Workshop on Control of multi-drug resistant organisms (MDRO) in healthcare settings

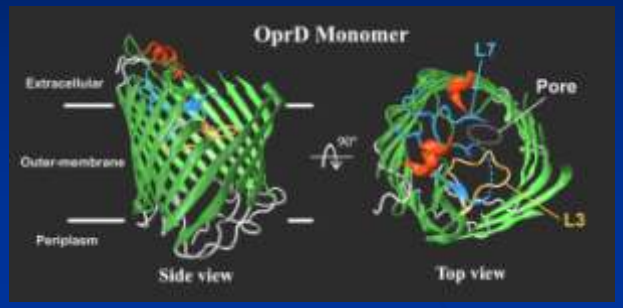
CRE in Hong Kong

1 March 2011
Lecture Theatre, Centre for Health Protection
Dr WK Luk

Carbapenem

- Imipenem
- Meropenem
- Ertapenem
- Doripenem
- Panipenem
- OprD (vs OmpC)
- Bind penicillin binding protein
- Broad spectrum – GP; GN; Anaerobic
- Stable to β-lactamase
- Main antibiotic for organism producing ESBL

Carbapenem Resistant Enterobacteriaceae CRE



www.pdbj.org/eprots/index_en.cgi?PDB%3A2ODJ

- Resistance mechanism

  1. Porin loss with β-lactamase

  2. Carbapenemase (MHT; combination disc, PCR)

  Other genera

  3. Efflux

  4. Change in penicillin binding protein

Carbapenemase genes

Carbapenemase genes.

Ambler Class A	9 families (KPC, SME, NMC-A, IMI, PER, GES, SFO, SFC, IBC)
Ambler Class B	6 families (VIM, GIM, SIM, NDM, IMP, SPM)
Ambler Class D	2 families (OXA, PSE)

World-wide epidemiology

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 hospital 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

Emerging CRE

- Many are colonisers and infection in community
- India Enterobacteriaceae ESBLs 70 - 90%, widespread use of antibiotics such as carbapenems necessary
- growing prevalence of ESBL producers
- drive a greater reliance on carbapenems.
- selection pressure for carbapenem resistance in Enterobacteriaceae,
- *Klebsiella pneumoniae* clones with KPC carbapenemase are a major problem in the USA, Greece, and Israel
- VIM metallo-carbapenemase have disseminated among *K pneumoniae* in Greece.

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

Karthikeyan K Kumarasamy, Mark A Toleman, Timothy R Walsh, Jay Bagaria, Fafhana Butt, Ravikumar Balakrishnan, Uma Chaudhary, Michel Doumith, Christian G Giske, Seema Irfan, Padma Krishnan, Anil V Kumar, Sunil Maharjan, Shazad Mushtaq, Tabassum Noorie, David L Paterson, Andrew Pearson, Claire Perry, Rachel Pike, Bhargavi Rao, Ujjwayini Ray, Jayanta B Sarma, Madhu Sharma, Elizabeth Sheridan, Mandayam A Thirunarayan, Jane Turton, Supriya Upadhyay, Marina Warner, William Welfare, David M Livermore, Neil Woodford

Lancet Infect Dis 2010; 10: 597–602

Published Online August 11, 2010

Summary

Background Gram-negative Enterobacteriaceae with resistance to carbapenem conferred by New Delhi metallo-β-lactamase 1 (NDM-1) are potentially a major global health problem. We investigated the prevalence of NDM-1, in multidrug-resistant Enterobacteriaceae in India, Pakistan, and the UK.

	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**

Medical Tourism

- an emerging trend worldwide
- all age groups traveling abroad to seek low-cost yet first-class medical treatments.
- US and UK top the list of health tourists traveling to Brazil, Hong Kong and India for medical treatments
- ~ 500,000 US citizens traveled out of the country to seek medical and dental treatments in 2005.
- the number is on a constant high
- getting treatments done at a fraction of cost
- also beating the long wait lists
- get to explore an exotic destination

