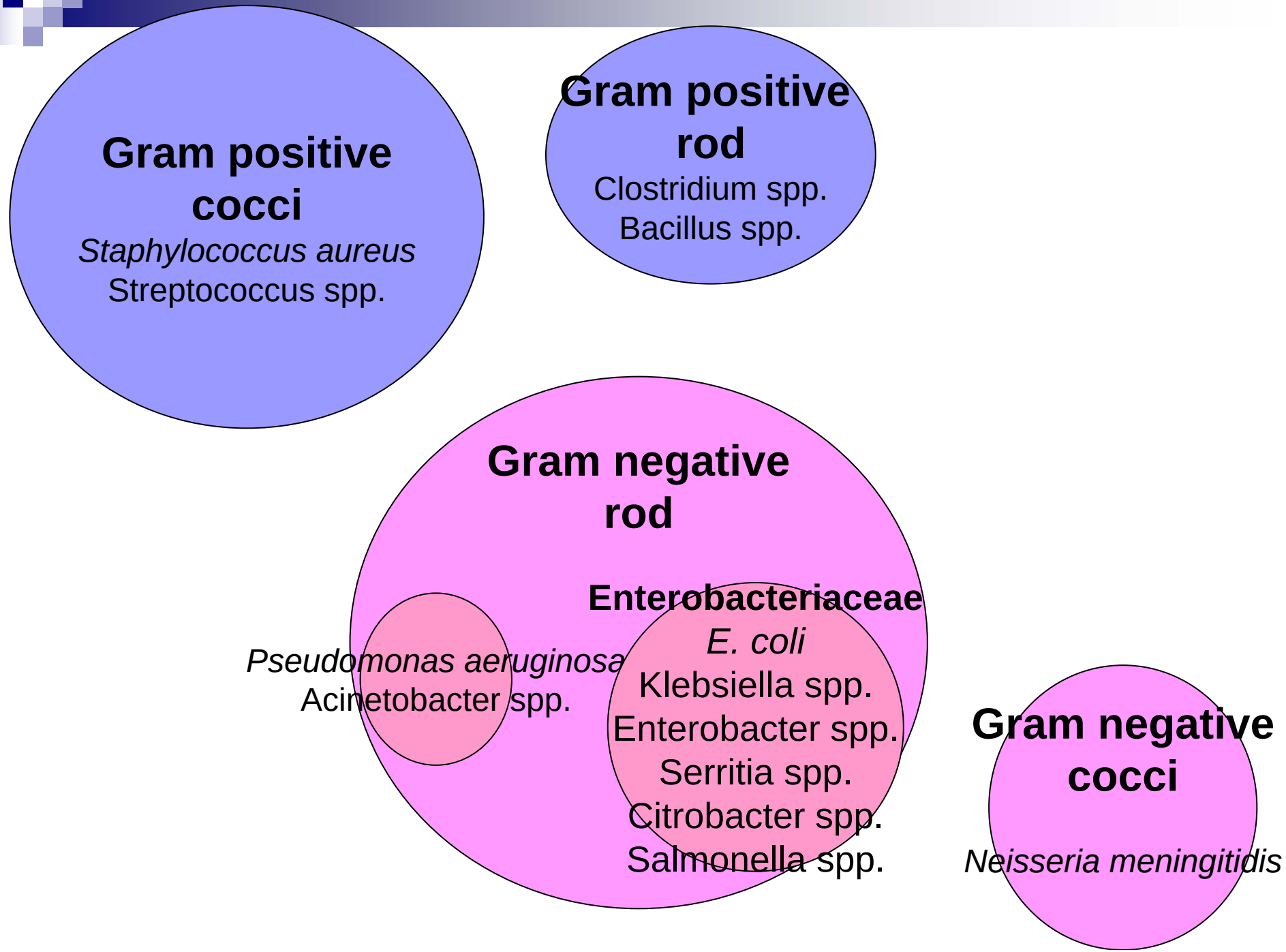
Infection Control Forum

HA Fact Sheet on Carbapenem resistant Enterobacteriaceae (CRE)

9th December 2010

Lecture Theatre,

G/F Centre for Health Protection


Gram positive cocci
Staphylococcus aureus
Streptococcus spp.
Gram positive rod
Clostridium spp.
Bacillus spp.
Gram negative rod
Enterobacteriaceae
E. coli
Klebsiella spp.
Enterobacter spp.
Serritia spp.
Citrobacter spp.
Salmonella spp.
Pseudomonas aeruginosa
Acinetobacter spp.
Gram negative cocci
Neisseria meningitidis

Department of Pathology

Division of Clinical Microbiology and Infection

Antibiogram 2006 (All specimen)

Period: From 01/01 to 31/12/2006
Specimen: All
% Susceptible
( ) No. of organism tested

