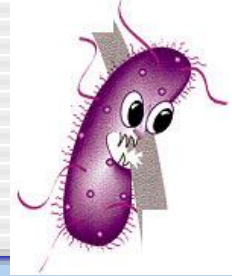
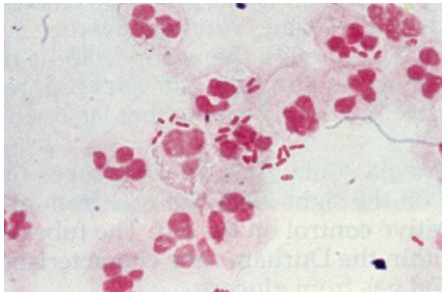
Inserm U914
Résistances Emergentes aux Antibiotiques

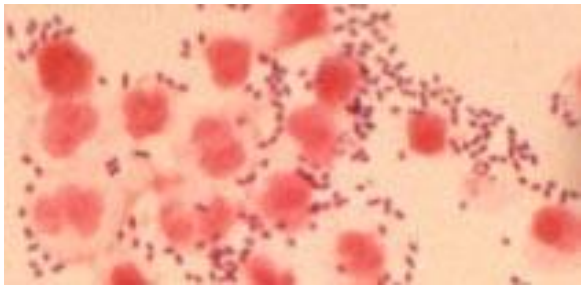
Mécanismes de résistance aux carbapénèmes chez les bacilles Gram-négatifs et diffusion dans le monde



Enterobacteriaceae



A. baumannii



P. aeruginosa

Quels avenirs pour les carbapénèmases?

XIII^{ème} journée Maurice Rapin:
Infections à l'hôpital,
vendredi 9 novembre 2012

T. Naas,
Hôpital de Bicêtre,
CNR associé Résistance aux carbapénèmes

UNIVERSITÉ PARIS SUD
FACULTÉ DE MÉDECINE

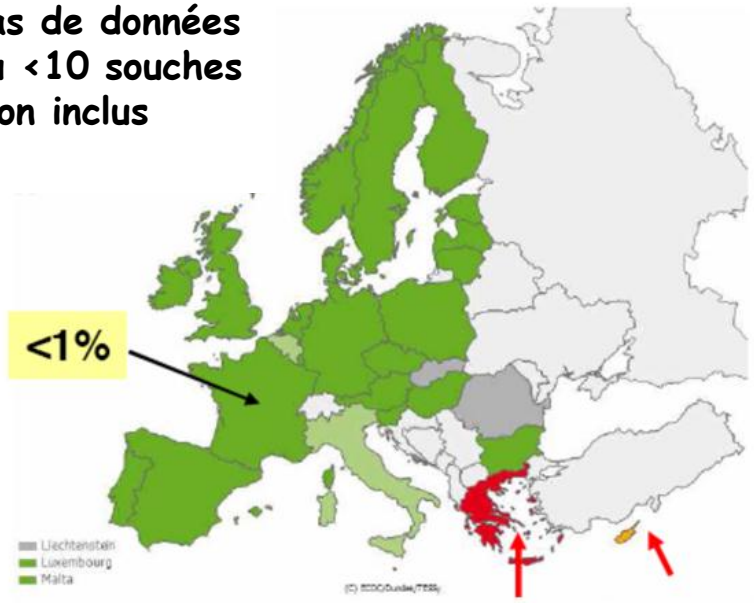
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

LabEx LERMIT
Laboratory of Excellence in Research on Medication and Innovative Therapeutics

Bactériémies à K. pneumoniae résistantes aux carbapénèmes EARSS, 2009-2010

- < 1%
- 1 à <5%
- 5 à <10%
- 10 à <25%
- 25 à <50%
- ≥50%
- Pas de données ou <10 souches
- Non inclus

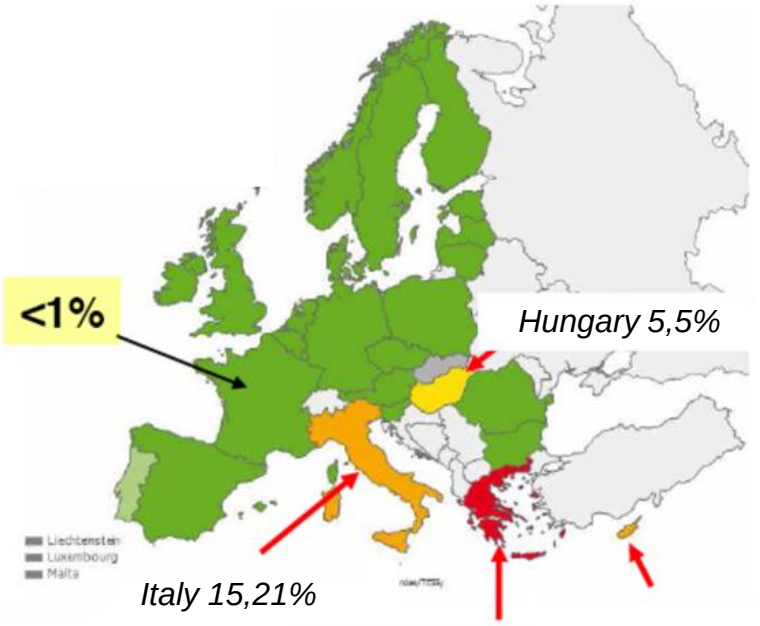
2009



Greece 36%

Cyprus 9,7%

2010



Italy 15,21%

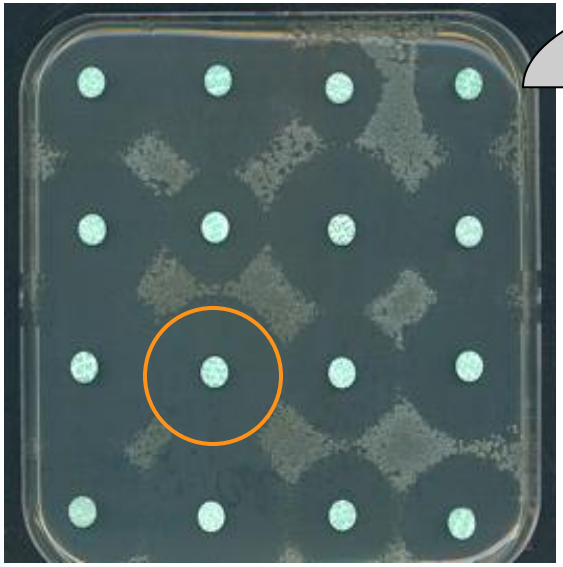
Greece 49%
(I/R 60%)

Cyprus 16%

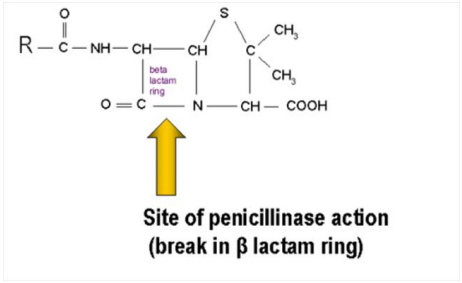
E. coli
de notre enfance

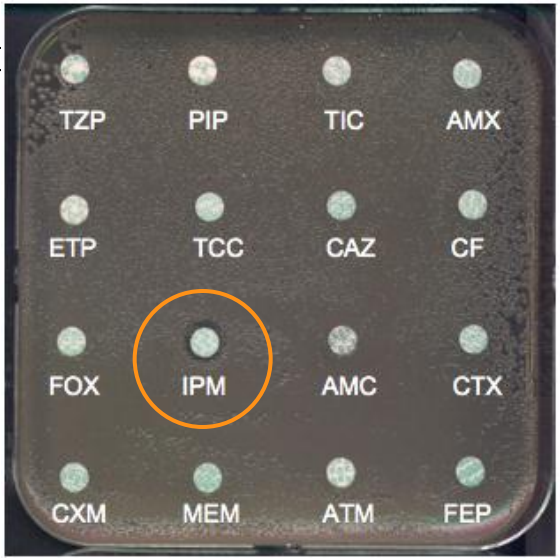
E. coli
des temps modernes

Le challenge avec les entérobactéries résistantes aux carbapénèmes



ß-lactamases





Carbapenemases
Mais pas uniquement

Les ß-Lactamases qui menacent les traitements des infections à bactéries G-?

AmpC plasmidique

bla_{CMY}, bla_{DHA}

BLSEs

bla_{CTX-M}, bla_{SHV} and bla_{TEM}
bla_{VEB}, bla_{PER}, bla_{GES}, bla_{TLA}, bla_{BES}....

Résistance aux C3G => S aux Carbapénèmes,

MAIS

Diminution de la perméabilité peut conduire à une R additionnelle aux Carbapénèmes

(Lee EH, Nicolas MH, Kitzis MD, Pialoux G, Collatz E, Gutmann L. *AAC* 1991, 35:1093-8.)

CTX-M/AmpC/impermeability/*K. pneumoniae*

Avant

Après
21 jours de traitement
Imipénème en monothérapie

International Journal of Antimicrobial Agents 35 (2010) 265–268

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Short communication

In vivo selection of imipenem-resistant *Klebsiella pneumoniae* producing extended-spectrum β-lactamase CTX-M-15 and plasmid-encoded DHA-1 cephalosporinase☆

Gaelle Cuzon[a], Thierry Naas[a,*], Michele Guibert[b], Patrice Nordmann[a]

Les ß-Lactamases qui menacent les traitements des infections à bactéries G-?

