



### Microbiology and the Evolution of MDROs

Dr Deirdre O'Brien  
Mercy University Hospital and  
South Infirmary Victoria University Hospital

Twitter: @Patient Care Conference 2017  
@SPC2016Cork #bugndrugs

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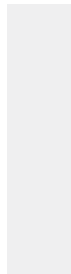
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### Talk outline

- What is a multidrug resistant organism (MDRO)?
- How do bacteria become resistant to antibiotics?
- Focus on resistance in *Enterobacteriaceae*




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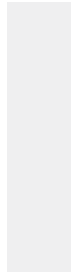
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### Multi-drug resistant organisms

- MRSA
- VRE (Vancomycin resistant Enterococci)
- Linezolid resistant VRE
- Multi-resistant Gram negative bacteria (ESBLs, MDRKP, CRE)
- Penicillin resistant *Streptococcus pneumoniae*
- Multi and extensively drug resistant TB
- Multi-drug resistant gonorrhoea.....




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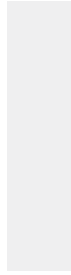
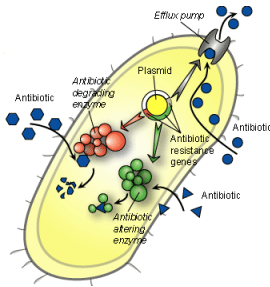
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## How do bacteria become resistant to antibiotics?




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## Intrinsic v Acquired Resistance

**Intrinsic resistance**  
"Born this way"

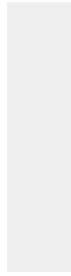
**Acquired Resistance**  
when a microorganism **obtains** the ability to resist the activity of a particular antimicrobial agent to which it was previously susceptible

Can arise as a result of:

- ❖ Genetic mutation
- ❖ Acquisition of foreign resistance genes
- ❖ Combination of these two mechanisms.

**Acquired resistance can be passed from one bacterium to another**

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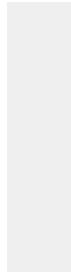
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## MDROs discussed in this talk

- ESBLs
- MDRKPs
- CRE/CPE




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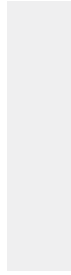
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## Enterobacteriaceae

- **Enterobacteriaceae family:** *E. coli*, *Klebsiella* spp, *Enterobacter* spp.
- Normal gut flora
- Common cause UTI in community
- Hospital acquired infections: UTI, pneumonia, intra-abdominal infections, wound infections, bloodstream infections




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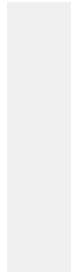
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## What are ESBLs (extended spectrum beta-lactamases) ?

- ESBLs are enzymes which confer resistance to beta-lactam antibiotics- ampicillin/amoxicillin, cephalosporins
- Produced by Gram negative bacteria eg. *E. coli*, *Klebsiella* spp., *Proteus* spp.




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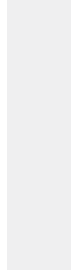
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## Where do ESBLs come from?

- Frequently plasmid encoded
- Plasmid= small DNA fragment that is capable of self replication and can be passed from one bacteria to another
- Plasmids containing enzymes for ESBL frequently carry genes encoding resistance to other antibiotics eg. aminoglycosides, quinolones




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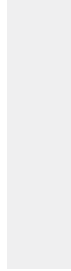
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### Where are ESBLs found?

- May live harmlessly in gut (similar to non-ESBL producing *E. coli*) but cause problems when enter urinary tract, bloodstream etc.




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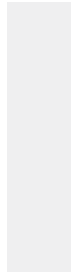
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### What kind of infections do ESBLs cause?

- Same range of infections as "regular" *E.coli*, *Klebsiella* spp. *Proteus* spp.
- Urinary tract infections
- Intra-abdominal infections
- Healthcare associated pneumonia
- Catheter related bloodstream infections
- Skin/ soft tissue (more unusual, these organisms tend to colonize rather than infect skin)




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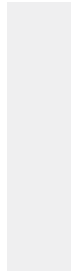
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### Who is at risk of infections caused by ESBL-producing bacteria?

- Gut colonization
- Length of ICU stay
- Presence of central venous or arterial catheters
- Emergency abdominal surgery
- Presence of a gastrostomy or jejunostomy tube
- Low birth weight
- Prior administration of any antibiotic
- Prior residence in a long-term care facility (eg. nursing home)
- Severity of illness
- Presence of a urinary catheter
- Ventilatory assistance
- Undergoing haemodialysis




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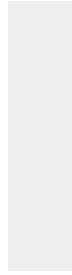
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## Can patients be cleared of ESBL carriage?

- Probably not
- No decolonisation regimen
- Likely that patients will carry the ESBL producing organism for some time
- Persists in gut (will become part of normal flora)
- Sometimes strain lost naturally
- Use of antibiotics will not help



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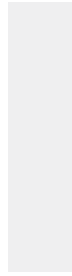
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## What do I tell patients/relatives?