Organism	Count	Amikacin	Amoxycillin + Clavulanic Acid	Ampicillin	Cefaclor	Cefepime	Cefoperazone + Sulbactam	Cefotaxime	Ceftazidime	Cefuroxime	Cefuroxime (Oral)	Cefuroxime (Parenteral)	Cephalothin	Ciprofloxacin	Clarithromycin	Clindamycin	Co-Trimoxazole	Erythromycin	Fusidic Acid	Gentamicin	Imipenem	Levofloxacin	Nitrofurantoin	Oxacillin	Penicillin G
Escherichia coli	2281	99	83	26				82	82		71	79	38	31			57			71	100	68	96		
		(2281)	(2281)	(2281)				(2281)	(2281)		(2281)	(2281)	(498)	(22)			(2281)			(2281)	(2281)	(2281)	(1783)		
Pseudomonas aeruginosa	787	99				95	95		95					91						98	97				
		(787)				(787)	(787)		(787)					(787)						(787)	(787)				
Staphylococcus aureus	746		100										100			76	99	76	98	93			100	100	10
			(746)										(746)			(654)	(746)	(746)	(654)	(746)			(92)	(746)	(746)
Klebsiella species	617	99	90	<1				87	87		79	82	81				79			93	100	89	60		
		(617)	(617)	(617)				(617)	(617)		(617)	(617)	(295)				(617)			(617)	(617)	(617)	(322)		
																							96		
				(449)																			(309)		
Haemophilus influenzae	441		100	75	100					100					93		65								
			(441)	(441)	(441)					(441)					(441)		(441)								
Streptococcus agalactiae (Group B)	405			100												64		52							100
				(134)												(271)		(271)							(271)
MRSA	325												0			14	92	16	95	39			100	0	0
													(325)			(259)	(325)	(325)	(259)	(325)			(66)	(325)	(325)
Proteus mirabilis	216	100	89	41				92	92		90	92	76				60			82	100	81	0		
		(216)	(216)	(216)				(216)	(216)		(216)	(216)	(63)				(216)			(216)	(216)	(216)	(153)		
Coagulase negative Staphylococcus	5		80										80			100	100	100	80	100				80	0
			(5)										(5)			(5)	(5)	(5)	(5)	(5)				(5)	(5)

Data of count <30 may not be representative
Please refer to medical microbiologist for interpretation

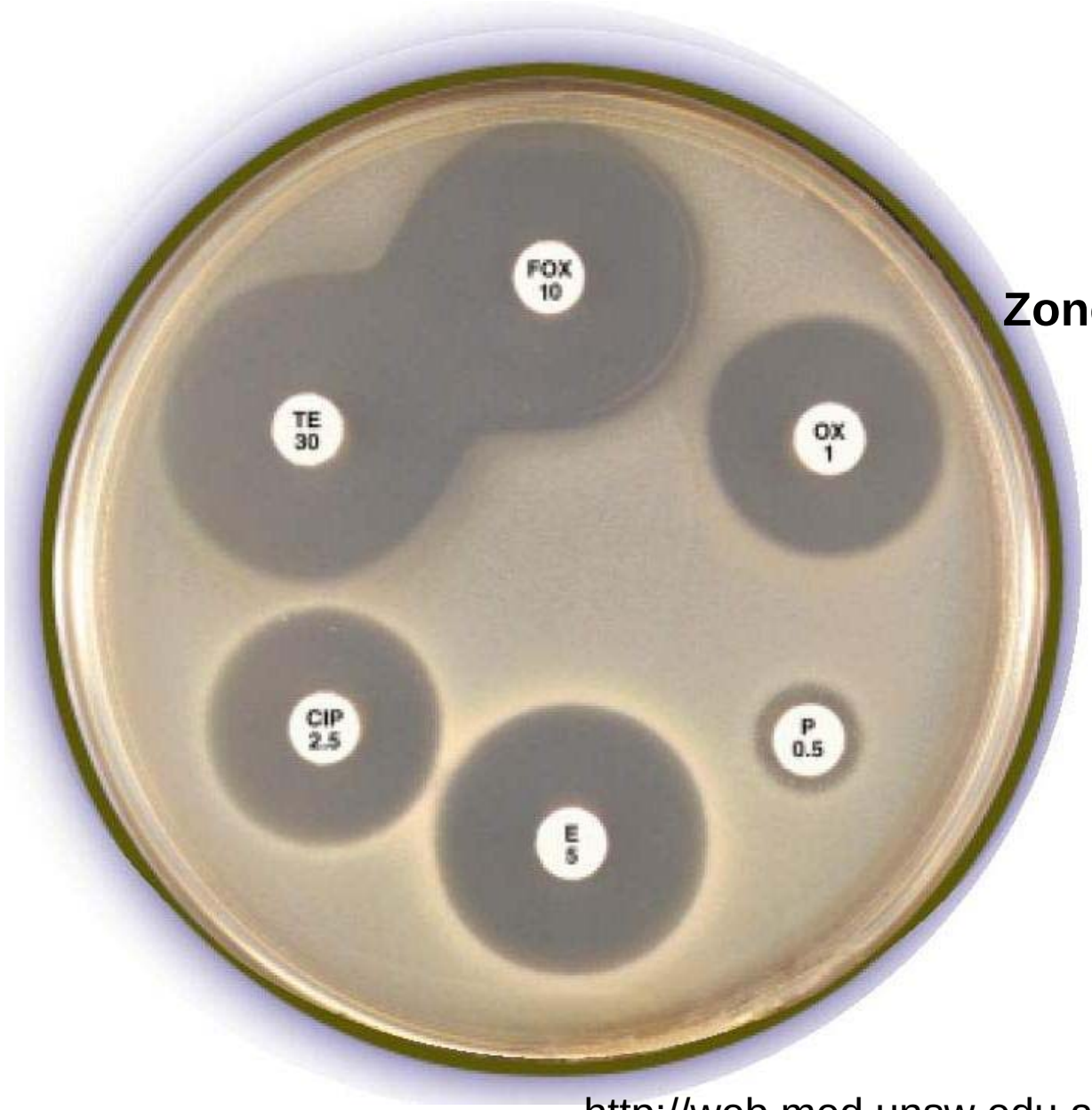
Carbapenem resistant Enterobacteriaceae (CRE)

