicrobial susceptibility testing
MALDI-TOF = Matrix-assisted laser desorption /ionization – time of flight mass spectrometry
WGS = whole genome sequencing

Agar plates

MacConkey

Selective for all Gram-negative bacteria (including Enterobacteriaceae and non-fermenters)

Chromogenic Media

Selective for resistant Enterobacteriaceae only (ESBL or CRE options available); several options

Antimicrobial susceptibility testing (AST)

Quantitative (MIC or breakpoint)

Agar or broth dilution (manual or autmoated), E-tests

Qualitative (R/I/S)

Disc diffusion; supplemental tests for mechanisms (e.g. ESBL, CRE)

MALDI-TOF, WGS, NAAT (PCR and Array Chips)

MALDI-TOF

Rapid and accurate speciation of bacteria from a colony; potential for detection of resistance genes

WGS

Whole genome sequence; gold standard typing method; costs coming down; can detect abx resistance genes

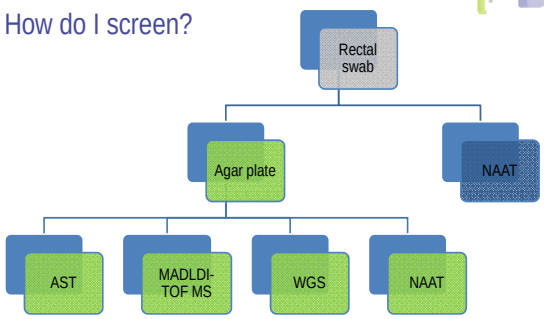
PCR

PCR can be used to detect a single or multiple genes of interest from a pure colony

Array Chips

>100 PCRs on a single chip for simultaneous detection of a range of genes and markers

How do I screen?



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NAAT direct from clinical specimens

PCR

Rapid real-time PCR kits available to detect resistance genes direct from clinical specimens; point of care tests coming

Rapid sequencing kits

Kits available for rapid sequence-based simultaneous detection of common organisms and resistance genes

Before you throw away the agar plates…

Molecular diagnostics are great but:

- but do not deal with changing epidemiology; struggle with target variability;
- are expensive;
- rely on validation of carriage sites;
- do not tell you about phenotypic susceptibility;
- have a limit of detection often around a couple of logs;
- and need to manage shared resistance genes between species, especially for MDR-GNR

See further details in talk by Dr Dan Diekema

Poll: which method is used by your clinical laboratory to detect CRE?

A) Chromogenic agar plate
B) Non-chromogenic agar plate
C) Molecular method (e.g. PCR)
D) Other
E) Don't know

Key questions

- Which interventions work?
- Are they different for Enterobacteriaceae and non-fermenters? (Probably, given their epidemiology.)
- What is the prevalence of CPE?
- How much do we believe a single negative screen? What is the duration of colonisation?
- Do we need rapid molecular diagnostics?
- Are there decolonisation strategies other than (virtually non) 'selective decontamination' using abx?

Summary

1. MDR-GNR are emerging worldwide and represent a unique threat.
2. CRE in particular combine resistance, virulence and the potential for rapid spread.
3. Prevalence in the US appears to be patchy, but increasing.
4. We do not yet know what is effective in terms of prevention and control, but screening and isolation of carriers seems prudent.
5. Diagnosis can be challenging, and relies on close liaison with the microbiology laboratory.

Learner objectives

1. Understand the importance of the rising threat from multidrug-resistant Gram-negative rods.
2. Understanding the microbial challenge, by building on our knowledge of other pathogens.
3. Gain updates on global prevalence, clinical overview, risk factors and prevention and control measures.
4. Discuss the strengths and weaknesses of the various diagnostic approaches for resistant Gram-negative rods.

Sept 16 2014: Not all resistant Gram-negative bacteria are created equal: Enterobacteriaceae vs. non-fermenters

1. Gain a microbiological overview of the various families of multidrug-resistant Gram-negative rods
2. Compare the features of the key families: Enterobacteriaceae (including CRE) and non-fermenters (including *A. baumannii*), especially at-risk population and epidemic potential.
3. Discuss how differences in epidemiology affect approaches to infection prevention and control.

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Questions?

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Resources

- CDC CRE Toolkit.
- AHRQ CRE Tookit.
- UK Public Health England CPE Tookit.

Acknowledgements

Pat Cattini
Image credit: 'Danger! Mines!' by Save the Wild UP.

Thank you!

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