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The role and contribution of reference laboratories in Europe (CPE microbiology / epidemiology)

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Microbiology reference labs in Europe

- **Public health microbiology:**
 - human, animal, food, water & environmental microbiology
 - focus on human health & disease
 - infectious disease detection
 - monitoring
 - outbreak response
 - provision of scientific evidence to prevent & control disease
- **2007, ECDC:**
 - National Microbiology Focal Points (NMFPs) in EU countries
- **2007-2010, NMFPs:**
 - survey of public health microbiology institutions in EU countries
 - **core activities of microbiology reference laboratories**



TECHNICAL REPORT

Core functions of
microbiology reference
laboratories
for communicable diseases

June 2010

www.ecdc.europa.eu

Microbiology reference labs in Europe

- **Remarkable variations in reference labs systems in the EU countries:**
 - reference laboratory definition
 - centralisation vs. broad distribution among various institutions
 - selection and evaluation methods
 - types of pathogens / diseases / specialised areas covered and their distribution among reference laboratories
- All diseases within the ECDC mandate (EP/EC Decision No 2119/98/EC) are covered by the EU reference lab network capacity
- **Core functions of microbiology reference laboratories:**
 - reference diagnostics (up-to-date methods, confirmation, atypical cases)
 - reference material resource (development/maintenance/access, provision)
 - scientific advice (advice/support/guidelines for health authorities & laboratories)
 - collaboration & research (regional/international networks/projects/initiatives)
 - monitoring, alert & response (surveillance, outbreak investigations, warnings)

AST / AMR reference labs in Europe

• AMR:

- recognised as one of the critical areas of public health microbiology
- included within the reference laboratory system in each European country
- since the 1990s international networking actions in Europe

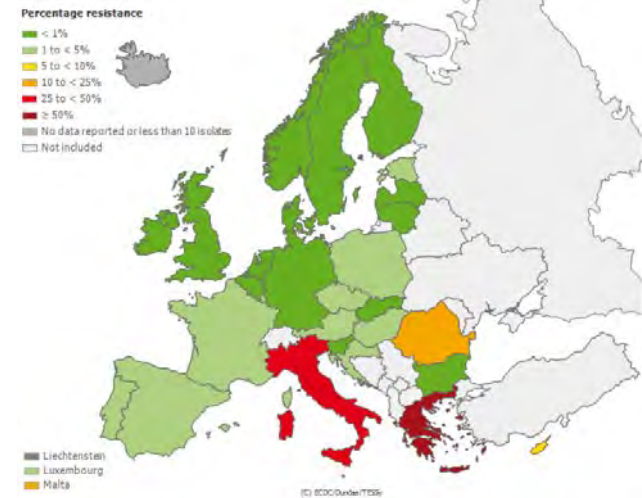
• EARSS / EARS-Net:

- AST / AMR reference labs network set-up at RIVM, The Netherlands
- since 2009 at ECDC
- network of national AMR surveillance systems; invasive cases data collection

E. coli carba-NS, 2013



K. pneumoniae carba-NS, 2013



AST / AMR reference labs in Europe

- European AST / AMR reference laboratories contribute to the activity of **EUCAST** (European Committee for Antimicrobial Susceptibility Testing), organised by ESCMID, ECDC and national European committees for susceptibility breakpoints:
 - country representatives of the EUCAST General Committee
 - 2011-2014: Subcommittee on the detection of resistance mechanisms of clinical and/or public health importance
- Guidelines for detection of major AMR mechanisms:
 - 2012, update 2013
 - include carbapenemase detection



EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance

**Version 1.0
December 2013**

EUCAST subcommittee for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance:
Christian G. Giske (Sweden, EUCAST Steering Committee and EARS-Net Coordination Group; chairman), Luis Martinez-Martinez (Spain, EUCAST Steering Committee), Rafael Cantón (Spain, chairman of EUCAST), Stefania Stefani (Italy), Robert Skov (Denmark, EUCAST Steering Committee), Youri Glupczynski (Belgium), Patrice Nordmann (France), Mandy Wootton (UK), Vivi Miriagou (Greece), Gunnar Skov Simonsen (Norway, EARS-Net Coordination Group), Helena Zemlickova (Czech republic, EARS-Net Coordination Group), James Cohen-Stuart (The Netherlands) and Marek Gniadkowski (Poland).