Reduced susceptibility noted 2008, but test for carbapenemase negative

In HK, likely first case detected 2009

What is CRE

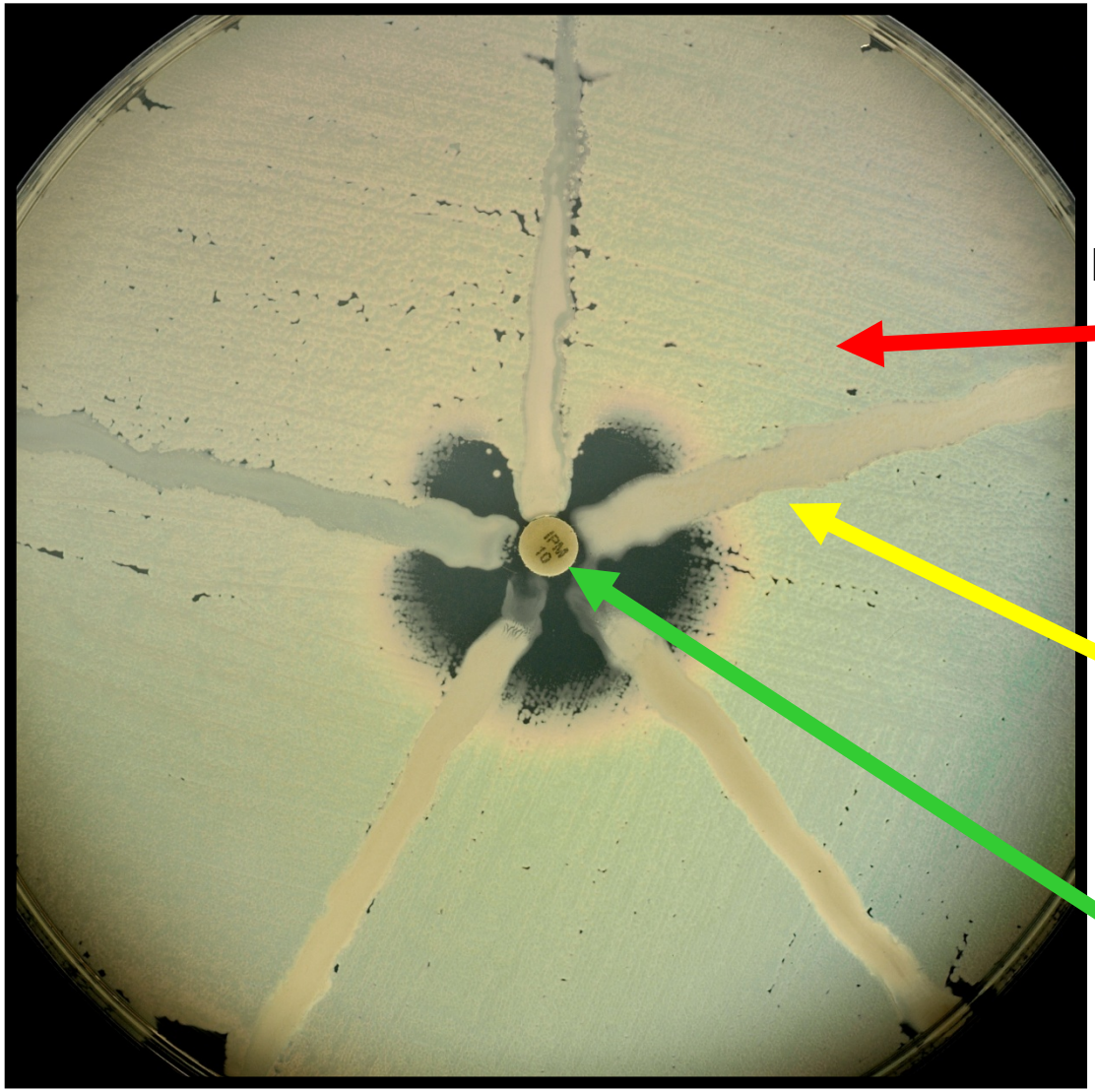
- Reduced susceptibility to Carbapenem
- Resistance mechanism
  - Porin loss + AmpC
  - Carbapenemase activity by MHT (false +ve possible)



Zone of inhibition

http://web.med.unsw.edu.au/pathology-cds/

Modified Hodge Test



Lawn of *E. coli* ATCC 25922
1:10 dilution of a
0.5 McFarland suspension

Test isolates

Imipenem disk

Described by Lee et al. CMI, 7, 88-102. 2001.

What is CRE

- Reduced susceptibility to Carbapenem
- Resistance mechanism
  - Porin loss + AmpC
  - Carbapenemase activity by MHT (false +ve possible)
  - Carbapenemase gene by PCR

Carbapenemases

Classification	Enzyme	Most Common Bacteria
Class A	KPC, SME, IMI, NMC, GES	Enterobacteriaceae (rare reports in *P. aeruginosa*)
Class B (metallo-β-lactamse)	IMP-4, VIM, GIM, SPM, NDM-1	*P. aeruginosa* Enterobacteriacea *Acinetobacter* spp.
Class D	OXA	*Acinetobacter* spp.

Why bother

- Risk of person to person transmission of E. coli
- Secondary transmission of E. coli O157 ~4%–16% (EID 1998)
- Infections are asymptomatic – detected as outbreak

- Carried in plasmid - what was once considered to be a problem of clonal spread has now become a global problem of interspecies dispersion.

CRKP (carbapenem resistant Klebsiella pneumoniae)

- Spreading & increasing
  - CRKP first described in North Carolina in 1999
  - Identified in 24 states and is recovered routinely in certain hospitals in New York and New Jersey now.