AmpC plasmidique

bla_{CMY}, bla_{DHA}

BLSEs

bla_{CTX-M}, bla_{SHV} and bla_{TEM}
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Résistance aux C3G
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MAIS

Diminution de la perméabilité peut conduire à une R additionnelle aux Carbapénèmes

(Lee EH, Nicolas MH, Kitzis MD, Pialoux G, Collatz E, Gutmann L. AAC 1991,

Carbapénèmases

- Metallo-enzymes (**bla_{VIM}**, **bla_{IMP}**), **bla_{NDM}**
- Oxacillinases ($bla_{OXA-23,-40,-58}$) and **bla_{OXA-48}**
- Classe A (bla_{NMCA}, bla_{IMI}, bla_{SME}), bla_{GES}, and **bla_{KPC}**

Carbapénèmases de classe A

✓ Chromosome-encoded

. NMCA → *Enterobacter cloacae*

. IMI-1, → *Enterobacter cloacae*

. Sme-1, -2 → *Serratia marcescens*

. SFC-1 → *Serratia fonticola*

✓ Plasmid-encoded

. KPC-1…13 → *Klebsiella pneumoniae, Enterobacteriacae*

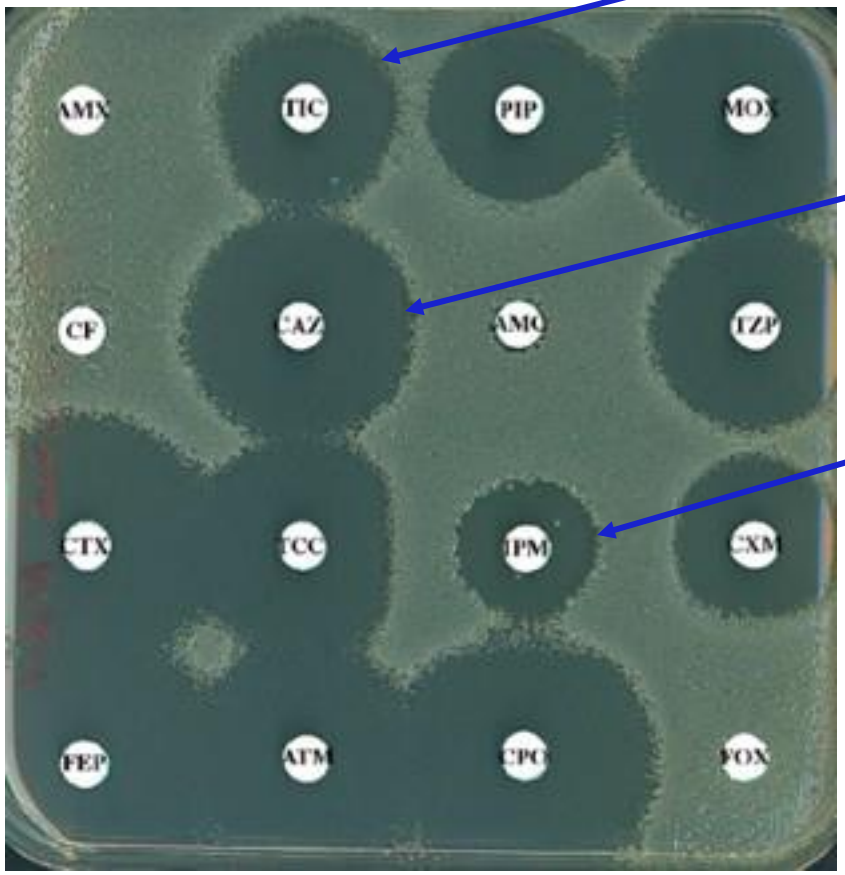
. IMI-2,-3 → *Enterobacter asburiae, E. cloacae, (E.coli)*

✓ Point mutant with reduced imipenem susceptibility

. SHV-38 → chromosome of *Klebsiella pneumoniae*

. GES-1-21 → plasmid of *P. aeruginosa, Enterobacteriacae*

Carbapénèmases chromosomiques de classe A
E. cloacae NOR-1 (NMC-A)

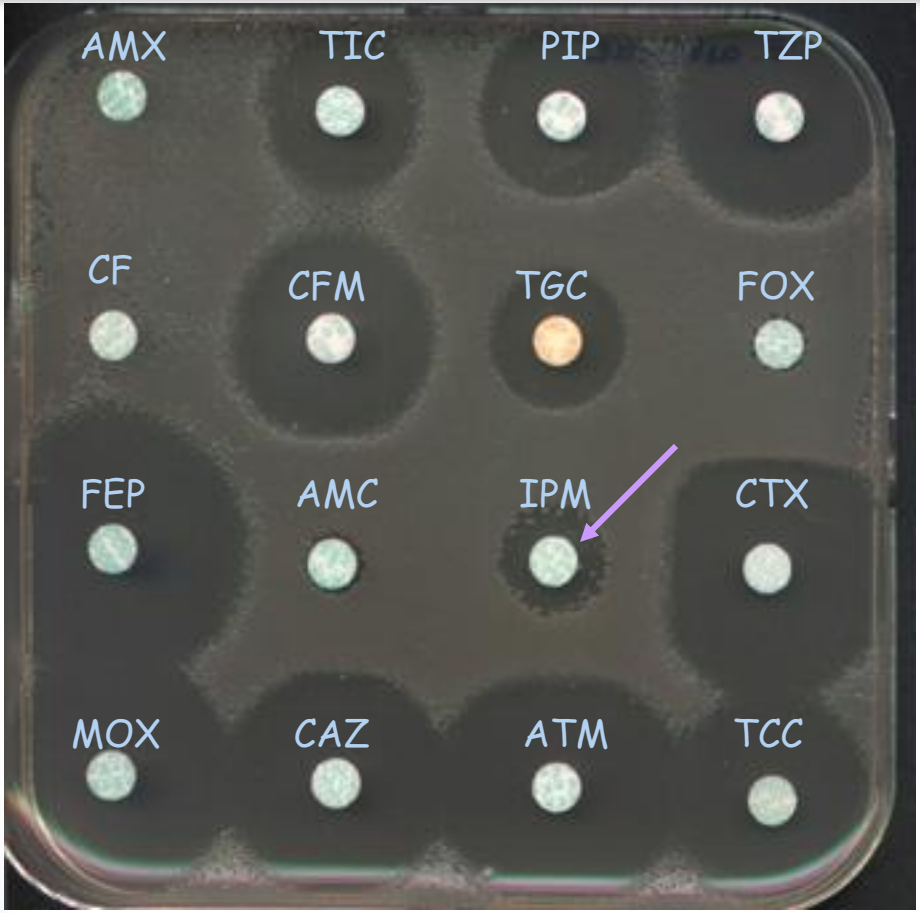


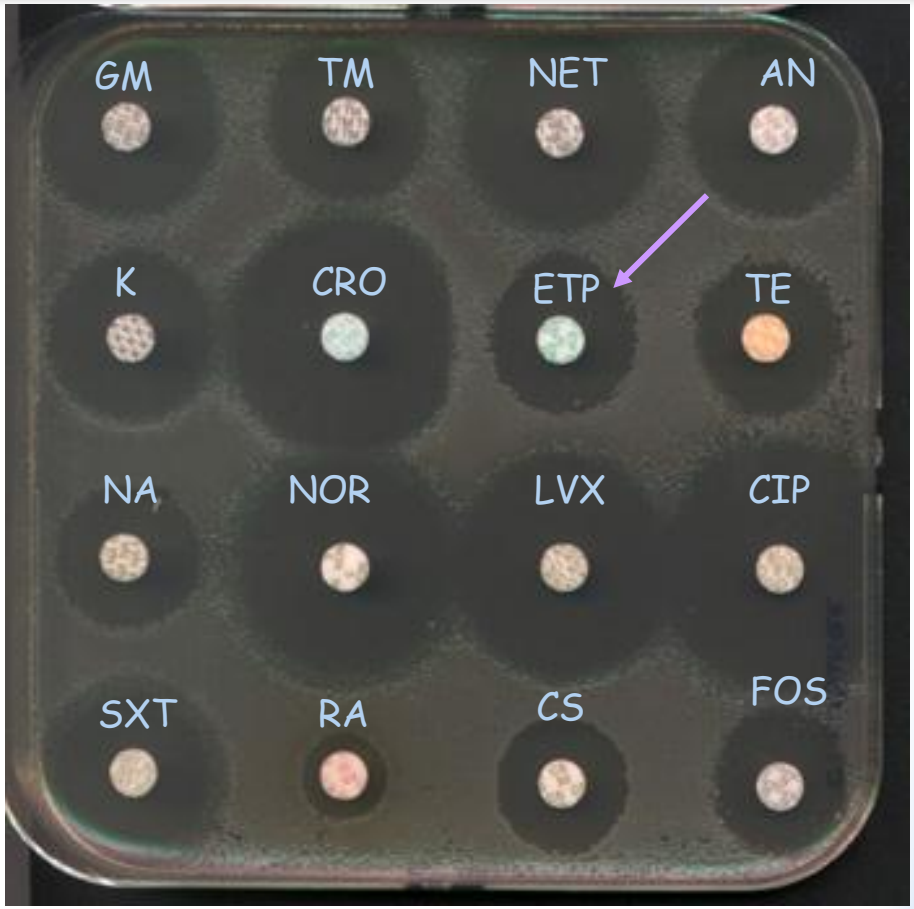
nmc-A et ampC
⇒ Inductible
et
⇒ hyper-production (ampD-)

(Naas T, Nordmann P. PNAS. 1994, 91:7693-7)

Enterobacter asburiae bla_{IMI-2} en France

G. Cuzon, D. Tandé, M.P. Henry, R. Le Berre, G. Le Lay, P. Nordmann, and T. Naas
(ECCMID 2010)





- fracture ouverte suite à chute dans rivière
- plasmide 90 kb

Isolats cliniques de Enterobacter sp. produisant bla_{IMI} en France

First detection of blaIMI-2 gene in a clinical *Escherichia coli* strain.
Rojo-Bezares et al.
AAC. 2012; 56:1146-7.