- Depends on whether colonized or infected
- Explain that patient has an infection (correlate results with clinical findings) which is resistant to many commonly used antibiotics
- Spread can be prevented through correct hand hygiene procedures



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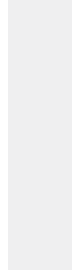
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## Treatment Options

- Trimethoprim and nitrofurantion
- Ciprofloxacin
- Aminoglycosides
- Fosfomycin
- ??piperacillin/tazobactam
- Carbapenems (ertapenem, meropenem)



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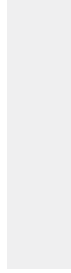
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### What is MDRKP?

- MDRKP= Multi-drug resistant *Klebsiella pneumoniae*
- *Klebsiella pneumoniae* that are ESBL positive and are resistant to ciprofloxacin and gentamicin
- Notifiable to HPSC




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### Invasive MDRKP, including MDRKP/Non-CRE and MDRKP/CRE: distribution of cases by year, 2014-2016

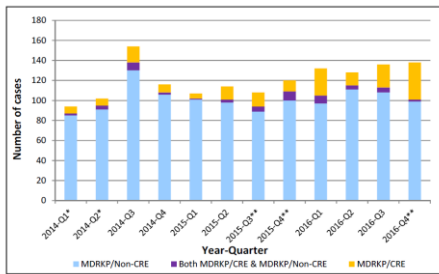


Figure 1. Quarterly MDRKP cases (CRE and Non-CRE): Q1 2014 – Q4 2016  
 \*No data from one tertiary hospital for Q1-2 2014; \*\* No data from one general hospital for Q3-4 2015 and Q4 2016




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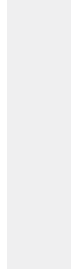
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### Why do I need to worry about ESBLs- should I not focus on CPE?

- Absolutely not!!!
- More ESBLs = more need to use meropenem= more CPE
- Infection caused by ESBL= more likely to have increased mortality, longer hospital stays and greater hospital costs




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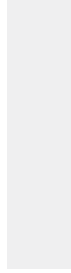
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## Carbapenems

- Carbapenems are **invaluable** for the treatment of infection due to multi-resistant Gram negative bacteria
- Meropenem, ertapenem, doripenem, imipenem




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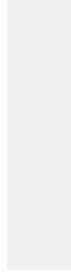
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## CRE or CPE?

- CRE= Carbapenem Resistant Enterobacteriaceae
- CPE= Carbapenemase Producing Enterobacteriaceae



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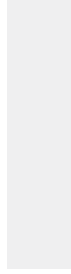
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- Carbapenem resistance is complex
- Many different species with many, many different mechanisms of resistance
- Carbapenemase producers primarily responsible for the increasing spread of CRE



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## Different carbapenemases...

- KPC
- OXA-48
- VIM
- NDM
- IMP

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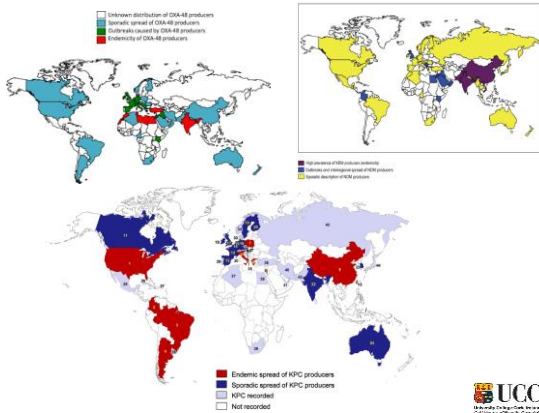
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## Treatment Options for CPE



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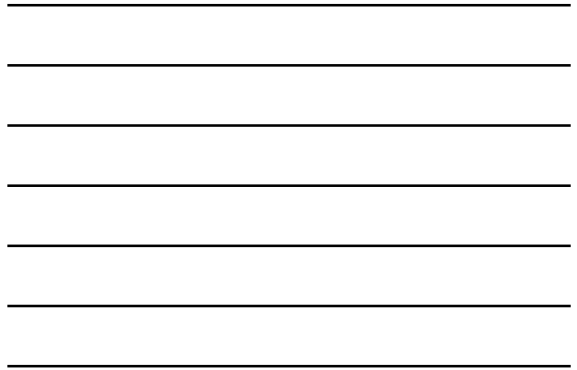
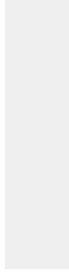
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the guardian

Antimicrobial resistance a 'greater threat than cancer by 2050'

UK Chancellor George Osborne to tell IMF that this people's vote could see without nuclear action

Deaths attributable to AMR every year compared to other major causes of death

the guardian

Antibiotics

US reports first case of bacteria resistant to antibiotic of last resort

In the end of the road for antibiotics unless we act urgently, says Centers for Disease Control and Prevention after superbug infects Pennsylvania woman

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Infusion with Penicillin G

penicillins: A Report of 2 Cases and a Brief Review of the Literature

Ann Intern Med. 1963;59:100-104. doi: 10.7326/0000-9000-59-1-100

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BAD BUGS, NO DRUGS

An antibiotic discovery blueprint: A Public Health Crisis Brews

July 2014

JAC

Has the era of untreatable infections arrived?