- Health-care--associated infections reported to CDC:
  CRKP in all *Klebsiella* isolates
  - 2000 <1%
  - 2007 8%

- Difficult to treat & Increase in mortality
  - Resistant to all beta-lactam
  - associated with increased mortality, length of stay, and increased cost

Europe carbapenem-resistant *Enterobacteriaceae*

- VIM-type MBLs and *K. pneumoniae* carbapenemases (KPC) are the most frequently isolated carbapenemases
- Overall, CRE are still rare causes of human infections in most parts of Europe, except for Greece and Cyprus

- 2009 European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS)
- carbapenem-resistance rates among invasive *K. pneumoniae* infections:
- Greece 43.5%
- Cyprus 17.0%
- Italy 1.3%
- Belgium 1.2%
- other 23 countries <1%

- Despite generally low rates, CRKP - cause of country-wide epidemics of HCAI in Greece, Israel, USA, Latin American countries and China, and of local outbreaks in Poland and Italy

www.eurosurveillance.org

Where are they come from?

Local

Imported

We describe two patients—one man aged 30 years and one woman aged 66 years—who were colonised with New Delhi metallo-β-lactamase-1 (NDM-1)-producing *Klebsiella pneumoniae* isolates after a journey to India during which they had no contact with health-care services.[1] In 2009, both patients returned from a low-budget holiday trip to India, where they visited, among other places, New Delhi. The patients ate and drank at local restaurants. They did not visit any medical-care facility but did take ciprofloxacin against enteritis. On their return,

Patient A
Urosepsis
ESBL+ *E. coli*

Patient B
Perianal abscess
MSSA
ESBL+ *E. coli*

Both
Rectal screening
CRKP

patient A was admitted to the hospital with urosepsis caused by an extended-spectrum β-lactamase (ESBL)-positive *Escherichia coli*, and patient B was admitted for treatment of a perianal abscess caused by a *Staphylococcus aureus* and an ESBL-positive *E coli*. The rectal screening cultures from both patients yielded carbapenem-resistant *K pneumoniae*. These strains caused no infections in the patients and there was no secondary transmission to other patients.

	Patient A		Patient B	
	MIC (mg/L)	Susceptibility*	MIC (mg/L)	Susceptibility*
Imipenem†	>32	R	>32	R
Meropenem†	>32	R	>32	R
Ertapenem†	>32	R	>32	R
Piperacillin–tazobactam	>32, 4	R	>32, 4	R
Cefuroxime	>64	R	>64	R
Cefotaxime	>8	R	>8	R
Ceftriaxone	>16	R	>16	R
Ceftazidim	>32	R	>32	R
Aztreonam	>32	R	>32	R
Ciprofloxacin	>4	R	>4	R
Gentamicin	>16	R	>16	R
Tobramycin	>4	R	>4	R
Amikacin	>16	R	>16	R
Cotrimoxazole	>8	R	>8	R
Nitrofurantoin	>64	R	>64	R
Tigecyclin	0·25	S	0·25	S
Colistin	≤1	S	≤1	S
Chloramphenicol	≤2	S	4	S

MIC=minimum inhibitory concentration. R=resistant. I=intermediate susceptible. S=susceptible
*Susceptibility defined by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints. †Tested by Etest: carbapenem MICs were all more than 32 mg/L. Tested by microbroth dilution: the MICs of strain A and B were for imipenem 2 (S) and 8 (I), meropenem 8 (I) and 16 (R), and ertapenem 2 (R) and 8 (R), respectively.

***Table*: Antimicrobial susceptibilities for NDM-1-positive *Klebsiella pneumoniae* isolated in patients A and B**

In many low-endemic countries, measures are taken to prevent the in-hospital spread of multiresistant strains by screening patients who received previous medical care in high-prevalence countries and subjecting them to barrier precautions awaiting the screening results. However, as shown in this study, travellers might also acquire carbapenemase-producing isolates with no history of medical care abroad; thus, this control strategy might fail. On admission, patients should therefore be asked whether they have recently travelled to India or Pakistan and, if positive, should be screened for NDM-1-positive enterobacteria. Additionally, because travel history is often unavailable, we advise screening of all enterobacteria isolated in the routine clinical laboratory for the

Tängdén . Foreign travel is a major risk factor for colonization with Escherichia coli producing CTX-M-type extended-spectrum beta-lactamases: a prospective study with Swedish volunteers. Antimicrob Agents Chemother. 2010 Sep;54(9):3564-8. Epub 2010 Jun 14. thomas.tangden@gmail.com

- Healthy volunteers traveling outside Northern Europe were enrolled.
- Rectal swabs and data on potential travel-associated risk factors were collected before and after traveling.
- A total of 105 volunteers were enrolled. Four did not complete the study, one carried ESBL+ *E. coli* before travel.
- 24 of 100 participants with negative pre-travel samples were colonized with ESBL-producing *E. coli* after the trip. (All CTX-M, mostly CTX-M-15). Co-resistance to several antibiotic subclasses was common.

Tängdén . Foreign travel is a major risk factor for colonization with Escherichia coli producing CTX-M-type extended-spectrum beta-lactamases: a prospective study with Swedish volunteers. Antimicrob Agents Chemother. 2010 Sep;54(9):3564-8. Epub 2010 Jun 14. thomas.tangden@gmail.com

- Risk factor acquisition of ESBLs
  - Travel to India the highest risk (88%; n = 7).
  - Gastroenteritis during the trip (P = 0.003).
- 5 of 21 volunteers completed the follow-up after 6 months had persistent colonization with ESBLs.
- This is the first prospective study demonstrating that international travel is a major risk factor for colonization with ESBL-producing Enterobacteriaceae.
- Considering the high acquisition rate of 24%, it is obvious that global efforts are needed to meet the emergence and spread of CTX-M enzymes and other antimicrobial resistances.