http://www.futureyears.com/health/medical-tourism/hong-kong/

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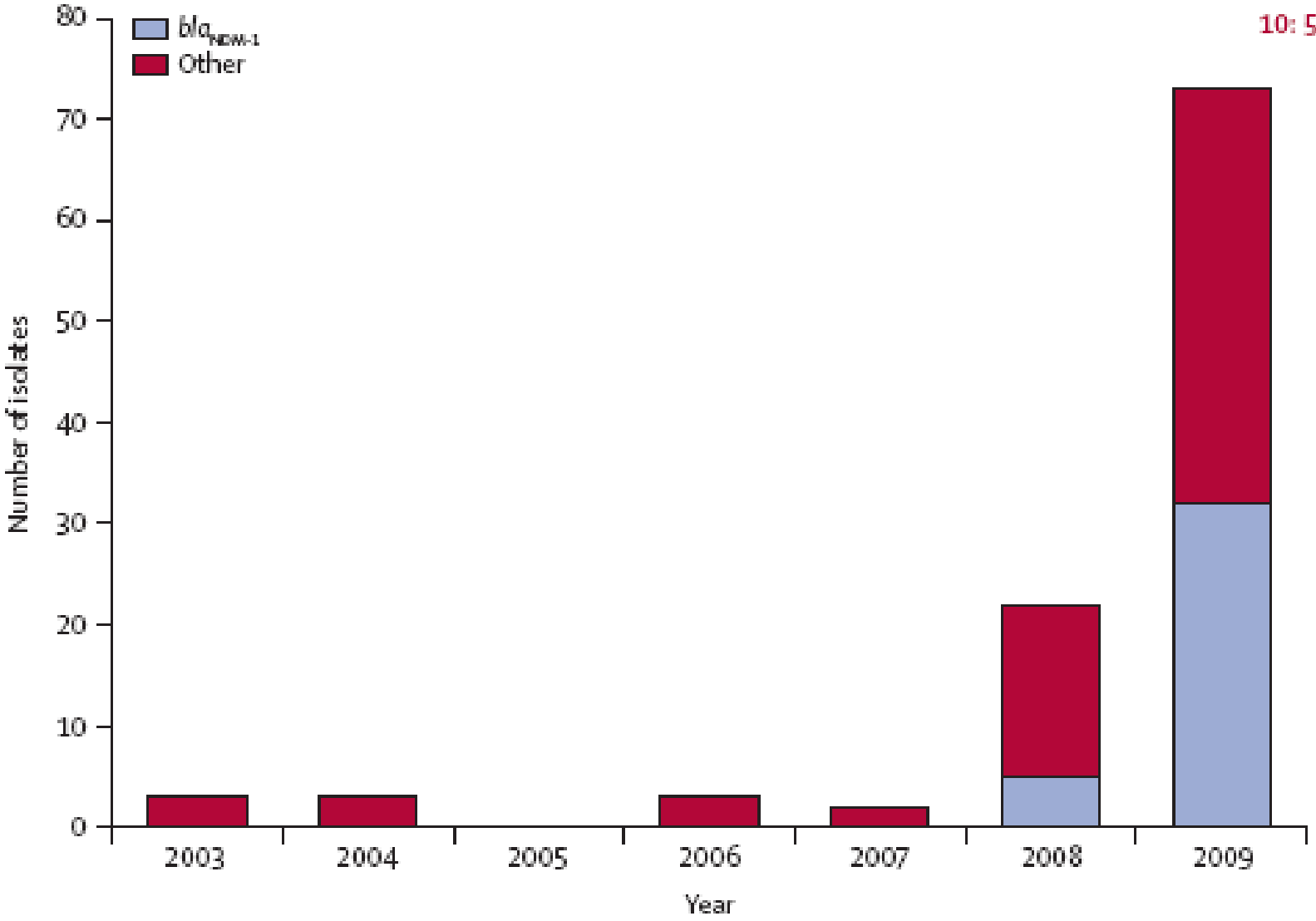


Figure 1: Numbers of carbapenemase-producing Enterobacteriaceae referred from UK laboratories to the UK Health Protection Agency's national reference laboratory from 2003 to 2009

The predominant gene is bla_{NDM-1}, which was first identified in 2008. The other group includes diverse producers of KPC, OXA-48, IMP, and VIM enzymes.

Division of Clinical Microbiology and Infection

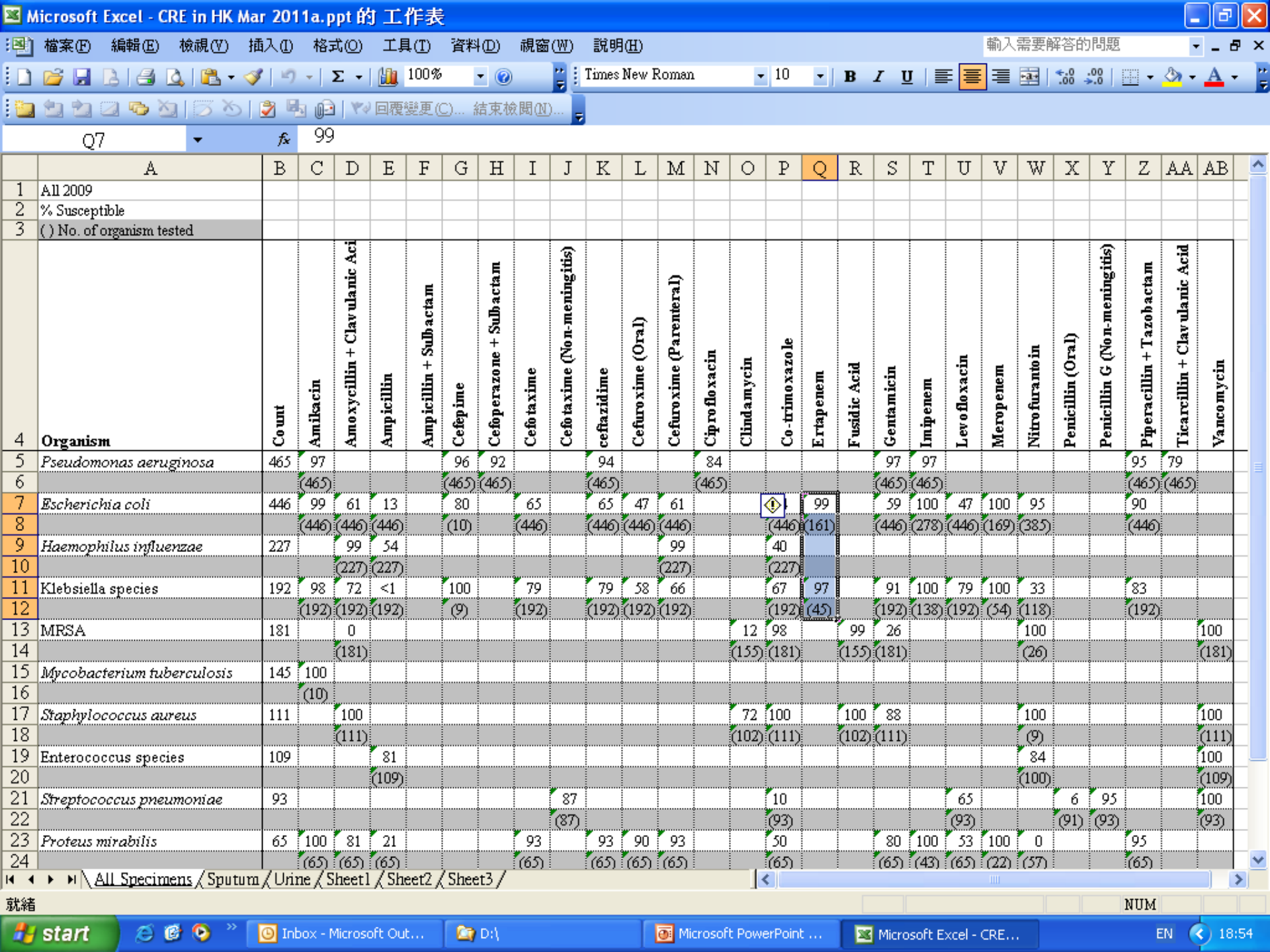
Antibiogram 2006 (All specimen)