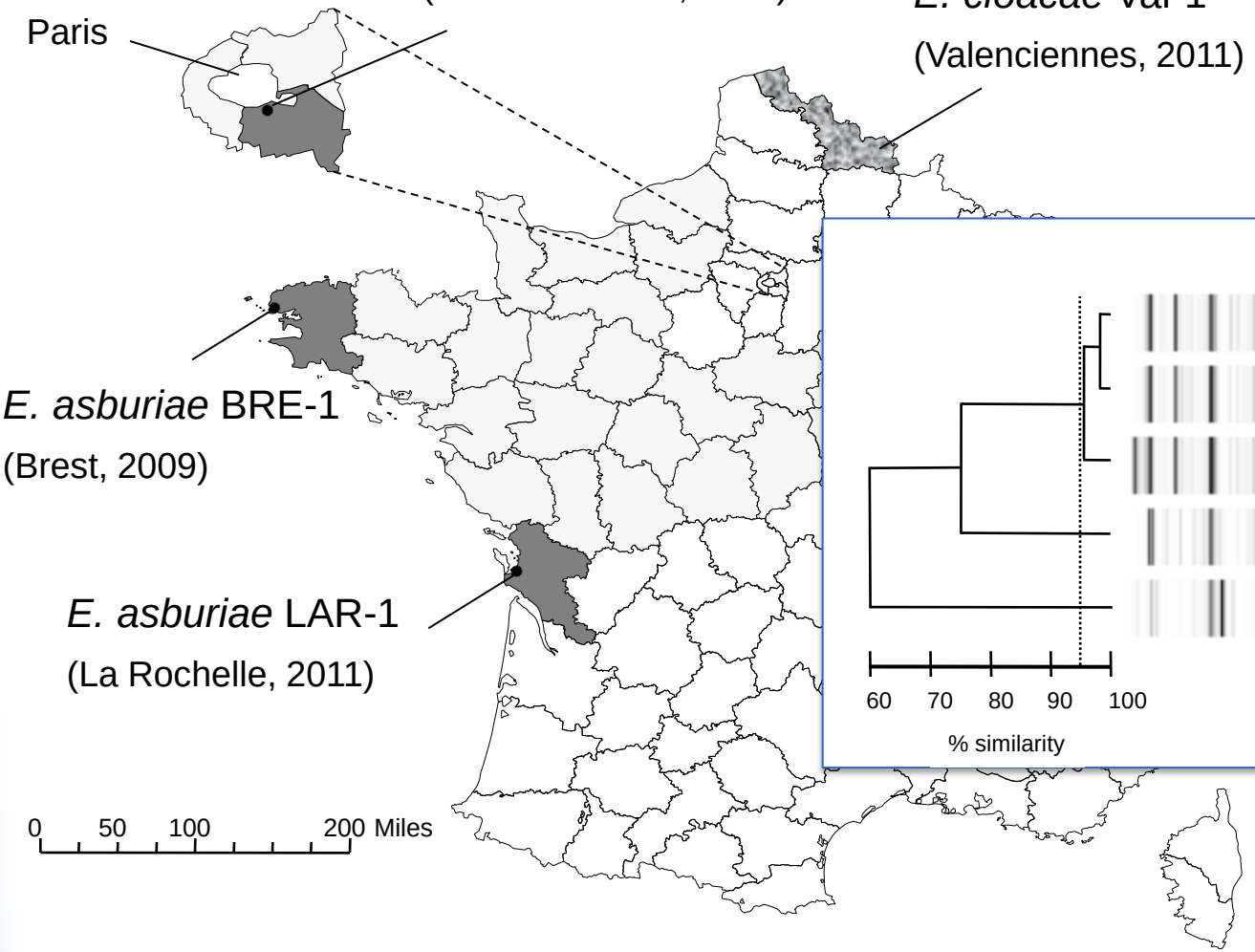
E. asburiae PAR-1
(Kremlin-Bicêtre, 2007)

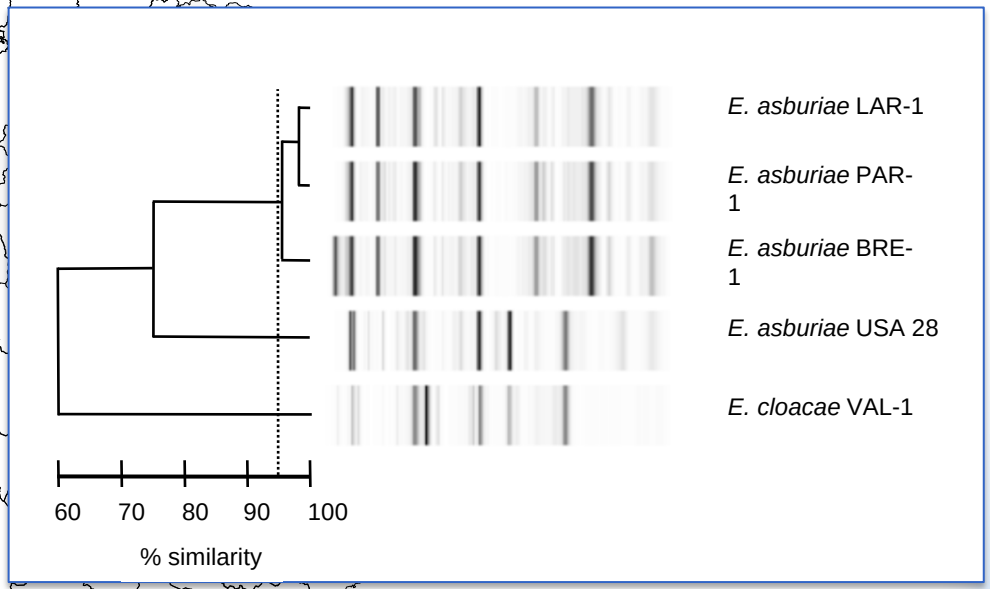
E. cloacae Val-1
(Valenciennes, 2011)

Paris

E. asburiae BRE-1
(Brest, 2009)

E. asburiae LAR-1
(La Rochelle, 2011)





Naas T, et al. AAC.2012; 56:1664-5
Bernusset S, et al. en préparation

GES et variants

Table 3. Key amino-acid substitutions of GES variants in relation to their hydrolytic spectra

GES variant	GenBank accession numbers	Country	Strain	Ambler position[a]					Hydrolysis profile[b]				Inhibition[c]
				62	104	126	170	243	CAZ	FOX	ATM	IPM	Ac clav
GES-1	AF156486	France, Argentina, Brazil, Portugal and The Netherlands	*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Serratia marcescens*	Met	Glu	Ala	Gly	Gly	+	–	–	–	S
GES-2	AF326355	South Africa	*P. aeruginosa*				Asn		+	–	–	+	P
GES-3	AB113580	Japan, China and Korea	*K. pneumoniae*	Thr	Lys				+	–	–	–	S
GES-4	AB116260	Japan	*K. pneumoniae*	Thr	Lys		Ser		+	+	–	+	P
GES-5	AY494717	Greece, Korea, China and Brazil	*Escherichia coli*, *K. pneumoniae* *P. aeruginosa*				Ser		+	+	–	+	P
GES-6	AY494718	Greece	*K. pneumoniae*		Lys		Ser		+	+	–	+	P
GES-7 (IBC-1)	AF208529	Greece	*Enterobacter cloacae*		Lys				+	–	–	–	S
GES-8 (IBC-2)	AF329699	Greece	*P. ae*			Leu			+	–	–	+	S
GES-9	AY920928	France	*P. ae*					Ser	+	–	+	–	S

[a]Only amino-acid changes as compared to GES-1 are indicate
[b]+ and –, hydrolysis and no hydrolysis, respectively.
[c]p means poorly inhibited and s means similarly inhibited as
CAZ, Ceftazidime; FOX, cefoxitin; ATM, Aztreonam; IPM, im