Hospital transmission

Preliminary evidence suggests that 13 of 77 patients from Italy and the UK were possible secondary cases linked to other hospitalised patients who had returned from India (Table 1). In Italy, two cases with no travel

hospital, an endoscope-related outbreak affected nine patients six month after a travel-associated case.

Progressive trend of resistance

- *Staphylococcus aureus*
- PSSA Penicillin
- PRSA Cloxacillin
- MRSA Vancomycin
- VISA Linezolid
- VRSA Linezolid

- *E. coli*
- *E. coli* Ampicillin
- β-lactamase Augmentin
- MDR Ceftazidime
- ESBL Carbapenem
- CRE Colistin

CRE

- For all acute care facilities,

  CDC and HICPAC recommend an aggressive infection control strategy, including managing all patients with CRE using contact precautions and implementing CLSI guidelines for detection of carbapenemase production.

HA CRE guideline

- Control
- Practical

Microsoft Word Document

ANTIMICROBIAL Stewardship Toolkit

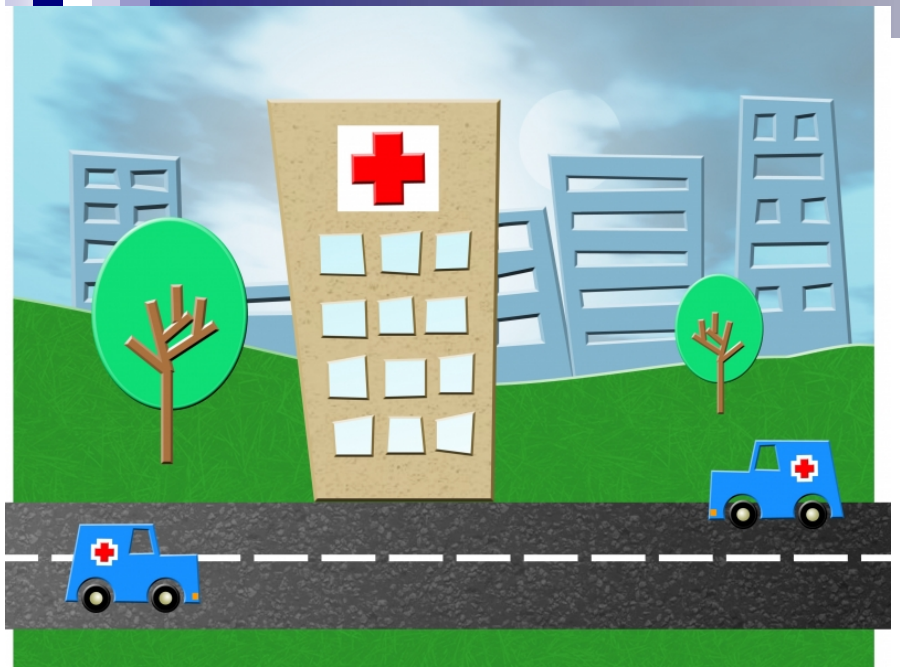
http://www.gnyha.org/UserFiles/Image/HomePage/antimicrobial.jpg

I Prudent antibiotic use

Antibiotic use and antibiotic resistance Hand in hand

http://whitememorial.com/images/residencies/pharmacy/ICU_rounds.jpg

Antibiotic Stewardship Program (ASP) should be in place to give advice on and monitor the appropriate use of antimicrobials in patient care.



http://news.wafti.org.uk/photos/UK/baby.jpg

II Early detection of CRE

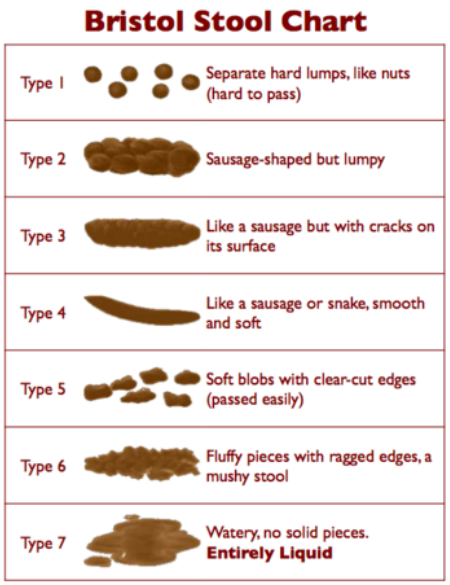
Laboratory detect resistance in clinical specimen

Active surveillance culture (ASC)

http://www.razor-gator.com/StaphPhotos/hospital_bed_large.jpg

hospitalized as in-patient outside Hong Kong in the last 6 months

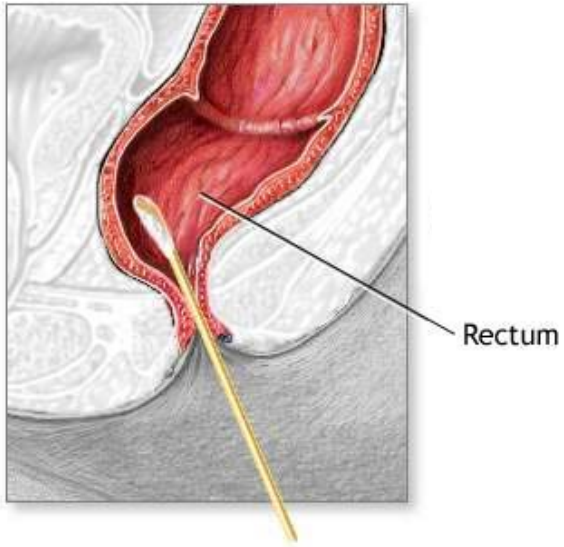
Patients staying in the same cubicle with any PCR +ve CRE case for ≥2 days and are still in the hospital should be screened for carriage



http://www.stop-heartburn-indigestion.com/image-files/bristol_stool_chart-350px456.png