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



Microsoft Excel - CRE in HK Mar 2011a.ppt 的 工作表

檔案(F) 編輯(E) 檢視(V) 插入(I) 格式(O) 工具(T) 資料(D) 視窗(W) 說明(H)

輸入需要解答的問題

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回覆變更(C)... 結束檢閱(N)...

Q7 99

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB
1	All 2009																											
2	% Susceptible																											
3	( ) No. of organism tested																											
4	**Organism**	**Count**	**Amikacin**	**Amoxycillin + Clavulanic Aci**	**Ampicillin**	**Ampicillin + Sulbactam**	**Cefepime**	**Cefoperazone + Sulbactam**	**Cefotaxime**	**Cefotaxime (Non-meningitis)**	**ceftazidime**	**Cefuroxime (Oral)**	**Cefuroxime (Parenteral)**	**Ciprofloxacin**	**Clindamycin**	**Co-trimoxazole**	**Ertapenem**	**Fusidic Acid**	**Gentamicin**	**Imipenem**	**Levofloxacin**	**Meropenem**	**Nitrofurantoin**	**Penicillin (Oral)**	**Penicillin G (Non-meningitis)**	**Piperacillin + Tazobactam**	**Ticarcillin + Clavulanic Acid**	**Vancomycin**
5	*Pseudomonas aeruginosa*	465	97				96	92			94			84					97	97						95	79	
6			(465)				(465)	(465)			(465)			(465)					(465)	(465)						(465)	(465)	
7	*Escherichia coli*	446	99	61	13		80		65		65	47	61				99		59	100	47	100	95			90		
8			(446)	(446)	(446)		(10)		(446)		(446)	(446)	(446)			(446)	(161)		(446)	(278)	(446)	(169)	(385)			(446)		
9	*Haemophilus influenzae*	227		99	54								99			40												
10				(227)	(227)								(227)			(227)												
11	Klebsiella species	192	98	72	<1		100		79		79	58	66			67	97		91	100	79	100	33			83		
12			(192)	(192)	(192)		(9)		(192)		(192)	(192)	(192)			(192)	(45)		(192)	(138)	(192)	(54)	(118)			(192)		
13	MRSA	181		0											12	98		99	26				100					100
14				(181)											(155)	(181)		(155)	(181)				(26)					(181)
15	*Mycobacterium tuberculosis*	145	100																									
16			(10)																									
17	*Staphylococcus aureus*	111		100											72	100		100	88				100					100
18				(111)											(102)	(111)		(102)	(111)				(9)					(111)
19	Enterococcus species	109			81																		84					100
20					(109)																		(100)					(109)
21	*Streptococcus pneumoniae*	93								87						10					65			6	95			100
22										(87)						(93)					(93)			(91)	(93)			(93)
23	*Proteus mirabilis*	65	100	81	21				93		93	90	93			50			80	100	53	100	0			95		
24			(65)	(65)	(65)				(65)		(65)	(65)	(65)			(65)			(65)	(43)	(65)	(22)	(57)			(65)		

All Specimens / Sputum / Urine / Sheet1 / Sheet2 / Sheet3

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MDRO situations in HA hospitals 2009 - 2010

Incidence	MRSA BSI	VRSA	VRE	ESBL +NR	CRE/ CRE PCR +ve	CRA/ MDRA	CRPA/ MRPA
2009	0.17 /1000 acute bed days	No	0.2% Sporadic outbreaks in hospitals	20-25%	0.05 to 0.07% / NA	39% MDRA= 2.6 to 4%	4.75% MRPA= 0.1%
2010	0.15 / 1000 acute bed days	No	0.4% (3 outbreaks involved 28 patients)	20-25%	0.19% / 13 cases	39% MDRA= 2.1%	4.62% MRPA= 0.1%
Trend	**Decreasing (12%↓cf 2009; 21%↓ cf 2007)**	**No**	**Slightly increasing**	**stable**	**Low but increasing**	**CRA: Stable MDRA: Slightly decreasing**	**stable**

MRPA=concomitant R to Imipenem, Ceftazidime, Amikacin and Ciprofloxacin

MDRA= concomitant R to Fluoroquinolones, Aminoglycosides, Cephalosporins and BL/BLase inhibitor combinations

末日惡菌親屬 在港爆發

【本報訊】本港再有病人帶有超級惡菌，衛生防護中心首次確認含有超級抗藥能力的肺炎克雷伯桿菌，包括一名曾在內地入院的港人及另一男子，兩人帶有惡菌而未有發病。

衛生防護中心專責小組，監控末 惡菌 NDM-1 在港情況以來，首次 KPC 碳青霉烯酶基因 及兩名公

另一名因腹痛在聯合醫院治療的24歲男子，尿液含有該抗藥惡菌，但他沒有出現尿道感染症狀，顯示惡菌只寄生在體內，病人並無外遊。

港大感染及傳染病中心總監何栢良表示，這種抗藥惡菌與末日惡菌同屬一個家族，現時只有兩種抗生素有效治療。他估計該名曾入住內地醫院的男子，是在內地醫院感染惡菌。至於24歲的男病人則屬社區感染，容