David M. Livermore\*

Antibiotic Resistance: Meeting and Addressing the Challenge

Journal of Antimicrobial Chemotherapy (2015) Vol. 60, Suppl. 1, i10-116

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IDSA

July 2014



**What levels of antimicrobial resistance are present in Ireland?**

**How do we compare to other countries?**



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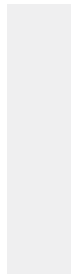
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### EARS-net

- EU Surveillance network for antimicrobial resistance
- Key pathogens
- Began 1999
- Excellent participation by Irish laboratories



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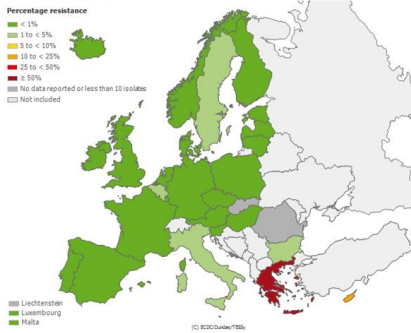
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**Proportion of Carbapenems (R+I) resistant *Klebsiella pneumoniae* isolates in participating countries in 2009**



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# CRE 2015

Figure 3.9. Klebsiella pneumoniae. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015




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# How are ESBLs, MDRKP and CPE transmitted?

- **Most important mode of transmission via transient carriage on the hands of healthcare workers**
- **Environmental spread**
- **Antimicrobial stewardship**




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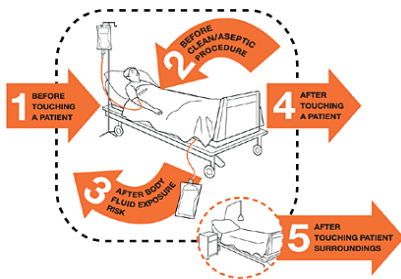
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# An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant Enterobacteriaceae

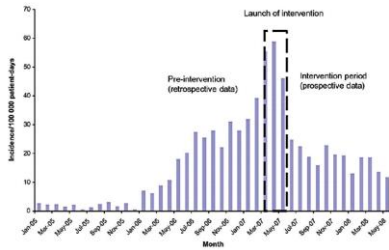
Mitchell J. Schwaber and Yehuda Carmeli  
National Center for Infection Control, Tel Aviv, Israel

Clinical Infectious Diseases 2014;58(5):697-703

- Nationwide spread of CRE in Israel 2006-failure to contain a local levels
- Acquisition rate of 55.5 cases per 100,000 patient days
- National intervention for CRE containment



## Acquisition rate reduced to 4.8 cases per 100,000 patient days..



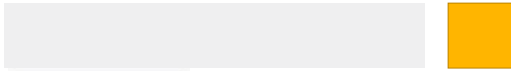
## What worked?

TABLE 1. Compliance with Infection Control Guidelines in 13 Post-Acute Care Hospitals as Noted on 5 Site Visits

Variable	2008	2010	2011	P
Infection control consultant	62	85	92	.055
Hand hygiene <sup>a</sup>				
Presence of ABHR in each room	85	92	100	.146
ABHR at site of care	15	54	85	<.001
Presence of antiseptic soap	15	92	85	<.001
Presence of sink in each room	23	31	46	.164
Paper towel availability	69	85	100	.032
Compliance audits	0	46	77	<.001
Appropriate use of barrier precautions in context of standard precautions <sup>b</sup>				
Gloves	31	69	92	.001
Gowns	54	77	77	.208
Masks	38	62	69	.118
CRE prevention program				
Placement of colonized patients in single rooms or cohorting	77	85	100	.082
Use of gown and gloves in contact isolation	46	92	100	.001
Designated medical equipment	92	100	100	.221
Admission screening cultures	15	69	77	.002
Contact screening	38	77	100	.001
Discontinuation of isolation per standard protocol	15	46	100	<.001
Total infection control score (average, out of possible 16)	6.8	11.6	14.0	<.001

NOTE. Data are percentage of compliant hospitals (n = 13), unless otherwise indicated. ABHR, alcohol-based hand rub; CRE, carbapenem-resistant Enterobacteriaceae.





• Farm animals account for 40% of antibiotic use in the UK

• 80% of all antibiotics in the US given to farm animals



Horizontal lines for notes.



EUROPEAN ANTIBIOTIC AWARENESS DAY

A European Health Initiative

Get better without using antibiotics

This leaflet explains the need to get the right treatment for common illnesses such as colds and coughs without encouraging antibiotic resistance.



Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

ANTIMICROBIAL STEWARDSHIP: "START SMART - THEN FOCUS"



Horizontal lines for notes.

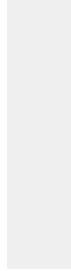
Public engagement essential.....



Horizontal lines for notes.

## Take home messages

- MDRO rates a major concern in Irish healthcare and globally
- Gram negative resistance is complex and our understanding of this is evolving
- Antimicrobial resistance a real threat to how we all practice medicine
- Stewardship and adherence to infection prevention and control practices our best (only) means to limit the spread



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