

Emergence of carbapenemase-producing *Enterobacteriaceae* in France, 2004 to 2011.

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Introduction - Context

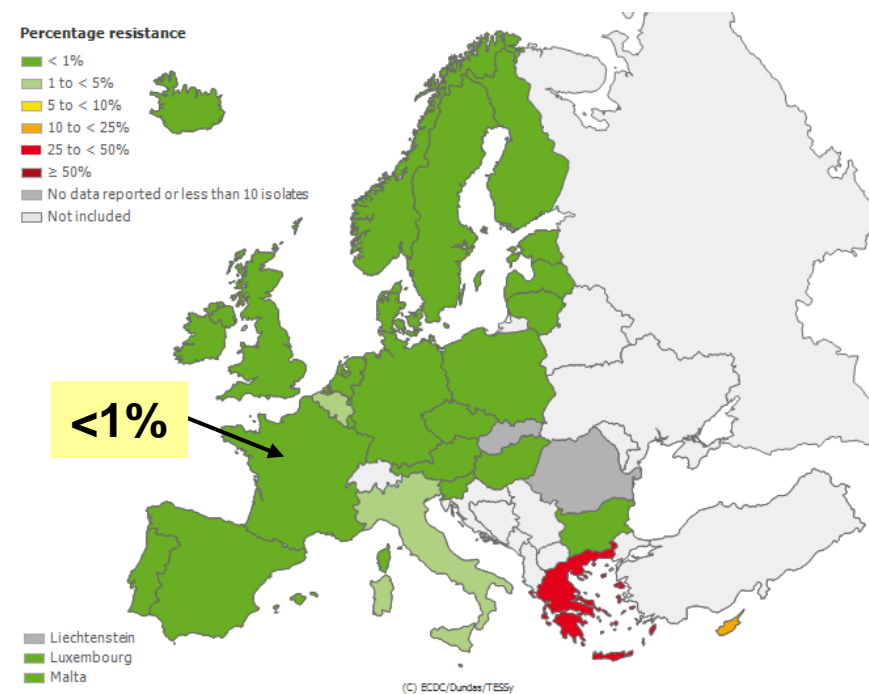
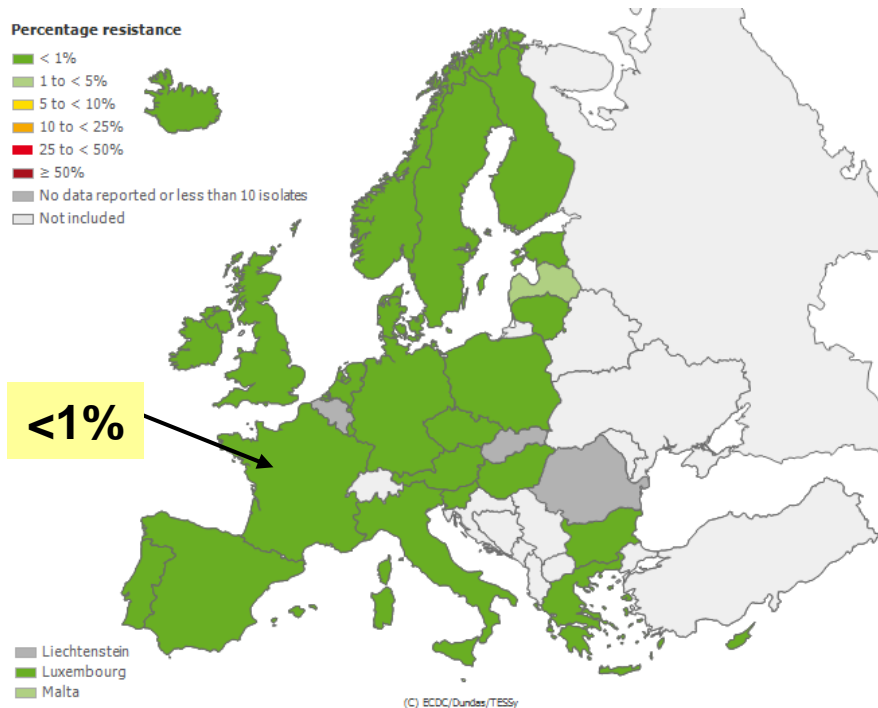
- *Enterobacteriaceae*
 - Increasingly resistant to antibiotics
 - Carbapenems: among the few last-line drugs for therapy against strains expressing extended-spectrum beta-lactamases.
- Carbapenemase-producing *Enterobacteriaceae* (CPE)
 - Resistance to carbapenems
 - Reported increasingly worldwide
 - Last step towards a therapeutic dead end