醫管局監察

【本報訊】本港病菌抗藥問題惡化，公立醫院數據顯示，抗碳青霉烯鮑氏不動桿菌越來越普遍，去年比率已達四成；包括末日惡菌 NDM-1 大腸桿菌在內的新型抗藥惡菌，去年也佔腸桿菌樣本的 0.05%，醫管局專家指，醫院內環境擠逼病人容易交叉感染，殺傷力不容忽視。

碳青霉烯（Carbapenem）屬於「重鎗」抗生素之一，桿 [illegible]，對這種抗生素呈抗藥性的樣本 [illegible] 種抗生 [illegible] 不動桿 [illegible]

樣本 [illegible] 近年 [illegible]

新種抗藥惡菌入血擺命

殺入社區無徵狀 公院兩人中招

【本報訊】再有新品種抗藥惡菌殺入本港！衛生防護中心首次發現兩名公立醫院病人帶有的肺炎克雷伯桿菌，含一種全新抗藥基因「KPC」，對常用的二線抗生素碳青霉烯類抗藥。兩人雖帶菌但無病發，其中一人已出院。港大感染及傳染病中心總監何栢良指，新惡菌已殺入社區，一般人帶菌可毫無徵狀，但「趁你病攞你命」，一旦入血隨時致命，促請當局加強監察。

KPC基因 經口糞傳播

其中一名帶菌的瑪麗醫院六十六歲男病人，上月曾入住上海一間醫院，其肛門樣本培植出含KPC基因的肺炎克雷伯桿菌。此菌為腸道細菌，主要經口糞傳播，病人現於東華醫院隔離，情況穩定。另一名廿四歲男病人因腹痛及腹瀉入聯合醫院，尿液樣本含同一惡菌，但未致尿道炎。病人最近無外遊，院方無使用抗生素，其病徵消退後已康復出院。化驗顯示，病人體內惡菌對抗生素慶大霉素有反應。

防護中心指出，兩宗個案無關連，目前世界各地均有發現KPC惡菌報告，包括歐美及內地，預計本港繼續有零星個案。該中心已設立監察系統，跟進惡菌散播情況。

何栢良懷疑該名六十六歲病人在內地中招，將惡菌帶入本港，但廿四歲病人無外遊史，反映他在社區感染。

他認為，兩宗個案或只屬冰山一角，促請當局加強監控，建議各公院為所有剛外遊返港的入院病人測試有否帶惡菌；「惡菌若在社區落地生根，比爆發流感或諾如病毒，對醫療系統打擊更大」。

惡菌隨時攻陷 公院急訂措

【本報訊】本港抗藥性惡菌正迅速擴散，醫管局鎖定的七種目標惡菌中，三惡菌有上升趨勢，但公立醫院「把關」措施不一，可能隨時被惡菌攻陷，構思將公院的感染控制措施規範化，設定「最低設防」指引，包括使用隔離病房、在病歷列明是否感染惡菌等。

疾衛生防護中心早前公布「十大惡菌排行榜」，顯示抗藥性惡菌有變種的風險，而七種常在公立醫院出現的惡菌中，醫管局發現三種有上升趨勢，包括碳青黴烯酶抗腸桿菌（CRE）、抗碳青霉烯鮑氏不動桿菌（CRAB）及革蘭氏陰性菌（ESBL+NR）。其中CRAB有明顯上升趨勢，醫管局化驗室樣本顯示，佔整體樣本三成九，而多樣化抗藥性鮑氏不動桿菌，亦佔整體樣本的百分之四。

惡菌入侵 醫護不察

醫管局總感染控制主任曾艾社說，醫院在感染控制仍有進步空間，有時惡菌入侵醫院後，醫護人員亦沒有察覺，「可能與醫護人手不足，病徵不明顯，即不少病人沒有發病，只算是帶菌者，以及交叉感染有關」。

醫管局構思將公立醫院的感染控制措施規範化，希望最快可在未來一、兩個星期落實。曾艾社說：「每間醫院都有感染控制措施，但大家的標準不同」，計劃將感染控制措施規範化，設定「最低設防」指引，要求各醫院至少做到指引的要求，再因應院內實際的情況，如惡菌感染率，可以自行增加感染控制措施。

醫管制定 設防指引

醫管局因應惡菌的傳播率、致命性，制定「最低設防」指引。曾艾社說，包括如何使用隔離病房、在病歷上列明病人是否感染惡菌，並將部分惡菌樣本轉交衛生防護中心化驗。他表示，受感染的病人有一套專門的治療用具，包括抽血帶、聽診器、血壓計等，減低交叉感染風險。

衛生防護中心成立的監測抗藥性細菌專家小組今日舉行首次會議。港大感染及傳染病中心總監何栢良表示，期望日後的監測範圍，可擴闊至私家醫院和動物飼養的層面。

他說，以往市民低估抗藥性惡菌對病人的影響，專家小組的工作重點是要讓市民及醫學界，了解抗藥性惡菌的來源，細菌對哪些常用抗生素有抗藥反應等，以便採取相應策略。衛生防護中心總監曾浩輝亦說，期望專家統一抗藥性的定義，全面收集數據後，半年內對本港抗藥惡菌的情況掌握得更好。

▲醫管局因應惡菌的傳播率、致命性，料制定「最低設防」指引

Epidemiology in HK

- All along, routine test for carbapenem resistance in isolates from clinical specimen
- Carbapenem resistant noted in 2008, further test showed not related to carbapenemase
- Carbapenemase - First detected case in 2009

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Review

Guideline for phenotypic screening and confirmation of carbapenemases in Enterobacteriaceae

James Cohen Stuart[a,*], Maurine A. Leverstein-Van Hall[a,b], on behalf of members of the Dutch Working Party on the Detection of Highly Resistant Microorganisms[1]

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Carbapenemase genes detected by PHLC (nucleotide sequencing if PCR +)

Carbapenemase genes.