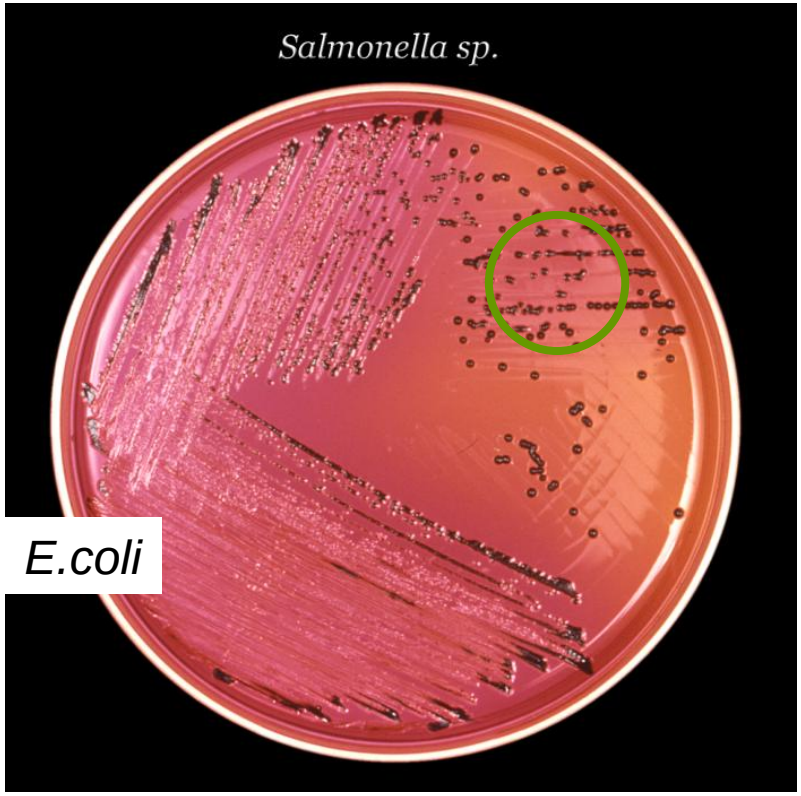
Image 3: Vancomycin minimum inhibitory concentration (MIC) E-test strip on a tap water agar. Density of bacterial growth is increased with increasing vancomycin concentration.

http://4.bp.blogspot.com/_qixgS1qi_5E/SHhC6syvOGI/AAAAAAAAADE/xi29AqkvWkg/s400/fig03.jpg



http://static.howstuffworks.com/gif/adam/images/en/rectal-culture-picture.jpg

Specified **“CRE screening”** in lab. request form



www.healthhype.com/microorganisms-types-harmf

http://www.consultantlive.com/image/image_gallery?img_id=1418906&t=1244053927771

Stool for culture vs stool for CRE screening

Screening of contact

- **Patient contact** (staying in the same cubicle with PCR +ve CRE case for ≥2 days) who has been discharged back to **RCHE**
- ICT to inform ICB
- *ICB nurse*