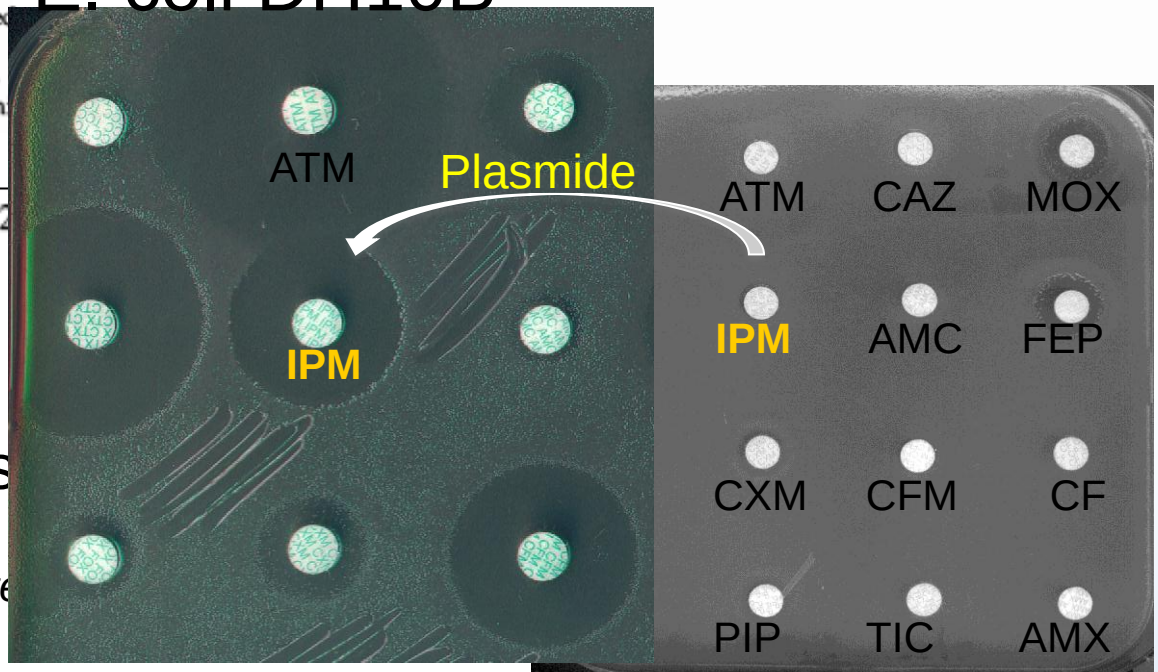
REVIEW

Clin Microbiol Infect 2008; **14** (Suppl. 1): 42–52

Minor extended-spectrum β-lactamases

T. Naas, L. Poirel and P. Nordmann

E. coli DH10B



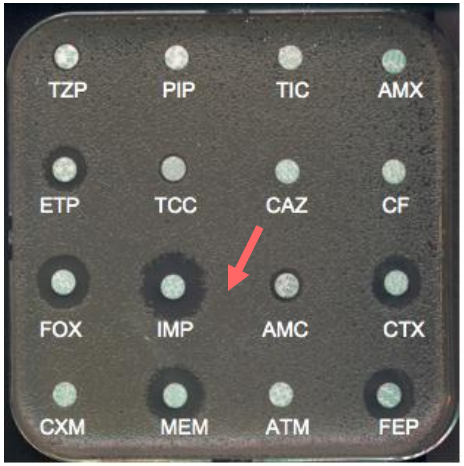
- plasmid
- intégron

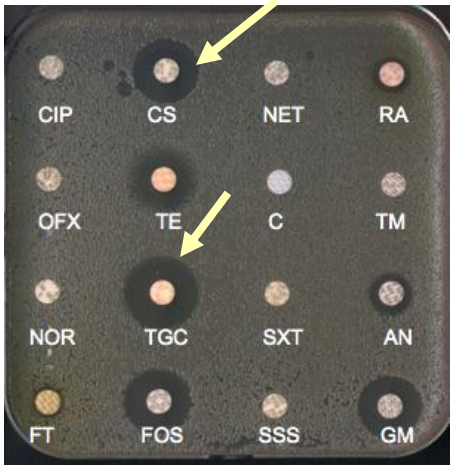
} Multi-résis

- *P. aeruginosa*, *Enterobacte*

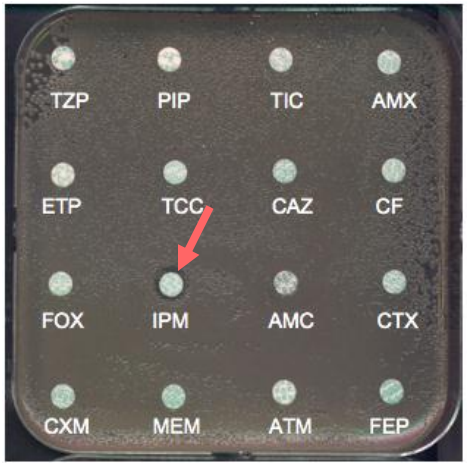
KPC, NDM et OXA-48

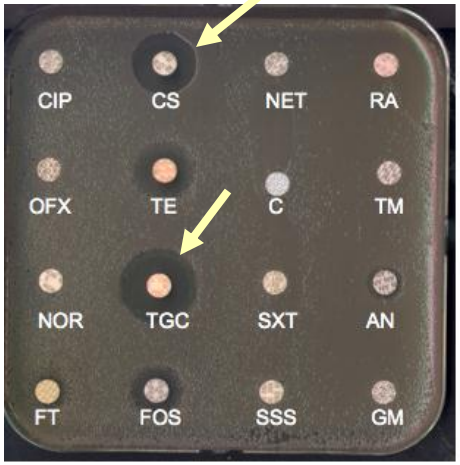
Kp KPC-2



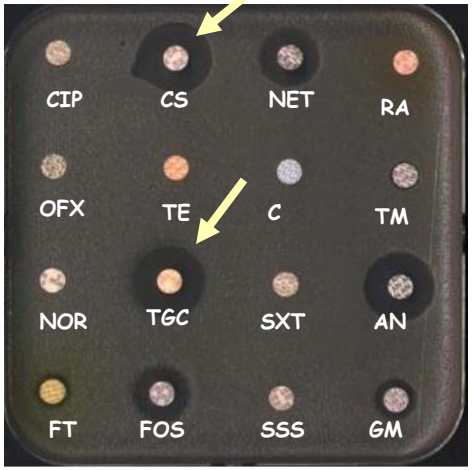


Kp NDM-1





Kp OXA-48



Les producteurs de carbapénèmases sont multi résistants

Les producteurs de carbapénèmases sont multi résistants

Les carbapénèmases ne viennent rarement seul…..

Letters to the Editor

***Klebsiella pneumoniae* Isolate Producing at Least Eight Different β-Lactamases, Including AmpC and KPC β-Lactamases**[▽]

ES. Moland et al. *AAC* 2007; 51:801-2.

Presence of Plasmid-Mediated Quinolone Resistance in *Klebsiella pneumoniae* Isolates Possessing bla_{KPC} in the United States[▽]

A. Endimiani et al. *AAC* 2008; 52:2680-82.

Detection of the new metallo-β-lactamase VIM-19 along with KPC-2, CMY-2 and CTX-M-15 in *Klebsiella pneumoniae*

S. Pournaras et al. *JAC* 2010; 65:1604-07.

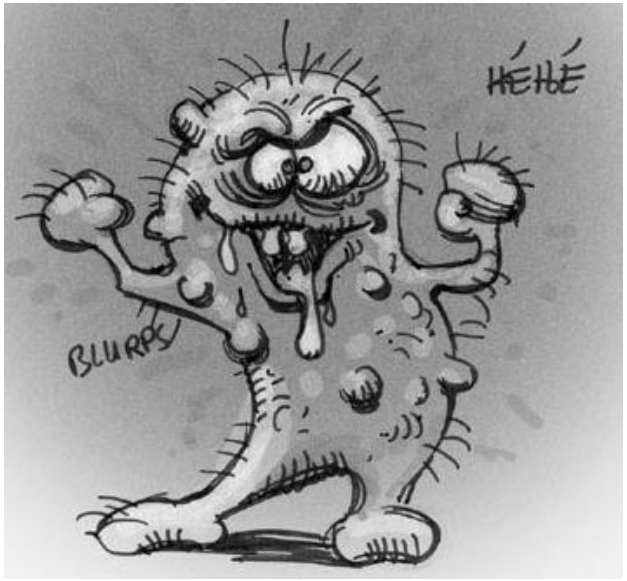
First Report of *Klebsiella oxytoca* Strain Coproducing KPC-2 and IMP-8 Carbapenemases[▽]

B. Li et al. *AAC* 2011; 55:3937-41.

The emerging NDM carbapenemases

P. Nordmann et al. Trends Microbiol. 2011; 19:588-95.

ß-lactamases: ESBLs, CMY4, NDM-1, OXA-48; rifampicin resistance Arr-2; aminoglycoside resistance AadA1; methylases; chloramphenicol resistance CmlA 7; erythromycin resistance EreC…..



Identification de producteur de carbapénèmases difficile

Global Spread of Carbapenemase-producing *Enterobacteriaceae*

Patrice Nordmann, Thierry Naas, and Laurent Poirel

Heterogeneous expression of carbapenemases in Enterobacteriaceae

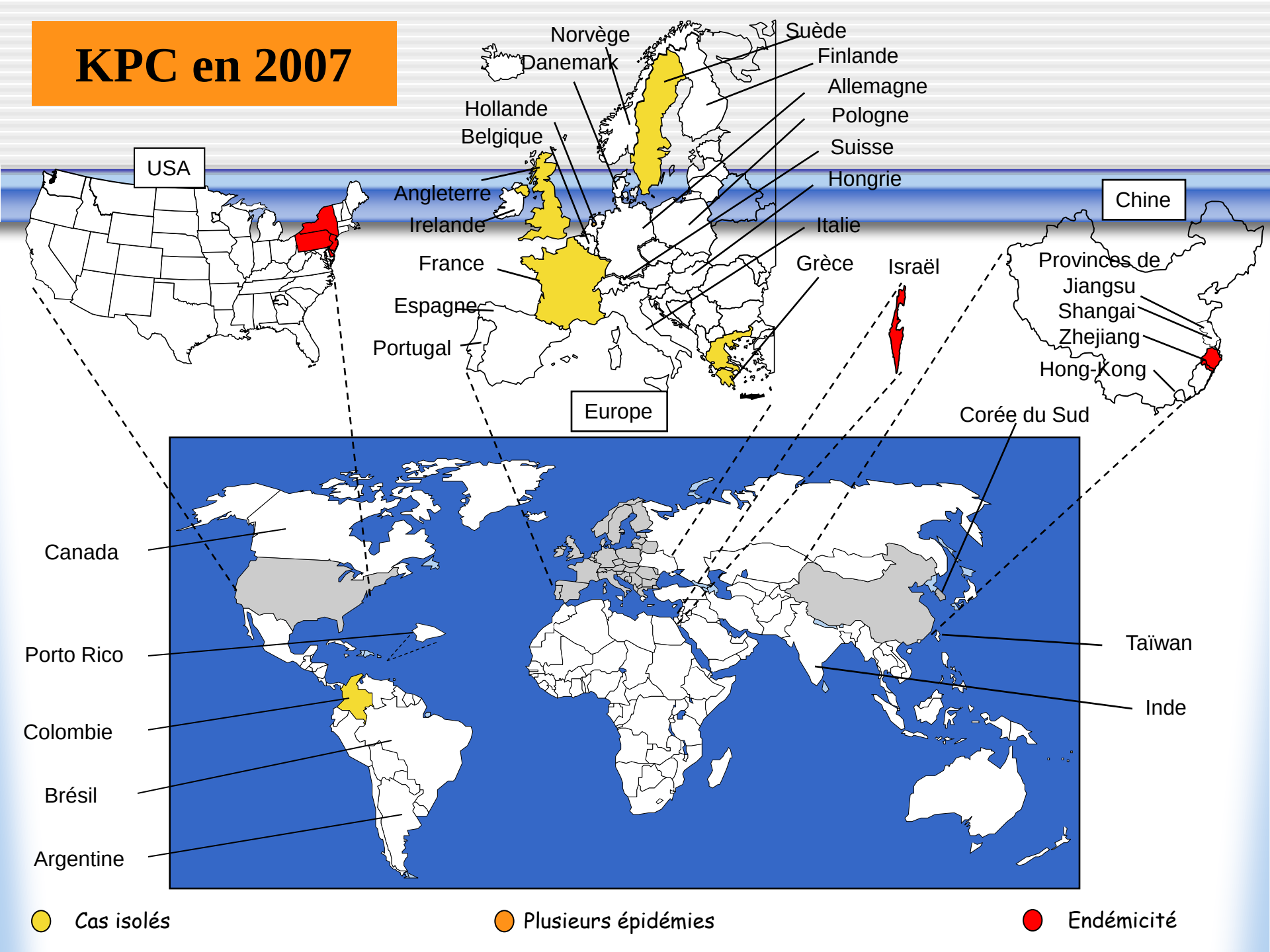
	MIC (mg/L)		
	Imipenem	Meropenem	Ertapenem
KPC	0.5 ; >64	1 ; 64	0.5 ; >64
MBL (including NDM-1)	0.5 ; >64	0.25 ; >64	0.5 ; >32
OXA-48-type	1 ; >64	0.5 ; 64	4 ; >64

Détection Difficile

Breakpoints (MIC, mg/l), 2011

	EUCAST		CLSI	
	S	R	S	R
Ertapenem	≤0.5	>1	≤0.25	≥1
Imipenem	≤1	>4	≤1	≥4
Meropenem	≤1	>4	≤1	≥4