Ambler Class A	9 families (KPC, SME, NMC-A, IMI, PER, GES, SFO, SFC, IBC)
Ambler Class B	6 families (VIM, GIM, SIM, NDM, IMP, SPM)
Ambler Class D	2 families (OXA, PSE)

Carbapenemases in Enterobacteria, Hong Kong, China, 2009

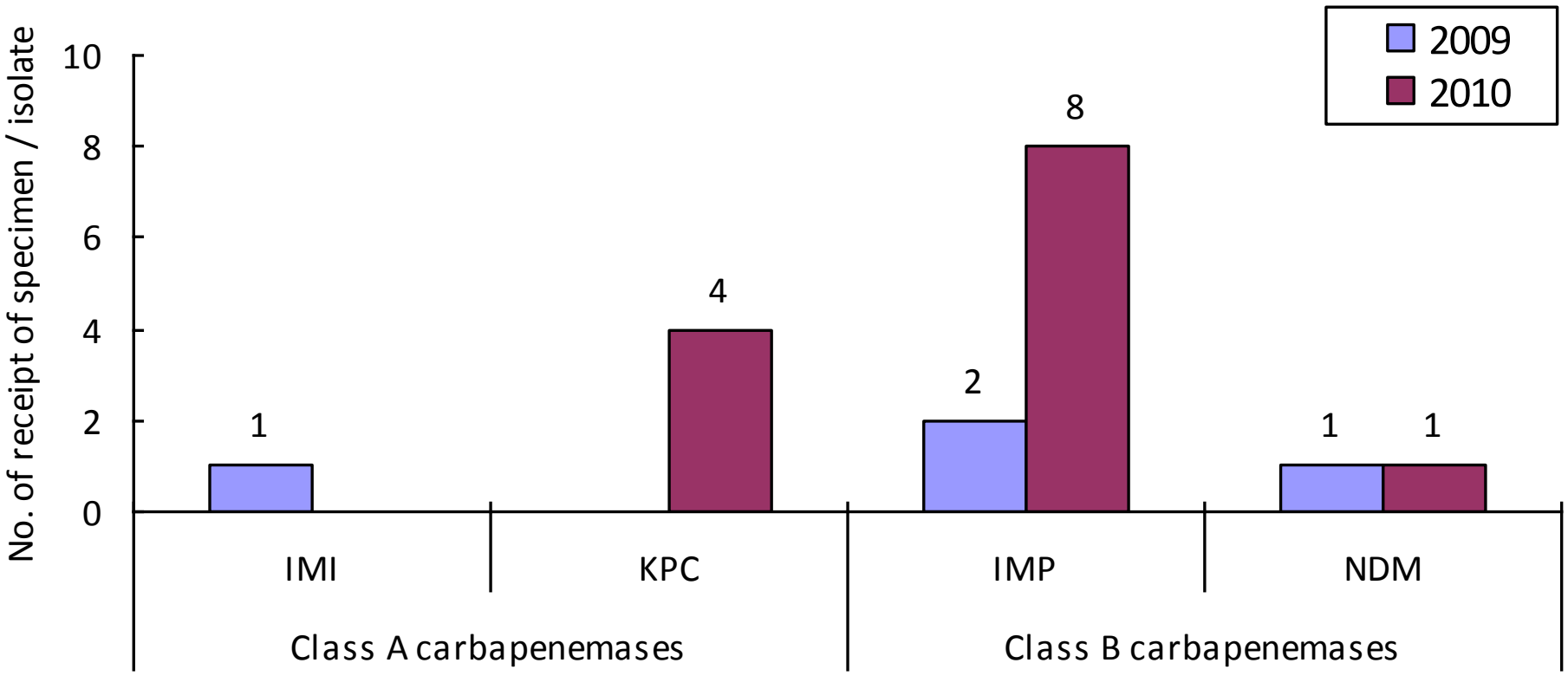
Table. Antimicrobial susceptibility results and ESBL detected for 4 carbapenemase-haboring enterobacteria isolates, Hong Kong, 2009*

Organism	Patient age, y/ sex	Patient location	Specimen	MIC, μg/mL (CLSI breakpoint for resistance)†									ESBL/ carbapenemase detected
				IMP (≥4)	MEM (≥4)	ERT (≥1)	NA (≥32)	CIP (≥4)	NIT (≥128)	AK (≥64)	GN (≥16)	SXT (≥80)	
Citrobacter freundii	69/M	Hospital	Sputum	8	≥16	≥8	≥32	≥4	128	≤2	8	≥320	IMP-4, CTX-M-9
Klebsiella pneumoniae	60/M	Hospital	Bedsore	≥16	≥16	≥8	≥32	≥4	≥512	16	≤1	≥320	IMP-4
Enterobacter cloacae	68/F	Hospital	Urine	≥16	≥16	≥8	4	≤0.25	64	≤2	≤1	≤20	IMI-3
Escherichia coli	64/M	Outpatient clinic	Urine	4	2	4	≤2	≤0.25	≤16	8	≥16	≤20	NDM-1

*ESBL, extended-spectrum β-lactamase; IMP, imipenem; MEM,meropenem; ERT, ertapenem; NA, nalidixic acid; CIP, ciprofloxacin; NIT, nitrofurantoin; AK, amikacin; GN, gentamicin; SXT, co-trimoxazole; NDM-1, New Delhi metallo-β-lactamase.
†CLSI, Clinical and Laboratory Standards Institute, updated June 2010.