  - contact the discharged patient and the relevant RCHE

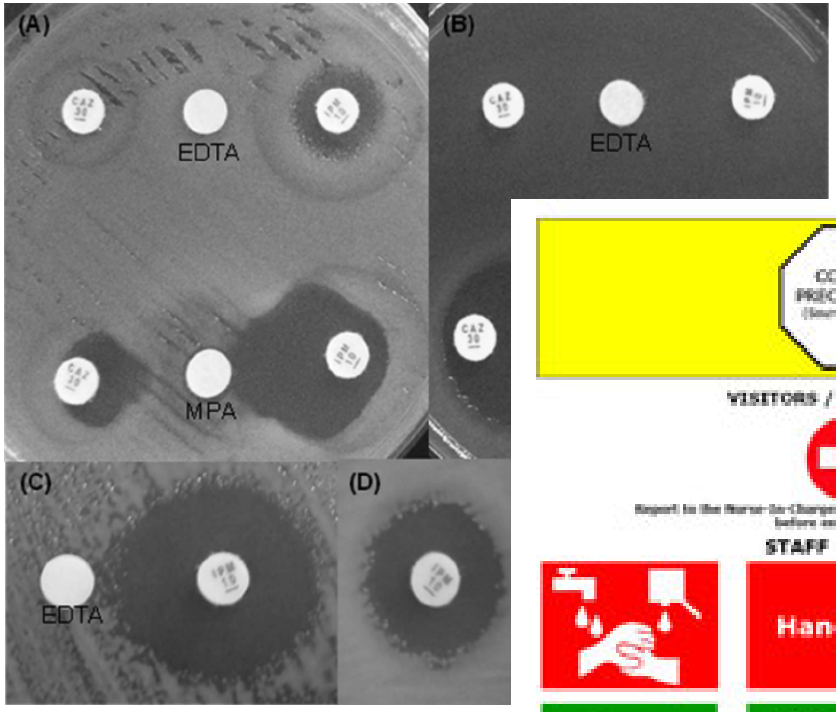
  - perform risk assessment

  - provide health advice specific to the setting of the RCHE

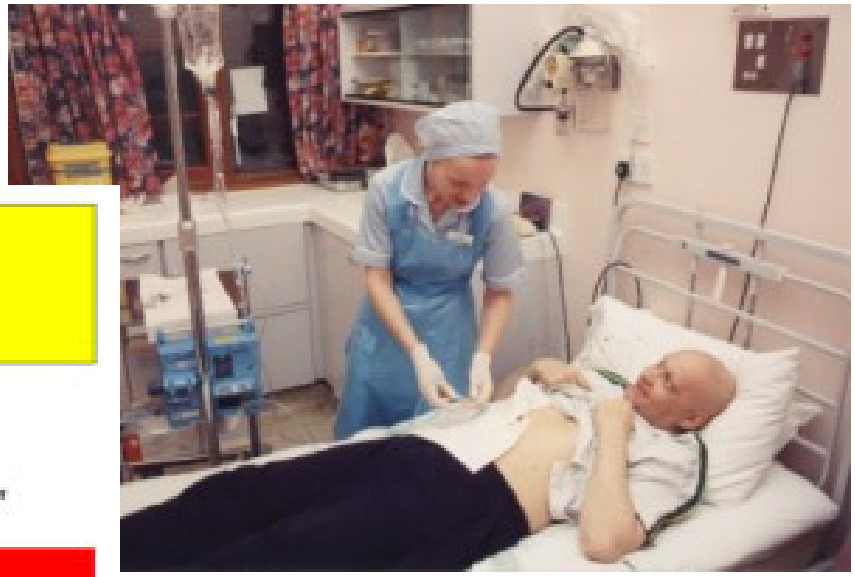
  - carry out other follow-up actions (e.g. screening) as necessary

  - If screening is recommended by ICB after risk assessment, CGAT of the RCHE will be asked to collect specimens from the patient. For those RCHEs without CGAT coverage, ICB nurse will arrange collection of the patient's specimens.
- Laboratories should follow established protocol on detection of CRE. Any CRE isolate should be sent to PHLC for PCR testing.

III Infection control measures *(apply to patient with carbapenemase producing CRE isolate and to be continued when PCR positive)*



http://jcm.asm.org/cgi/reprint/4



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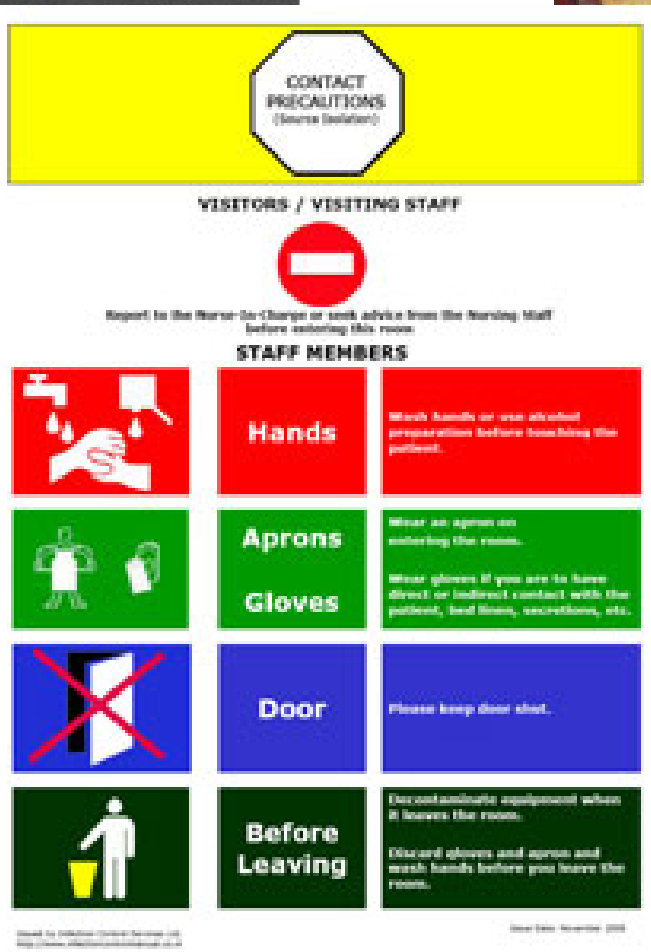

Lab. send isolate to PHLC for CRE PCR

www.infectioncontrolmanual.co.ni/principles/c...

III Infection control measures *(apply to any patient with carbapenemase producing CRE isolate e.g. MHT positive and to be continued when PCR positive)*

A. Single room isolation

- Preferred for patient with *carbapenemase producing CRE*.
- Should be for patient infected/colonized with a PCR +ve CRE isolate.
- Discontinue single room isolation when the infected site has been cleared of CRE and, eradication of carriage in gut, i.e. culture negative for at least 2 consecutive stool/ rectal swabs collected at 48 hours interval.

B. Contact Precautions

- Signage on Contact Precautions should be placed accordingly,
- Wear gown & gloves when direct contact with patient or his/her immediate environment / equipment is likely,
- Change gloves between tasks performed even on the same patient when contamination has occurred. Perform hand hygiene after removal of gloves.

C. Hand hygiene:

- Perform hand hygiene before and after touching the patient, before aseptic procedures, after body fluid exposure and after touching the patient's surroundings.
- Alcohol-based hand-rub should be placed at the patient's bedside.