KPC en 2007

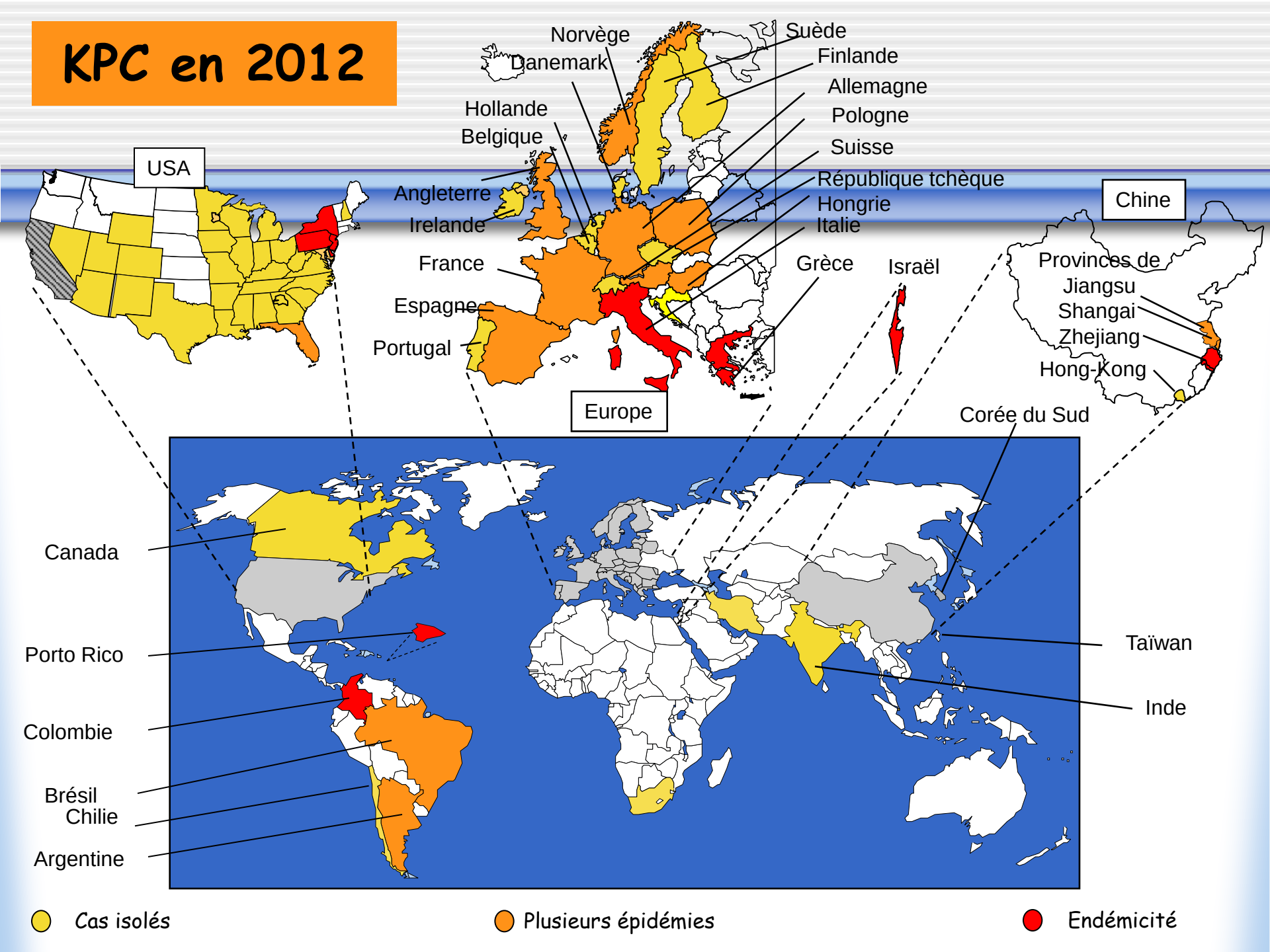


Cas isolés

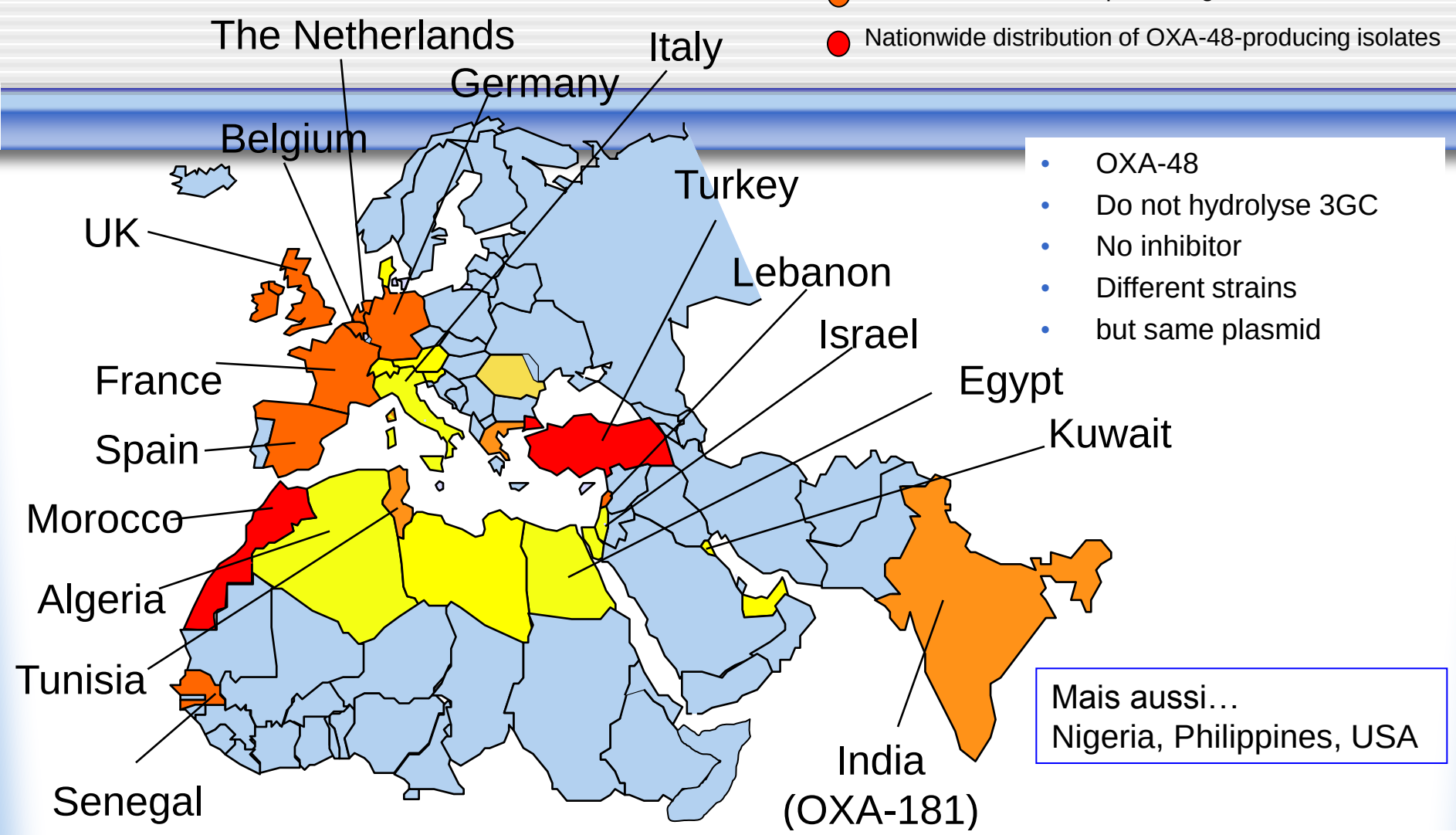
Plusieurs épidémies

Endémicité

KPC en 2012


Norvège
Suède
Danemark
Finlande
Allemagne
Hollande
Pologne
Belgique
Suisse
USA
République tchèque
Angleterre
Hongrie
Irelande
Italie
France
Grèce
Israël
Espagne
Portugal
Europe
Chine
Provinces de
Jiangsu
Shangai
Zhejiang
Hong-Kong
Corée du Sud
Canada
Taïwan
Porto Rico
Inde
Colombie
Brésil
Chilie
Argentine
Cas isolés
Plusieurs épidémies
Endémicité

OXA-48: an European spread?



- OXA-48
- Do not hydrolyse 3GC
- No inhibitor
- Different strains
- but same plasmid

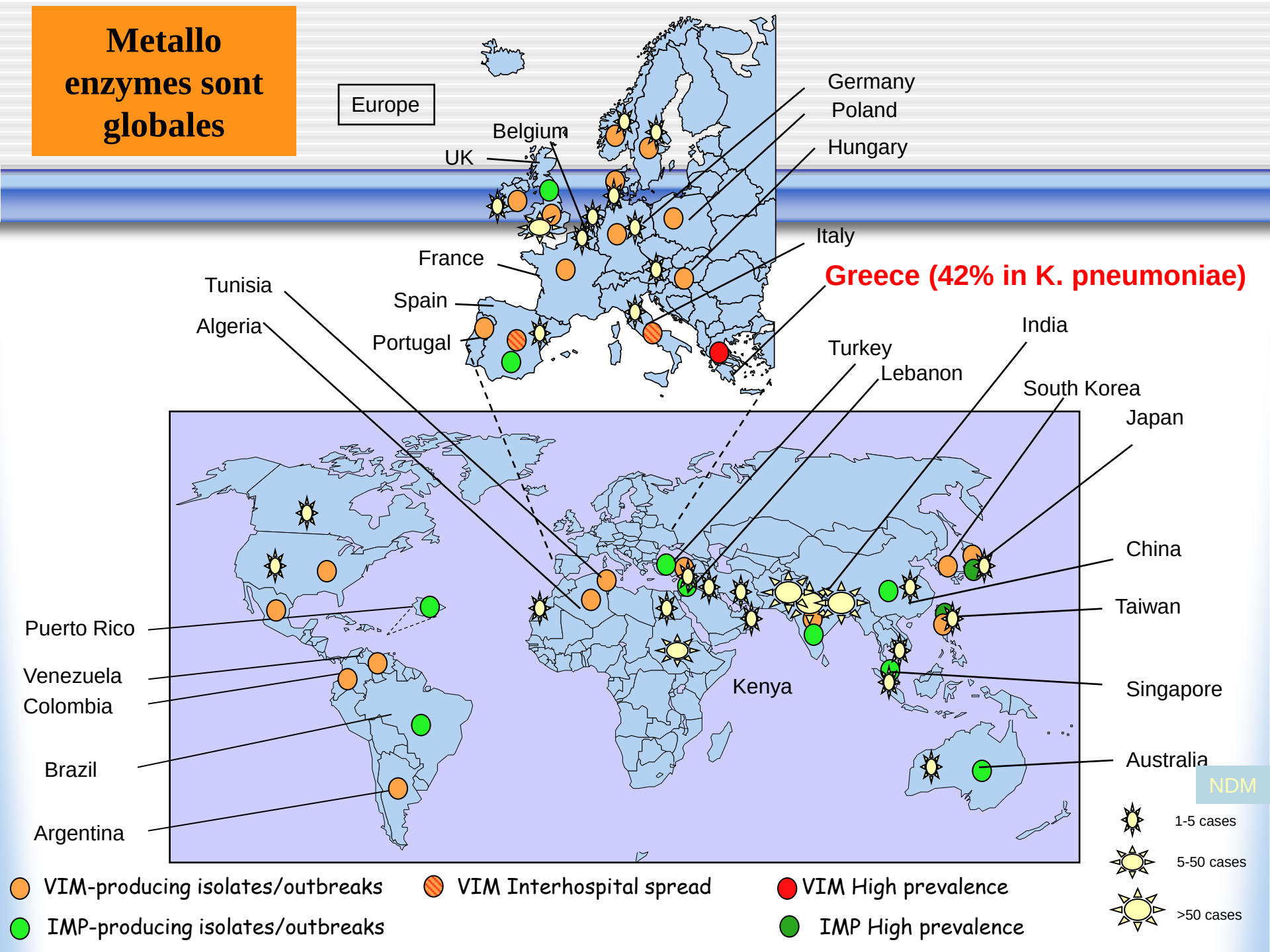
Mais aussi…
Nigeria, Philippines, USA

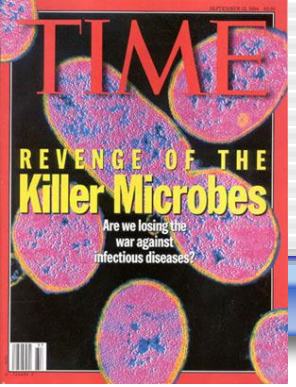
Global Spread of Carbapenemase-producing *Enterobacteriaceae*

Patrice Nordmann, Thierry Naas, and Laurent Poirel

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 10, October 2011

Metallo enzymes sont globales





Secrets de ces « success stories » ?