Chu YW. EID Jan 2011

Enterobacteriaceae with reduced susceptibility to carbapenems mediated by various molecular classes of carbapenemases
2009 - 2010



Carbapenemase by PCR	2009	2010
	4	13

CHP

末日惡菌06年已「登陸」香港

【記者陳凱迎報道】屬末日惡菌家族的帶碳青霉烯酶基因肺炎克雷伯桿菌（KPC），原來早在06年已「登陸」香港。一名經常往返港美並曾於美國切除膽囊的75歲女士，當年被發現其尿液樣本帶有KPC，相信她於美國感染惡菌但無病發；專家指，帶惡菌者一旦入院，有機會於本港醫院內造成爆發，對免疫力較差的病人帶來極大威脅。

本港首宗末日惡菌（NDM-1）個案在09年錄得，但其實相類的惡菌早已靜悄悄地傳入本港。該名帶有KPC的女士本身患有高血壓和糖尿病，在05年曾於紐約切除膽囊，回港後到本港的普通科門診覆診，06年8月尿液樣本被發現帶有對多種藥物呈抗藥性的KPC，但她本身毫無症狀，白血球數量亦正常，毋須處方抗生素，只被提醒要注意個人衛生。經基因檢測，發現上述女士帶有的惡菌，與於美國常見的KPC類似，相信該女士是於美國感染惡菌。

患者入院播惡菌

負責進行檢測的港大感染及傳染病中心總監何栢良指出，曾於外地入院的病人感染惡菌後雖未必有病徵，但他們回港後可於社區傳播惡菌，一旦入住本港醫院更有機會造成院內爆發，對於免疫力較低的病人，例如已接受器官或骨髓移植的病人，會造成極大威脅。

港院發現四個案

事實上，本港公立醫院在去年便發現四宗帶有KPC的個案，當中三人曾於外地接受醫療程序，餘下的一宗個案並無外遊紀錄，但曾因腹痛入住本地三間公立醫院，其中一家公院曾接收帶KPC病人，懷疑該個案因此間接感染惡菌。為防惡菌爆發，醫管局由去年12月起，主動為在入院前一年曾於外地接受治療的病人抽樣本檢測，以確定他們是否帶有惡菌。

2009-2010

www.factsabouthongkong.com/hongkongmaps.htm

Clinical Features

- Many from clinical specimen of hospitalised patient
- Specimen types include urine, bile, wound, sputum
- Mostly colonisation
- KPC, IMP no recent history of travel
- NDM-1 history of travel to India

Health Protection Report
weekly report

Volume 3 Number 4 Published on: 30 January 2009

Current News

- Case of viral haemorrhagic fever in traveller recently returned from Nigeria
- National Resistance Alert: carbapenemases in Enterobacteriaceae
- Call for applications for European intervention epidemiology fellowships

Microbiologists should be suspicious of any Enterobacteriaceae isolate with resistance or reduced susceptibility to carbapenems, except for *Proteus* and *Morganella* spp. with borderline resistance to imipenem only (an inherent trait of these genera) and *Enterobacter* spp., eight with borderline resistance to ertapenem only (usually associated with high level chromosomal β-lactamase expression). Suspect isolates should be sent to ARMRL for further investigation. Based on current experience, most will prove to have resistance contingent on combinations of an ESBL or AmpC β-lactamase together with impermeability but a minority will be confirmed as carbapenemase producers. Where these enzymes are found we urge the need for stringent infection control and the Centre for Infections Laboratory of Healthcare-Associated Infection will be happy to advise on this aspect. It should be stressed that producers can be difficult to recognize. The *K. pneumoniae* clone with the KPC carbapenemase is typically susceptible only to gentamicin, tigecycline and polymyxins and has clear resistance to all carbapenems, but many other producers have only low-level resistance and variable (though usually considerable) resistance to other agents. Laboratories should be especially alert to carbapenem-resistant isolates from patients with a history of hospitalization in countries where carbapenemase-producing Enterobacteriaceae are prevalent – particularly Greece, Turkey, Israel and the USA, as these have been a repeated source of introduction to the UK.

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 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
Urosepsis
ESBL+ *E. coli*

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

Both
Rectal screening
CRKP

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.

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- 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.

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.

TABLE 1. Suggested action plan for rapid implementation of infection control measures in settings with sporadic occurrence or complete absence of carbapenemase-producing Gram-negatives

Screening of all patients in contact with an index case
Epidemiological investigation with root cause analysis in cases of nosocomial cross-transmission events with more than two secondary cases
Measures to keep staff and hospital administration informed
Stringent infection control aimed at containment and ultimate eradication of nosocomial clusters
Coordination and supervision by public health authorities

Carmeli Y. CMI 2010:16;102-111

HA CRE guideline

- Control
- Practical

Action - HA protocol

- Antibiotics
- Laboratory detection
  - Clinical specimen
  - Active surveillance screening
- Isolation and precautions
- Contact tracing
- Environmental cleansing
- Alert & reporting especially on patient with CRE PCR +ve discharged to elderly home

Laboratory protocol

- Clinical specimen
- All isolates from all specimens – full range of ST including carbapenem (ertapenem)
- Active screening in selected cases
- History of travel with hospitalisation outside HK in recent 6 months
- Stool or rectal swab for CRE screening
- (secondary screening of patients with chronic wounds/ indwelling urinary catheters or endotracheal intubation or on dialysis are not included at this stage)

CRE screening takes 5 days

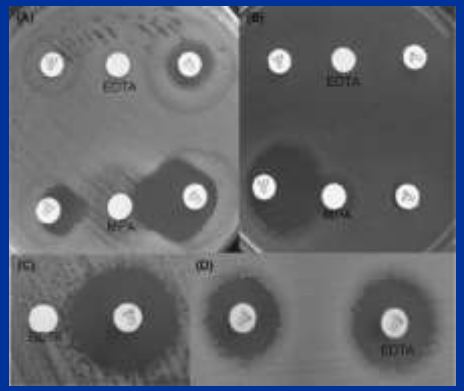
Day 1

Day 2

Day 3

Inform ICT
Send isolate to PHLC

Day 5



Day 4

susceptibility testing

CP when you send the swab

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Performance Standards for Antimicrobial Susceptibility Testing; Twentieth Informational Supplement (June 2010 Update)