D. Patient care equipment

- Dedicate non-disposable items (e.g. stethoscopes, blood pressure cuffs, wheelchairs, physiotherapy equipment, and trolleys) for single patient use.
- These items should be properly disinfected before use on another patient.

http://greenwoodenvironmental.typepad.com/.a/6a01156f7046e5970c0115706cef41970b-800wi

III Infection control measures *(apply to any patient with carbapenemase producing CRE isolate e.g. MHT positive and to be continued when PCR positive)*

E. Environmental decontamination

- Frequent cleansing (i.e. at least twice daily) is recommended for "high-touch" surfaces (e.g. doorknobs and bedrails) with freshly prepared disinfectant (e.g. 1:49 diluted 5.25% sodium hypochlorite solution; or 70% alcohol for metallic surfaces).
- Adopt a system of environmental cleansing for isolation case which could be differentiated from other patients. Disposable wipe can be an option.
- Provide training to designated staff, with a standard protocol, on environmental decontamination. Monitoring on compliance should be conducted.
- For PCR positive case, perform terminal environmental cleansing after the transfer out of the patient.

F. Minimize patient transport. Perform procedures at the patient's bedside where possible. Otherwise, thorough cleansing and disinfection should be done on the area after use by the patient.

G. Visitors should be advised to observe the appropriate infection control precautions according to the extent of contact with the patient.

H. Effective and reliable decolonization therapy for carriers is not available and cannot be recommended at present.

IV Alerts and Reporting

http://www.mdrelay.org/images/CapTelphone.jpg

http://www.personal.psu.edu/aes284/twtc/images/computer.jpg

Inform the Chief Infection Control Officer's (CICO) Office

- patient with PCR +ve CRE
- when an outbreak of CRE is suspected.

Label in the CMS alert by ICT

- 'Carbapenamase producing Enterobacteriaceae detected' for patient with CRE tested positive by the MHT
- Revise CMS alert to "CRE PCR +ve" if PCR tested positive.

The alert should be removed when the patient has been eradicated of CRE.

When CRE PCR +ve patient is re-admitted, take appropriate infection control precautions and inform the ICT.

V Patient transfer / discharge arrangements

- Inform ICT on inter-hospital or intra-hospital transfer of CRE PCR +ve patient.
- Receiving ward and the NEAT team should be informed of CRE in the patient and the need for contact precautions.
- Terminal cleansing and disinfection of the room should be performed upon discharge of the patient.

V Patient transfer / discharge arrangements

http://blog.galenhealthcare.com/wp-content/uploads/2010/1

Patients from institutions (e.g. RCHE) with CRE PCR +ve can be discharged:

1) When screening cultures taken consecutively at 48 hours interval were negative

給感染或帶有多重抗藥性細菌病人的資料單張和出院指導

多重抗藥性細菌的種類

細菌的抗藥性是指抗生素未能有效抑制或殺死細菌，導致細菌所引起的感染難以治癒。多重抗藥性細菌是指一些以多種常用抗生素治療，也不能治癒的細菌。雖然現時仍可使用其他抗生素予以治療，但是這些抗生素的效能可能較弱或會引起較多的副作用。以下是常見多重抗藥性細菌的例子：

1. 抗甲氧西林金黃葡萄球菌 (一般稱爲耐藥性金黃葡萄球菌) / 萬古霉素中介耐藥性金黃葡萄球菌/抗萬古霉素金黃葡萄球菌 (MRSA/VISA/VRSA)
2. 超廣譜β-內酰胺酶耐藥性細菌 (ESBL)
3. 抗萬古霉素腸道鏈球菌 (VRE)
4. 抗碳青霉烯腸道桿菌 (CRE)
5. 抗碳青霉烯鮑氏不動桿菌 / 耐多藥鮑氏不動桿菌 (CRA/MDRA)
6. 耐多藥絲膿假單胞菌 (MRPA)

病徵

多重抗藥性細菌可導致各類型與醫護環境相關的感染，如肺炎、尿道感染、傷口感染以至菌血症。雖然多重抗藥性細菌可寄存於沒有感染症狀的人士身上多月甚或多年，但它們較易入侵免疫力較弱或病情危殆的病患者，並引發感染。這些高危人士在感染後的情況一般較爲嚴重，或會致命，往往治療方法的選擇亦是有限。

傳染病，通常透過直接接觸受污染的物件、環境或人與人之間
欠佳可導致多重抗藥性細菌在醫院環境和社區之間廣泛及交叉傳播。其他因素包括皮膚損傷/傷口、或擠迫的環境等，亦有助於散播這些細菌。

一般感染控制措施

要預防及控制多重抗藥性細菌散播，醫護人員、病人及其家屬需特別留意並履行下列事項：

1 保持良好的個人衛生，例如每天更換衣服及洗澡。

頁3之1

2) With education pamphlet

3) Inform ICB before discharging the patient

V Patient transfer / discharge arrangements

- Asymptomatic patients with CRE prolonged carriage (e.g. 8 weeks or more)

  - should be risk assessed jointly by the hospital ICT, CICO and ICB before discharge back to RCHE.

V Patient transfer / discharge arrangements

- Patient o be discharged home should be given the education pamphlet on infection control precautions.
- CRE PCR +ve patients who are only identified after discharge from hospital should be contacted for information and education on infection control precautions.

Information sheet and discharge advice for the patient with Multiple-Drugs Resistant Organisms (MDROs) infection or colonization

Adobe Acrobat 7.0 Document

Adobe Acrobat 7.0 Document

Thank you