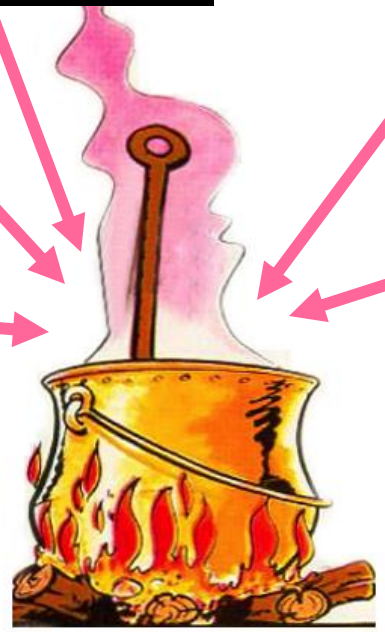
Insertion Sequences
Role in expression

plasmid borne
Self-transferable

Active transposon at high frequency
No target site specificity

ß-lactamase with specific Hydrolytic properties

Present in epidemiologically efficient strains
Enterobacteriaceae, P. aeruginosa and A. baumannii



resistance phenotype

difficult to detect

epidemiological behaviour

Higher mortality rate and length of hospitalization

Pourquoi faut-il être vigilant ?
« Association de malfaiteurs »

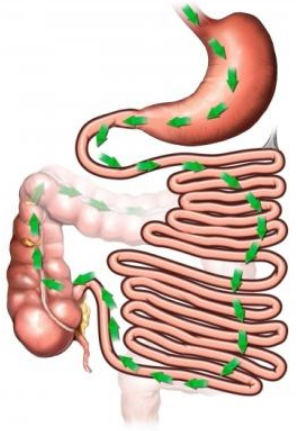
=> KPC: *K. pneumoniae* ST258

=> OXA-48: *K. pneumoniae* different clones, but emergence of ST395 clone (Cuzon et al. JCM, 2011, Potron, CMI, 2011), emergence also in *E. coli*

=> VIM, IMP: *K. pneumoniae*

=> NDM: *E. coli* et tous les autres

- **1st human bacterial pathogen**
- **1st community-acquired pathogen**
- **1st cause of urinary tract infections and diarrhea**



Infections à EPC: Taux de mortalité élevé (3x)

KPC, VIM, NDM and *E.coli* ST131

Antimicrob. Agents Chemother. October 2011 vol. 55 no. 10

Production of KPC-2 Carbapenemase by an Escherichia coli Clinical Isolate Belonging to the International ST131 Clone

Dearbháile Morris*, Fiona Boyle, Catherine Ludden, Iris Condon, James Hale, Nuala O'Connell, Lorraine Power, Teck Wee Boo, Hiran Dhanji, Christian Lavallee, Neil Woodford and Martin Cormican

- F, 84 ans
- Maison de retraite, Irlande
- Pas de voyage
- Infection urinaire

When Carbapenem-Hydrolyzing β-Lactamase KPC Meets Escherichia coli ST131 in France

Thierry Naas*, Gaelle Cuzon, Olivier Gaillot, René Courcol and Patrice Nordmann

- F, 64 ans
- Gérontologie, Lille
- Pas de voyage
- Infection urinaire

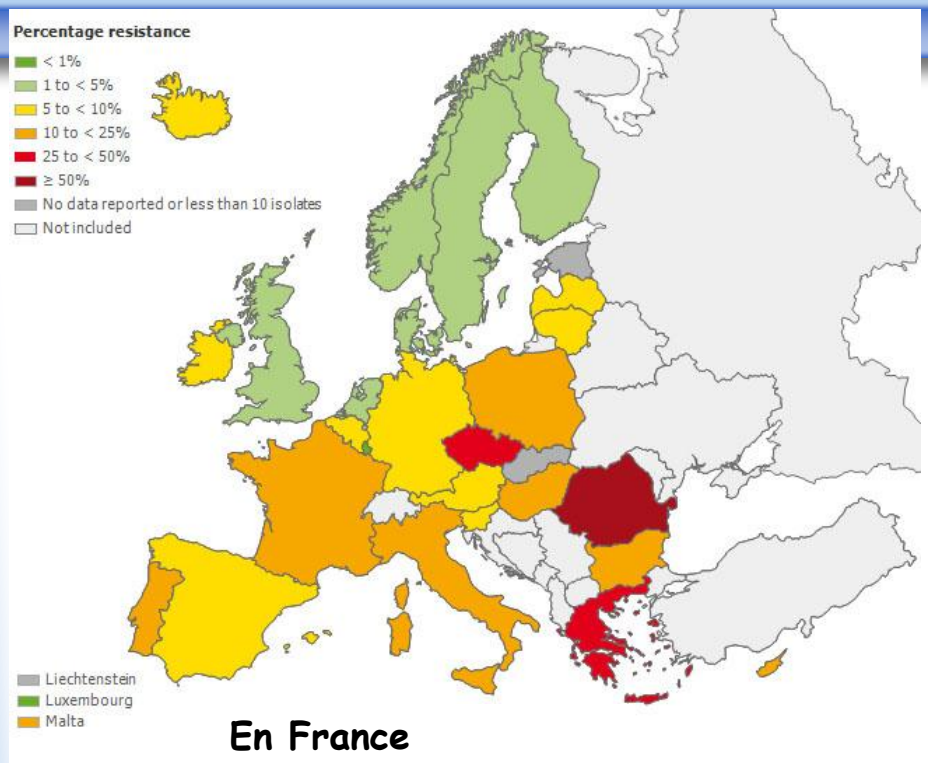
***Escherichia coli* O25b:H4-ST131**

Mais aussi VIM et NDM……

- Mantengoli E., et al. 2011. Escherichia coli ST131 producing extended-spectrum beta-lactamases plus VIM-1 carbapenemase: further narrowing of treatment options. Clin. Infect. Dis. 52:690–691.
- Peirano G., Schreckenberger P. C., Pitout J. D.. 2011. The characteristics of NDM-1-producing Escherichia coli that belong to the successful and virulent clone ST131. Antimicrob. Agents Chemother. 55:2986–2988.