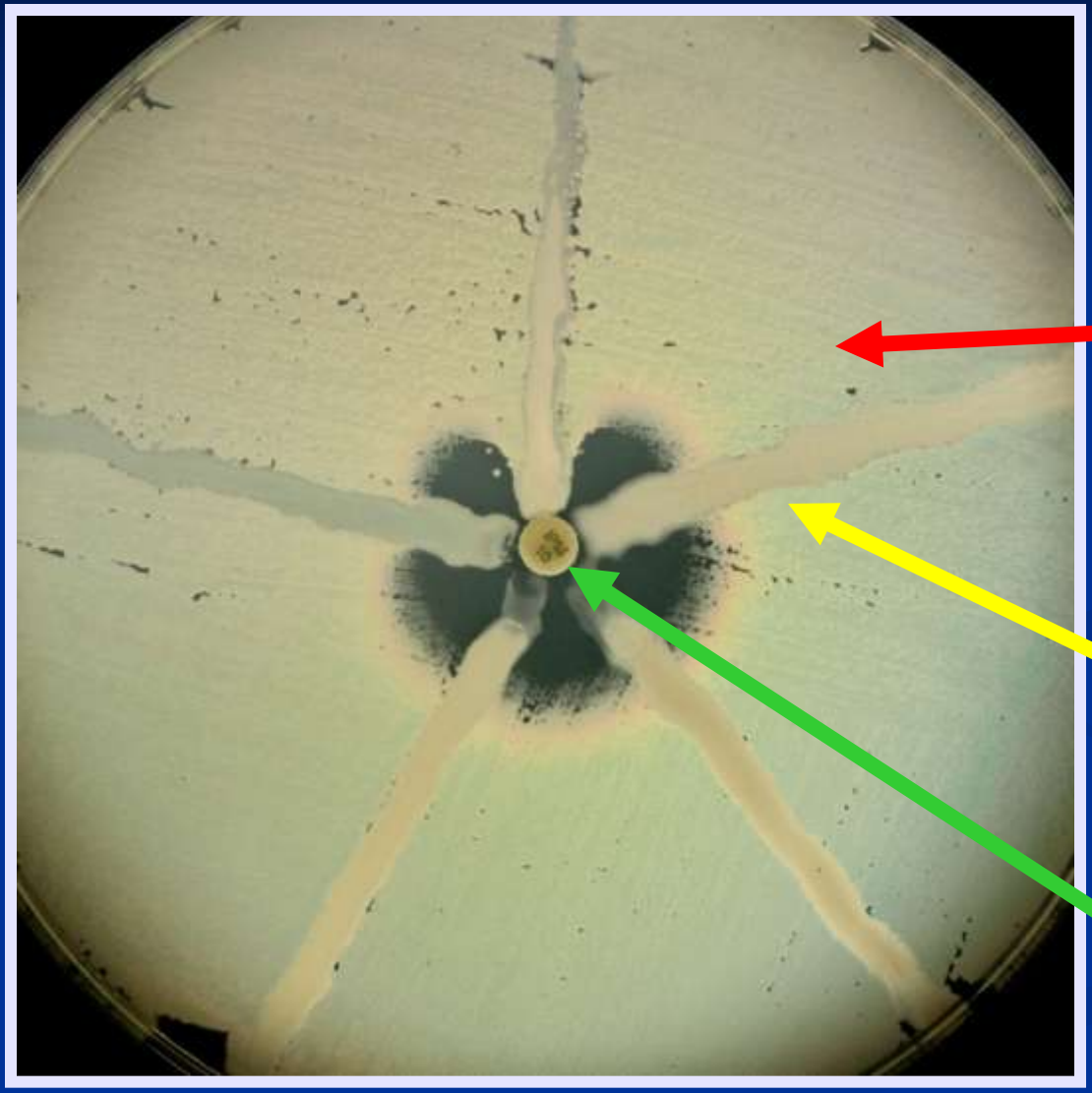
New Interpretive Criteria for Carbapenems and *Enterobacteriaceae*:

	Disk diffusion (mm)			**MIC (µg/mL)**		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Doripenem	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4
Ertapenem	≥ 23	20–22	≤ 19	≤ 0.25	0.5	≥ 1
Imipenem	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4
Meropenem	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4

Old Interpretive Criteria for Carbapenems and *Enterobacteriaceae*:

	Disk diffusion (mm)			**MIC (µg/mL)**		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Ertapenem	≥ 19	16–18	≤ 15	≤ 2	4	≥ 8
Imipenem	≥ 16	14–15	≤ 13	≤ 4	8	≥ 16
Meropenem	≥ 16	14–15	≤ 13	≤ 4	8	≥ 16