E. coli and *K. pneumoniae* : proportion of carbapenem resistant isolates from patients with invasive infections, 2009



% of carbapenem resistant *E. Coli* isolates, 2009

% of carbapenem resistant *K. pneumoniae* isolates, 2009





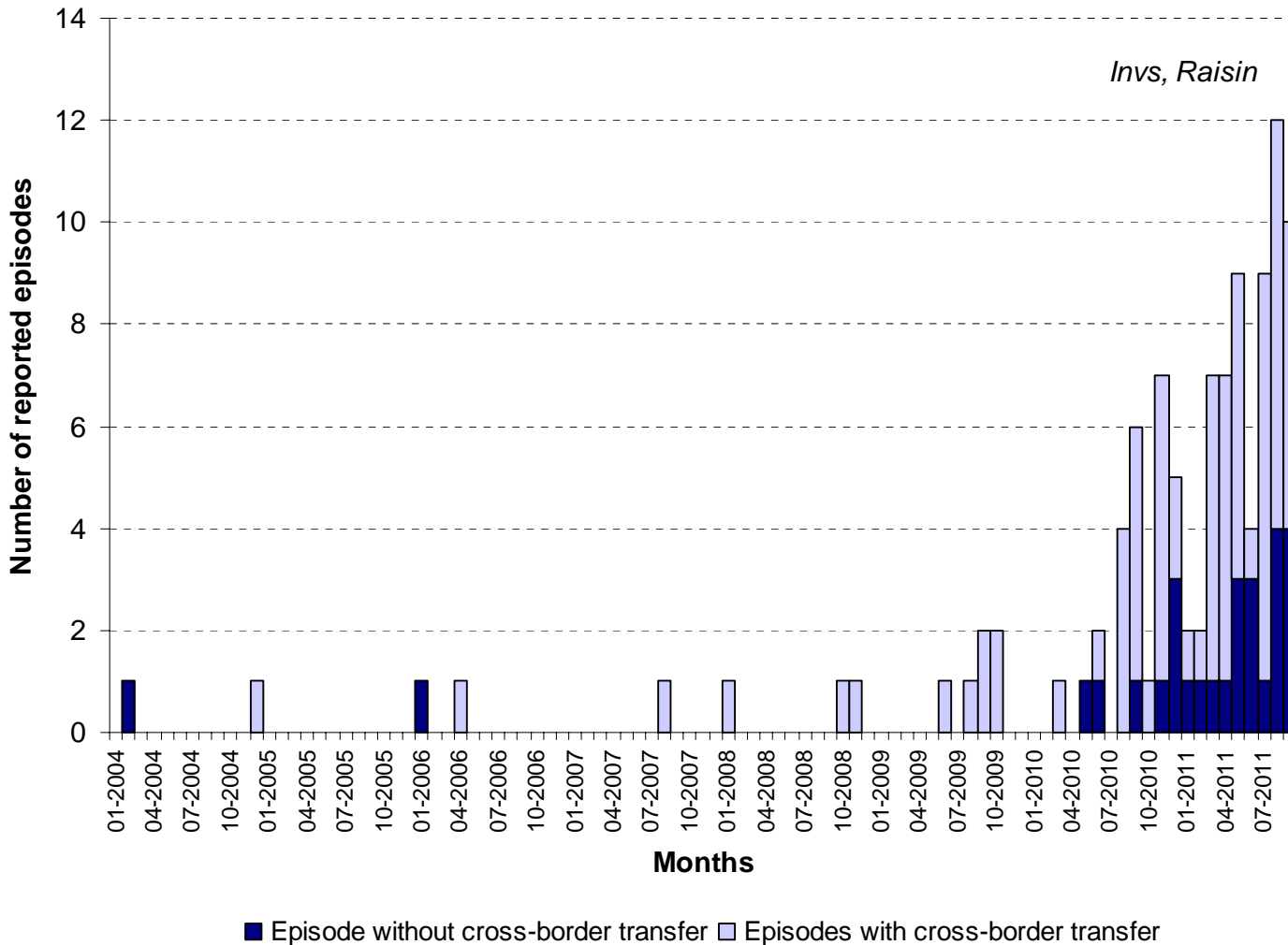
Objectives

- Review, quantify and describe the characteristics of CPE episodes reported to InVS
 - from February 2004 (when the first case were notified in France)
 - to September 2011

Methods

- Episodes with CPE
 - Notified by healthcare facilities through the French national Healthcare – Associated Infections Early Warning and Response System (HAI-EWRS)
 - Reported directly by microbiologists to InVS
- Study retrospective : before August 2010
prospective : since August 2010
- Definitions:
 - a case = a patient infected or colonised by a CPE confirmed by a reference or expert laboratory
 - an episode = one sporadic case or several cases related by an identified chain of transmission
- Data updated on 27 September 2011