P. aeruginosa (EARSS 2010)

Résistance à la Ceftazidime



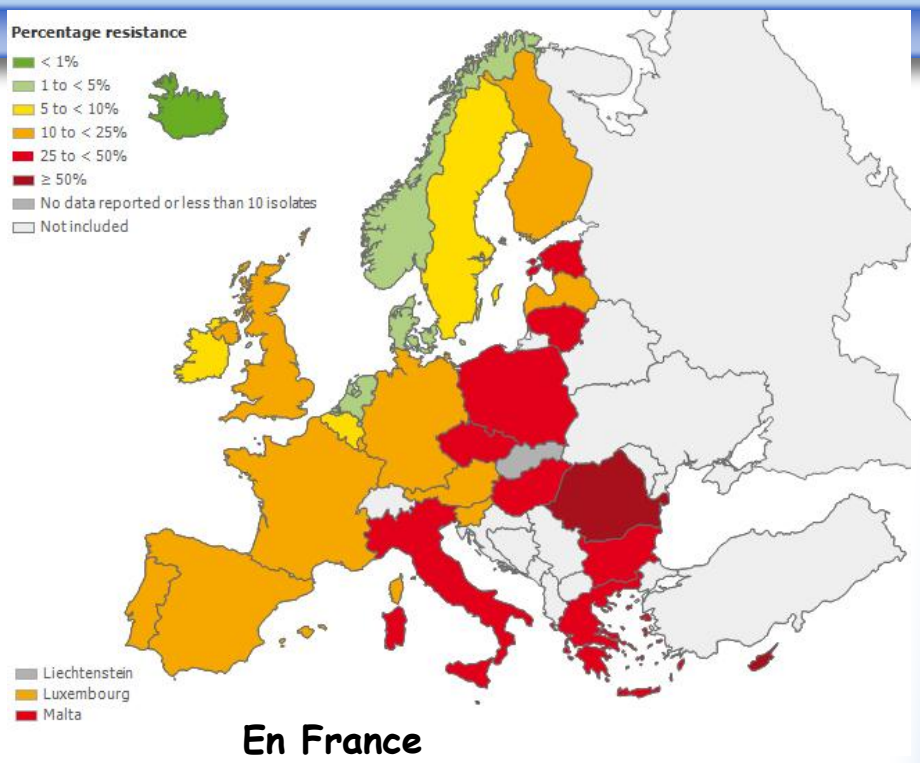
En France

2007	6.76 %
2008	8.02 %
2009	16.77 %
2010	12.69 %

AmpC hyper-produite

Mais aussi BLSE

Résistance à la l'imipénème



En France

2007	14.13 %
2008	14.23 %
2009	17.39 %
2010	17.79 %

Défaut de la porine D2

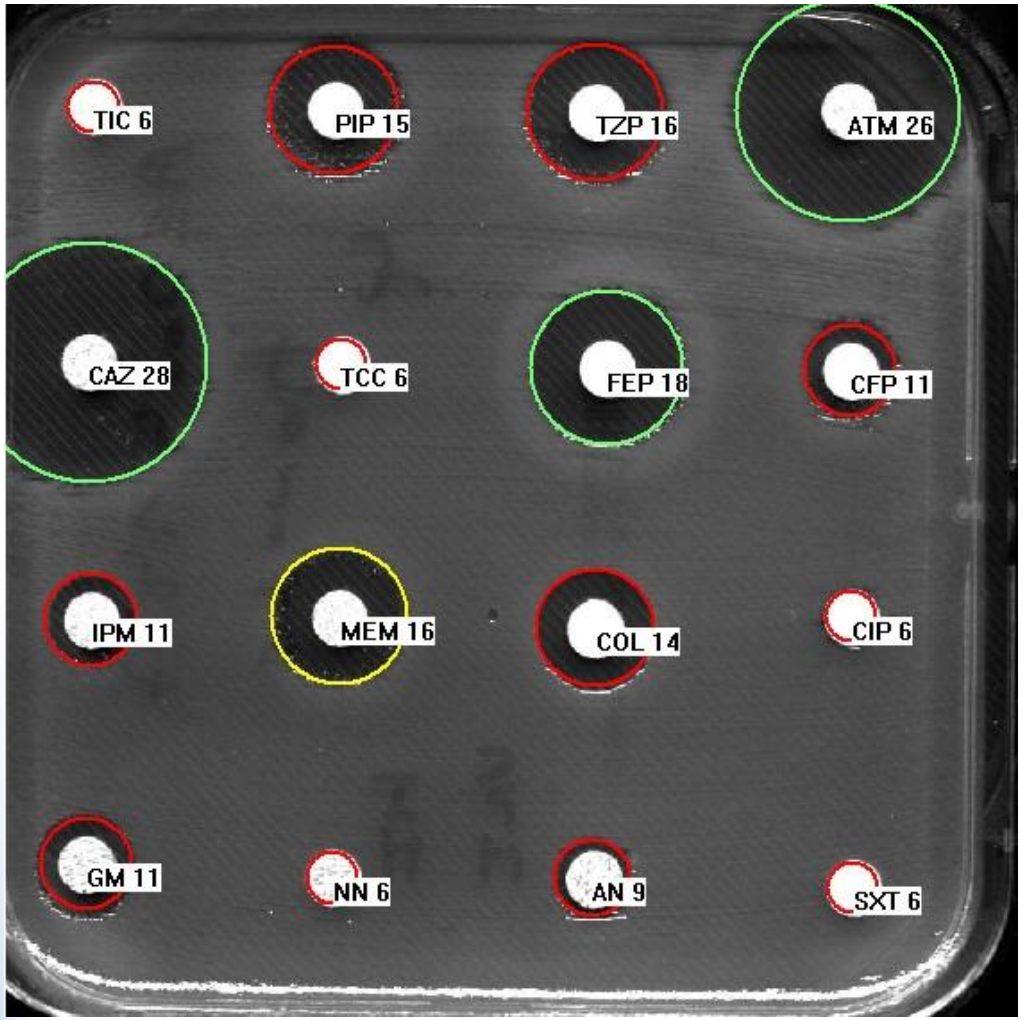
Mais aussi MBL (VIM +++)

OXA-198, an Acquired Carbapenem-Hydrolyzing Class D β-Lactamase from *Pseudomonas aeruginosa*▽

Farid El Garch,[1]* Pierre Bogaerts,[1] Carine Bebrone,[2] Moreno Galleni,[2] and Youri Glupczynski[1]

Laboratoire de Bactériologie, CHU Mont-Godinne, Université Catholique de Louvain, B-5530 Yvoir, Belgium,[1] and Laboratory of Biological Macromolecules, Centre for Protein Engineering, Department of Life Sciences, University of Liege, Liège, Belgium[2]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2011, p. 4828–4833



38% identité OXA-48

- Intégron
-Plasmide 46kb
- Forte hydrolyse de l'imipénème

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 2011, p. 3929–3931 Vol. 55, No. 8
0066-4804/11/$12.00 doi:10.1128/AAC.00226-11

Emergence of NDM-1 Metallo-β-Lactamase in *Pseudomonas aeruginosa* Clinical Isolates from Serbia[▽]

Branko Jovcic,[1]# Zorica Lepsanovic,[2]# Vesna Suljagic,[2] Gorjana Rackov,[2] Jelena Begovic,[1] Ljubisa Topisirovic,[1] and Milan Kojic[1]*

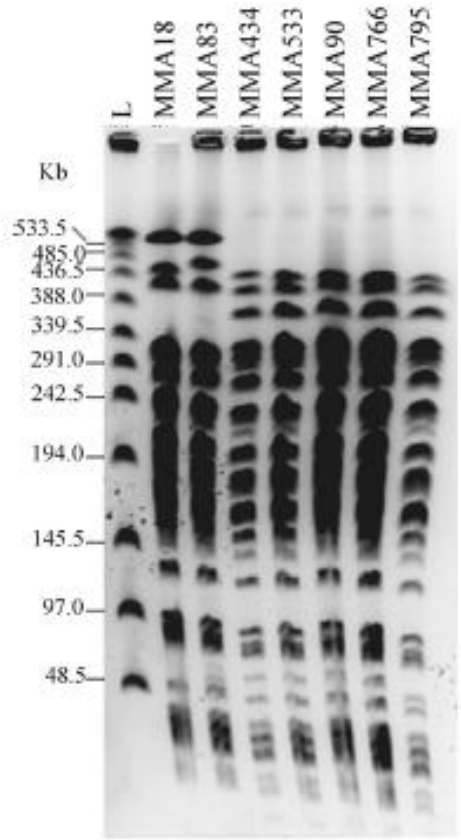


FIG. 1. PFGE profiles of *P. aeruginosa* isolates carrying the bla_{NDM-1} gene (MMA18, MMA83, MMA434, MMA533, MMA90, MMA766, and MMA795). L, λ concatemers (New England Biolabs).

Class B ß-lactamases: many more to come

Enzyme	Espèce	Pays (isolement)
IMP-1	*Enterobactericeae*	Japon
	A. xylosoxydans, A faecalis	
	P. aeruginosa	Japon, Singapore
	P. stutzeri, P. putida, P. fluorescens	Japon, Singapore
	B. cepacia	Japon
	A. baumannii	Japon, Corée, Italie
	A. junii	Angleterre
IMP-2	*P. aeruginosa*	Japon
	A. baumannii	Italie, Japon
	A. lwoffi	Japon
IMP-3	*S. flexneri*	Japon
IMP-4	*A. baumannii*	Hong-Kong
	C. youngae	Chine
	K. pneumoniae, E. coli	Australie
IMP-5	*A. baumannii*	Portugal
IMP-6	*S. marcescens*	Japon
IMP-7	*P. aeruginosa*	Canada, Malaisie
IMP-8	*K. pneumoniae, E. cloacae*	Taiwan
IMP-9	*P. aeruginosa*	Chine
IMP-10	*P. aeruginosa, A. xylosoxydans*	Japon
IMP-11	*P. aeruginosa*, *A. baumannii*	Japon
IMP-12	*P. putida*	Italie
IMP-13	*P. aeruginosa*,	Italie
…		
IMP-39		

Enzyme	Espèce	Pays (isolement)
VIM-1	*P.aeruginosa*	Italie, Grèce
	A. baumannii	Italie
	A. xylosoxydans	Italie
	P. putida	Italie
	E. coli	Grèce
VIM-2	*P. aeruginosa*	France, Grèce , Italie, Japon, Corée, Portugal,
	A. baumannii	Italie, Corée
	E. cloacae	Corée
	S. marcescens	Corée
	P. putida	Corée, Taiwan, Japon
	P. stutzeri	Taiwan
	A. xylosoxydans	Corée
	C. freundii	Taiwan
VIM-3	*P. aeruginosa*	Taiwan
	C. freundii	Taiwan
VIM-4	*P. aeruginosa*	Grèce , Suède
VIM-5	*P. aeruginosa*	Turquie
	K. pneumoniae	Turquie
VIM-6	*P. putida*	Singapore
VIM-7	*P. aeruginosa*	USA
…		
VIM-37		

DIM-1	*P. aeruginosa*	Hollande (2009)
KHM-1	*C. freundii*	Japon (2008)

NDM-1,7	*K. pneumoniae*	Inde (2009)
	A. baumannii	*Egypt, France, ,Algeria*
	P. aeruginosa	Serbia

SPM-1	*P. aeruginosa*	Brésil (1997)
GIM-1	*P. aeruginosa*, Enterobactericeae	Allemagne (2003)
SIM-1	*A. baumannii*	Corée (2005)
AIM-1	*A. baumannii*	Australie (2007)

P. aeruginosa et KPC

KPC-2, KPC-3, KPC-5

Colombie

(Villegas, AAC, 2007)

Porto Rico

(Cai, AAC, 2008)

Trinidad et Tobago

(Akpaka, JCM, 2009)

USA

(Poirel, AAC, 2010)

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2011, p. 2968–2970 Vol. 55, No. 6
0066-4804/11/$12.00 doi:10.1128/AAC.01633-10

Detection of the KPC Gene in *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* during a PCR-Based Nosocomial Surveillance Study in Puerto Rico▽

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Received 24 November 2010/Returned for modification 14 January 2011/Accepted 17 March 2011

A 6-month, PCR-based, island-wide hospital surveillance study of beta-lactam resistance in *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* was conducted in Puerto Rico. Of 10,507 isolates, 1,239 (12%) unique, multi-beta-lactam-resistant isolates from all geographical regions were identified. The KPC gene was detected in 61 *E. coli*, 333 *K. pneumoniae*, 99 *P. aeruginosa*, and 41 *A. baumannii* isolates, indicating the widespread dissemination of the KPC gene in clinically significant nosocomial isolates.

TABLE 1. Numbers of KPC-positive *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii* isolates among the total number of isolates and the multi-beta-lactam-resistant isolates

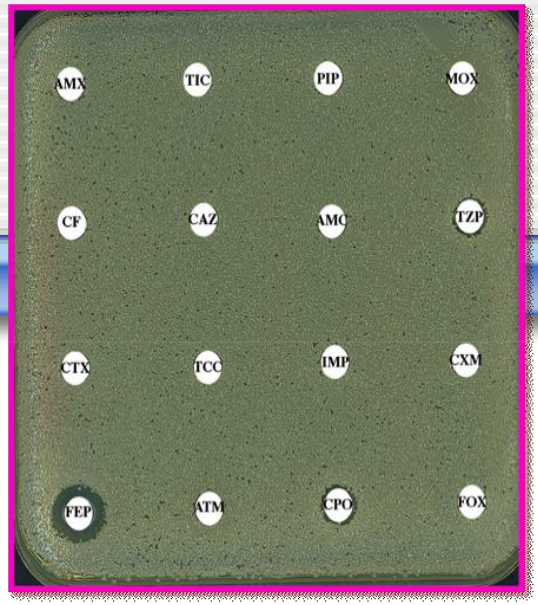
Organism	No. of isolates			No. of KPC producers/ total (%)	
	Total	MβLR	KPC producers	All isolates	MβLR isolates
E. coli	4,329	219	61	61/4,329 (1.4)	61/219 (33)
K. pneumoniae[a]	2,805	457	333	333/2,805 (12)	333/457 (73)
P. aeruginosa	2,415	272	99	99/2,415 (4.1)	99/272 (44)
A. baumannii	958	291	41	41/958 (4.3)	41/291 (14)
Total	10,507	1,239	534	534/10,507 (5)	534/1,239 (43)

[a] $P \leq 0.05$.