Modified Hodge Test



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

Test isolates

Imipenem disk

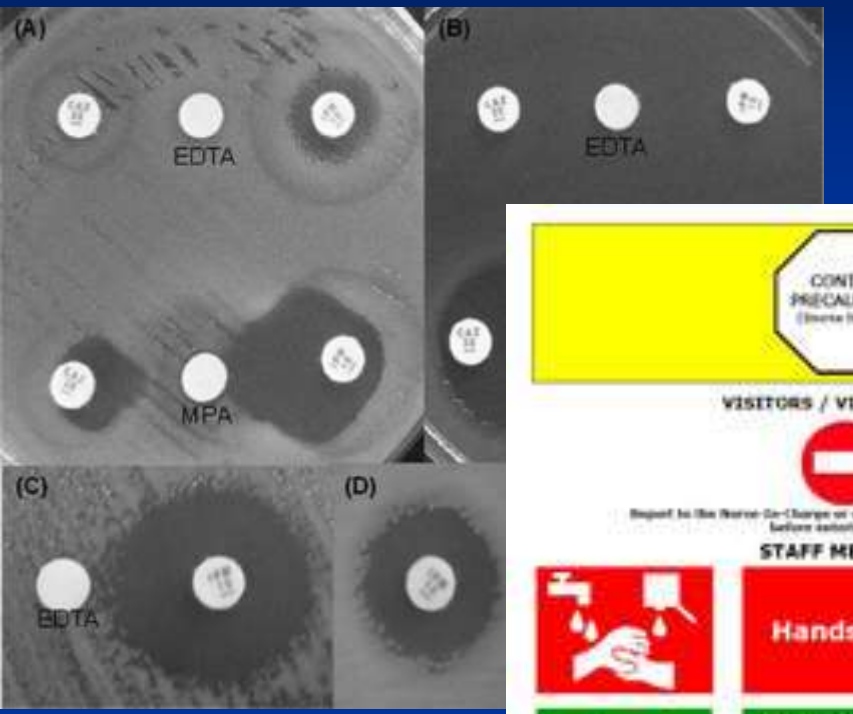
Described by Lee et al. CMI, 7, 88-102. 2001.

Secondary Test

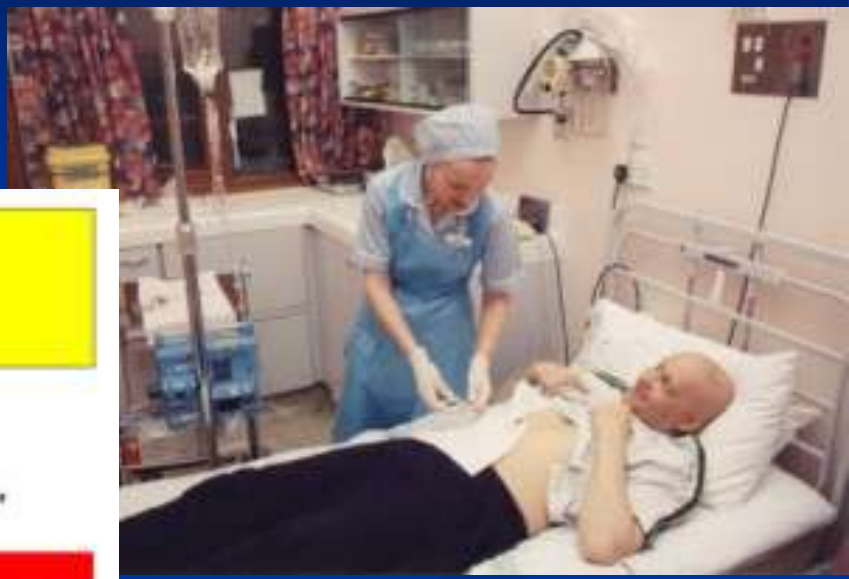
1. Modified Hodge Test (MHT) false Pos
2. Carbepenem disks (IMI, MEM, ERT) with EDTA and phenylboronic acid (>5mm zone different) JAC 2010;65:1664

- If either positive, send to PHLC for specific genes by PCR for confirmation

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



w.cancerhelp.org.uk/prod_consump/groups/cr_co
@cah/@gen/documents/image/crukmig_1000img-
g

Lab. send isolate to PHLC for CRE PCR

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

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

IV Alerts and Reporting

http://www.madr…es/CapTelphone.jpg

http://www.persona…jpg

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

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

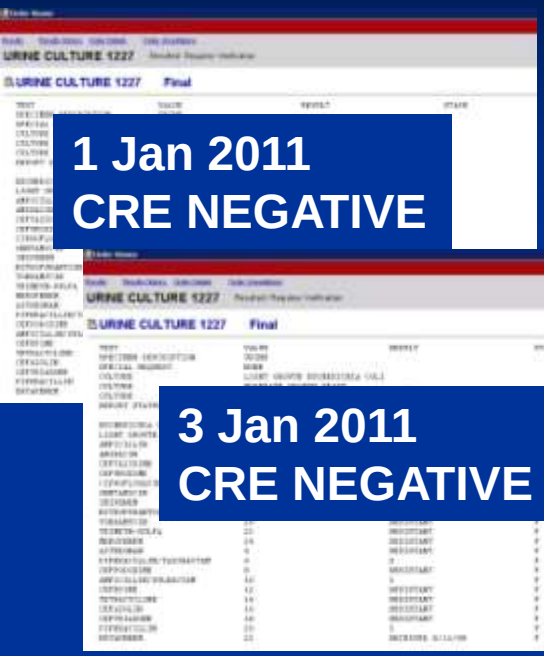
Label in the CMS alert by ICT

- '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



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療。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. 耐多藥綠膿假單胞菌 (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...
...次往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轉播。其他因素包括皮膚損傷/傷口，或携帶的環境等，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 1 之 1

2) With education pamphlet

3) Inform ICB before discharging the patient

Active surveillance culture

New Delhi metallo-β-lactamase (NDM-1)

Year	No. of case	Patients' background
2009	1	Oct 2009 (GOPC) 66-year-old man patient attending a government out-patient clinic
2010	1 (detected by active surveillance culture of rectal swab)	Dec 2010 History of hospitalization outside HK

Klebsiella pneumoniae Carbapenemase (KPC)

Year	No. of case	Patients' background
2009	0	
2010	4 (2 detected by active surveillance culture of rectal swabs)	Nov 2010 66-year-old man with a history of previous hospital admission in China in Oct 2010 Nov 2010 24-year-old man admitted for abdominal pain with no travel history Dec 2010 (2 cases with history of hospitalization outside HK)

Thank You