Episodes of CPE infections or colonisations, by month, France, 1 January 2004 – 27 September 2011 (N=104)



104 episodes

2009: 6

2010: 28

2011(September): 62


Bacterial species involved in CPE reported episodes (N=104)

Bacterial species	Number of episodes	
	N	%
<i>Klebsiella pneumoniae</i>	67	59
<i>Escherichia coli</i>	25	22
<i>Enterobacter cloacae</i>	14	12
<i>Enterobacter aerogenes</i>	3	3
<i>Citrobacter freundii</i>	3	3
<i>Proteus mirabilis</i>	1	<1
<i>Serratia marcescens</i>	1	<1
<i>Providencia stuartii</i>	1	<1
Total	115*	100

* 2 or 3 enterobacteriaceae with the same carbapenemase involved in 9 episodes

Epidemiological characteristics of CPE episodes (N=104)

- 249 cases identified
 - Infected: 68 (29%)
 - Colonised: 170 (71%)
- - 238 cases described
- 1 to 44 cases by episode
- Secondary cases: 22 episodes (21%)
For these episodes:
 - Mean number of cases: 8 cases
 - Median number of cases: 3 cases
- 2 episodes with co-index cases
- Deaths: 51
 - Crude lethality rate (deaths of all cases, wether infected or colonised): 20%



Episodes associated with cross-border transfer within one year (N=76)

- 73% of all episodes

Context	Number of episodes	(%)
Direct transfer from a foreign hospital	50	(66%)
Hospitalisation in a foreign hospital	13	(17%)
Resident in France, travel abroad without reported hospitalisation	7	(9%)
Resident abroad without reported hospitalisation	6	(8%)
Total	76	(100%)

Carbapenemase type, by country where index cases had been hospitalised or stayed abroad (N=76)

Country	KPC	OXA-48	VIM	NDM-1	Total
Greece	16 ²⁰⁰⁷		4 ²⁰⁰⁴		19*
Morocco	2 ²⁰¹¹	15 ²⁰¹⁰			17
India	2 ²⁰¹¹			9 ²⁰¹⁰	9*
Italy	3 ²⁰¹⁰		2 ²⁰⁰⁸		5
Algeria	1 ²⁰¹⁰	2 ²⁰¹⁰	1 ²⁰⁰⁸		4
Egypt	1 ²⁰¹¹	2 ²⁰⁰⁹	1 ²⁰¹⁰		4
Turkey		4 ²⁰¹⁰			4
Tunisia		3 ²⁰¹¹			3
Senegal		3 ²⁰¹¹			3
Koweit		2 ²⁰¹¹			2
Israël	1 ²⁰¹¹	1 ²⁰¹¹			2
Iraq				1 ²⁰¹⁰	1
USA	1 ²⁰⁰⁶				1
Spain		1 ²⁰¹¹			1
Serbia				1 ²⁰¹¹	1
Total	27	33	8	11	76

^N Year of 1st report

^a two carbapenemases involved in a same episode

Carbapenemase type, by country where index cases had been hospitalised or stayed abroad (N=76)

Country	KPC	OXA-48	VIM	NDM-1	Total
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Episodes without cross-border transfer and carbapenemases involved (N=28)

KPC	OXA-48	VIM	NDM-1	IMI	IMP	Total
1 2010	21 2010	2 2004	3 2010	1 2011	1 2004	28 ^a

^a two carbapenemases involved for one episode

- 27% of all episodes without cross-border transfer identified
 - 75% of which involved OXA-48.
 - occurred in 4 regions, 12 French départements
- Suggesting the beginning of an autochthonous circulation of OXA-48 CPE in France ?



Limitations of the study

- Completeness of reporting can not be guaranteed
- Recent emphasis on CPE in the scientific litterature, national recommendations and media reports could have triggered better reporting and may partly explain the sharp increase in the last years
- A chain of transmission resulting from contact with an unknown traveller from abroad cannot be excluded



Conclusion

- CPE episodes are emerging in France
- their number significantly increased during the last 3 years
- Most of them are related with cross-border transfer
 - To be aware of the risk of the spread of multidrug resistance by cross-border transfer of patients
 - To identify rapidly CPE by screening carriers among patients transferred from hospitals in countries with high CPE prevalence and implement adequate control measures
 - To reinforce strongly appropriate control measures in countries where CPE are endemic
- Possible beginning of an autochthonous circulation of OXA-48
 - Sustained vigilance needed when carbapenem resistance is suspected in *Enterobacteriaceae* isolated from **any** patient

Acknowledgments

- Healthcare professionals
- Infection control units
- Interregional infection control coordinating centres (CClin)
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- For more information : <http://www.invs.sante.fr/epc>

Thank you for your attention.