10.507 souches
534 souches KPC+ (5%)

1.239, Multi ß-lactam R (12%)
534 souches KPC+ (43%)

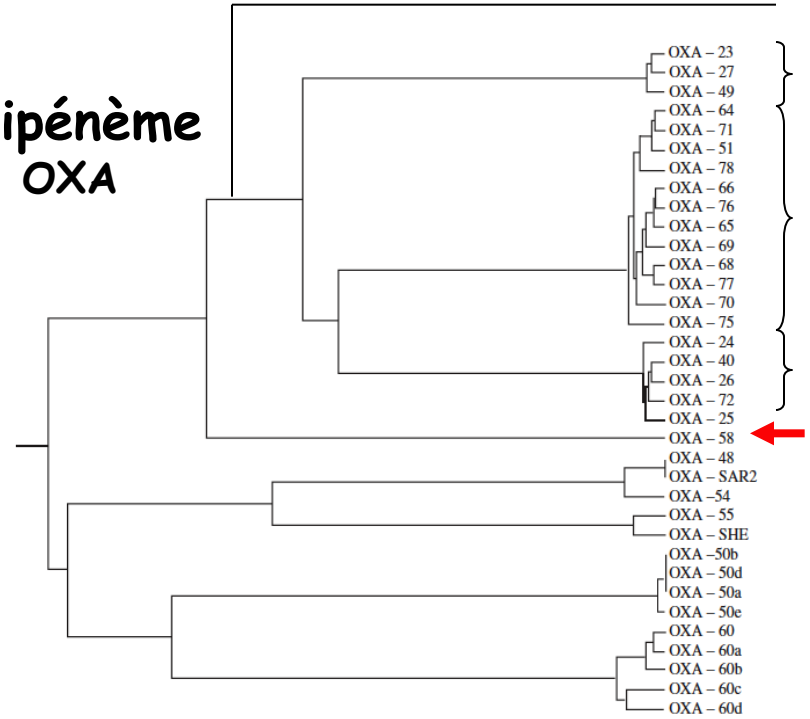
Résistance aux carbapénèmes chez *A. baumannii*



Cette résistance peut être le résultat de:

- Carbapénèmases de classe B
- Carbapénèmases de classe D (oxa)
- impermeability
- ou combination de ces mécanismes

Résistance à l'imipénème
Par production d'OXA



OXA-143

OXA-23 subgroup

OXA-51 subgroup

OXA-40 subgroup

OXA-58

POIREL, NAAS, NORDMANN, AAC 2010

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

Acinetobacter Infection

L. Silvia Munoz-Price, M.D., and Robert A. Weinstein, M.D.

ACINETOBACTER IS A GRAM-NEGATIVE COCCOBACILLUS (FIG. 1)[1,2] THAT during the past three decades has emerged from an organism of questionable pathogenicity to an infectious agent of importance to hospitals worldwide.[3,4] Approximately one quarter of the PubMed citations for "nosocomial acinetobacter" in the past 20 years appeared in 2005 and 2006. Acinetobacter infections have long been clinically prominent in tropical countries, have been a recurrent problem during wars and natural disasters, and have recently caused multihospital outbreaks in temperate climates. Most alarming are the organism's ability to accumulate diverse mechanisms of resistance, the emergence of strains that are resistant to all commercially available antibiotics,[5] and the lack of new antimicrobial agents in development.[6] At more than 300 U.S. hospitals surveyed by the Centers for Disease Control and Prevention (CDC), rates of carbapenem resistance in 3601 isolates of *Acinetobacter baumannii*, clinically the most important of 25 acinetobacter genospecies,[1] increased from 9% in 1995 to 40% in 2004.[7]

From Medical Specialists, Dyer, IN (L.S.M.-P.); and the Division of Infectious Diseases, Stroger (Cook County) Hospital, Ruth M. Rothstein CORE Center, and Rush Medical College — all in Chicago (R.A.W.). Address reprint requests to Dr. Munoz-Price at Medical Specialists, 919 Main St., Ste. 202, Dyer, IN 46311, or at simunozprice@gmail.com.

N Engl J Med 2008;358:1271-81.

Evolution of antimicrobial resistance

Table 1. Patterns of resistance (MIC in mg/l) of *A. baumannii*.

Antimicrobial agent	Study year and ref.							
	1993 [4]	1993 [5]	1996 [6]	2003 [7]	2003 [8]	2004 [9]	2007 [10]	2007 [11]
Ampicillin	98	91	88	–	–	98	–	–
Piperacillin	67	36	72	–	–	95	–	–
Ampicillin/sulbactam	48	–	34	21	–	54	–	49
Ceftazidime	45	32	42	45	27	85	97	88
Imipenem	0	0	2	5	3	48	38	71
Tobramycin	50	98	–	25	–	79	–	–
Amikacin	28	64	28	13	15	66	22	86
Ciprofloxacin	30	94	4	57	49	90	97*	93
Minocycline/doxycycline	2	–	–	–	–	35	7	–

*Levofloxacin instead of ciprofloxacin.

Vila J. and Pachón J. (2008) Expert Opin. Pharmacother. 9:587-599

Falagas M, et al: Trends in antimicrobial resistance of *Acinetobacter baumannii* clinical isolates from hospitalised patients in Greece and treatment implications
Clin Microbiol Infect 2007; 13:816

Table 1. Antimicrobial resistance of *Acinetobacter baumannii* isolates from patients in intensive care units in Greece

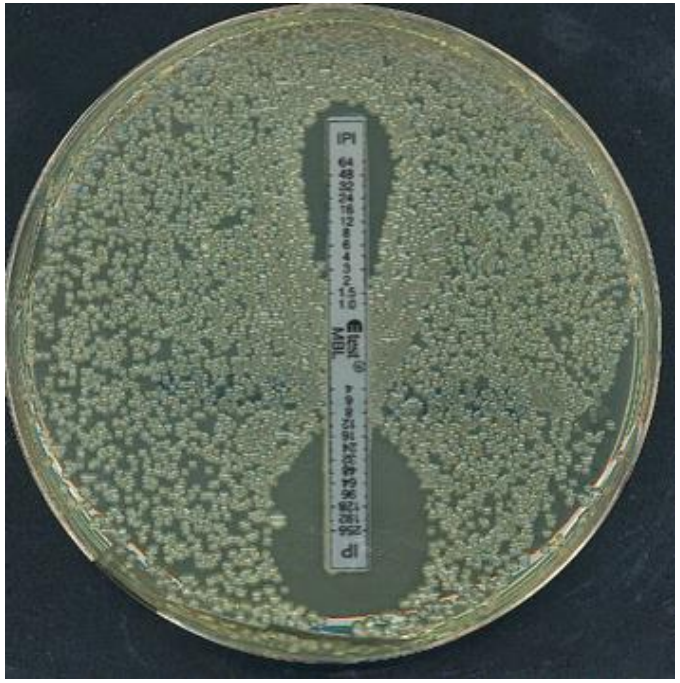
	Proportion of isolates with full or intermediate resistance										
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006[a]
Ampicillin–sulbactam	ND	46	40	ND	ND	ND	44	65	63	55	57
Piperacillin–tazobactam	ND	ND	ND	ND	ND	ND	84	91	96	96	98
Ceftazidime	ND	96	92	93	88	85	88	94	98	95	95
Cefepime	ND	81	84	ND	ND	ND	91	95	97	92	94
Imipenem	0	16	17	ND	10	27	44	66	64	78	91
Amikacin	ND	78	82	81	79	82	86	86	86	84	90
Ciprofloxacin	93	88	86	86	90	91	94	97	98	99	98
MDR[b]	ND	ND	ND	73	68	63	74	79	86	86	86

[a] Data available for the first semester of 2006.

[b] Multidrug-resistant (resistance to ceftazidime, ciprofloxacin, and amikacin).

Metallo-ß-lactamases et *A. baumannii* (très rares en France)

- VIMs
- IMPs



Metallo-ß-lactamases et *A. baumannii* (étaient rares en France?)

Coexistence of bla_{OXA-23} with bla_{NDM-1} and *armA* in clinical isolates of *Acinetobacter baumannii* from India

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Keywords: mixed carbapenemases, IS*Aba1*, high-level resistance to aminoglycosides

Mais aussi en France:

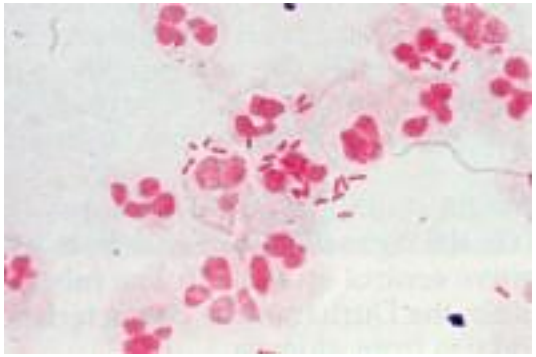
NDM-1-producing- *Acinetobacter baumannii* from Algeria. A Boulanger, T Naas, N Fortineau, S Figueiredo, and P Nordmann (AAC sous presse)

Et Chine, Egypt, Allemagne, Maroc, Israel …..

Conclusions

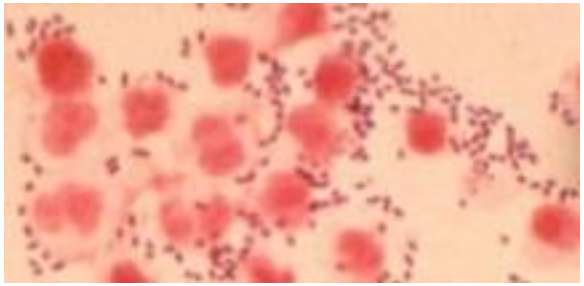
Enterobacteriaceae

1) KPC, OXA-48, NDM
2) ESBL/AMPC + impermeability
3) VIM, IMP, GIM



A. baumannii

1) Oxacillinases
2) NDM, GES, KPC



P. aeruginosa

1 VIM, IMP
2 KPC, NDM, GIM
3 OXA-198?