CPE reference labs / units in Europe

- **CPE reference units function within different structures:**
 - antibiotic / AST / AMR reference centres (e. g. Czech Republic, Poland, United Kingdom)
 - AMR Gram-negatives centres (e. g. Belgium, Germany)
 - specific CPE units (e. g. France)
- **Own / national activities** (often of international impact)



Carbapenemase-Producing *Enterobacteriaceae* in Spain in 2012

Jesús Oteo,³ David Saez,³ Verónica Bautista,³ Sara Fernández-Romero,³ Juan Manuel Hernández-Molina,³ María Pérez-Vázquez,³ Belén Aracil,³ José Campos,^{3,c} the Spanish Collaborating Group for the Antibiotic Resistance Surveillance Program

Antibiotic Laboratory, Bacteriology Department, Centro Nacional de Microbiología, Majadahonda, Madrid, Spain³; Microbiology Department, Hospital Universitario Carlos Haya, Málaga, Spain³; Consejo Superior de Investigaciones Científicas, Madrid, Spain³

J Antimicrob Chemother 2014; 69: 1777–1784
doi:10.1093/jac/dku084 Advance Access publication 25 April 2014

Journal of
Antimicrobial
Chemotherapy

NDM carbapenemases in the United Kingdom: an analysis of the first 250 cases

Anu Jain¹, Katie L Hopkins¹, Jane Turton¹, Michel Doumith¹, Robert Hill¹, Richard Loy¹, Daniele Meunier¹, Rachel Pike¹, David M. Livermore^{1,2} and Neil Woodford^{1*}

¹Antimicrobial Resistance and Healthcare Associated Infections Reference Unit, Public Health England, London NW9 5EQ, UK; ²Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK



Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio



Comparison of the SUPERCARBA, CHROMagar KPC, and Brilliance CRE screening media for detection of *Enterobacteriaceae* with reduced susceptibility to carbapenems^{☆☆☆}

Delphine Girlich, Laurent Poirel, Patrice Nordmann^{*}

Service de Bactériologie-Virologie, INSERM U914 "Emerging Resistance to Antibiotics", Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine et Université Paris Sud, K-Bicêtre, France

RAPID COMMUNICATIONS

NDM-1- or OXA-48-producing *Enterobacteriaceae* colonising Polish tourists following a terrorist attack in Tunis, March 2015

R Izdebski¹, K Bojarska¹, A Baraniak¹, E Literacka¹, M Herda¹, D Żabicka¹, A Guzek², M Półgrabia², W Hryniewicz², M Gniadkowski (gniadkow@cls.edu.pl)¹

¹ National Reference Centre for Susceptibility Testing & Department of Molecular Microbiology, National Medicines Institute, Warsaw, Poland
² Military Institute of Medicine, Warsaw, Poland

CPE reference labs / units in Europe

- **International activities:**
 - **Group of European experts**, including several reference labs:
 - ESGARS (ESCMID) Meeting on Metallo- β -lactamases, Siena 2005
 - ESCMID Consensus Conference on Carbapenamases and Carbapenem-resistant Gram-negatives, Athens 2008
 - detection, surveillance, infection control, clinical issues
 - set of significant position papers or reviews



International Journal of Antimicrobial Agents 29 (2007) 380–386

INTERNATIONAL JOURNAL OF
Antimicrobial
Agents

www.elsevier.com/locate/ijantag

Discussion

Metallo- β -lactamases as emerging resistance determinants in Gram-negative pathogens: open issues

Giuseppe Cornaglia^{a,*}, Murat Akova^b, Gianfranco Amicosante^c, Rafael Cantón^d, Roberto Cauda^e, Jean-Denis Docquier^{f,g}, Mikhail Edelstein^h, Jean-Marie Frère^g, Miklós Fuziⁱ, Moreno Galleni^g, Helen Giamarellou^j, Marek Gniadkowski^k, Raffaella Koncan^l, Balázs Libisch^l, Francesco Luzzaro^l, Vivi Miriagou^m, Ferran Navarro^{n,o}, Patrice Nordmann^p, Laura Pagani^q, Luisa Peixe^r, Laurent Poirel^p, Maria Souli^j, Evelina Tacconelli^e, Alkiviadis Vatopoulos^s, Gian Maria Rossolini^f

on behalf of the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS)

EDITORIAL

10.1111/j.1469-0691.2009.03114.x

The emerging threat of acquired carbapenemases in Gram-negative bacteria

G. Cornaglia¹ and G. M. Rossolini²

REVIEW

10.1111/j.1469-0691.2009.03115.x

Controlling the spread of carbapenemase-producing Gram-negatives: therapeutic approach and infection control

Y. Carmeli¹, M. Akova², G. Cornaglia³, G. L. Daikos⁴, J. Garau⁵, S. Harbarth⁶, G. M. Rossolini^{7,8}, M. Souli⁹ and H. Giamarellou⁷

REVIEW

10.1111/j.1469-0691.2009.03116.x

Acquired carbapenemases in Gram-negative bacterial pathogens: detection and surveillance issues

V. Miriagou¹, G. Cornaglia², M. Edelstein³, I. Galani⁴, C. G. Giske⁵, M. Gniadkowski⁶, E. Malamou-Lada⁷, L. Martínez-Martínez⁸, F. Navarro⁹, P. Nordmann¹⁰, L. Peixe¹¹, S. Pourmaras¹², G. M. Rossolini¹³, A. Tsakris¹⁴, A. Vatopoulos¹⁵ and R. Cantón¹⁶

CPE reference labs / units in Europe

- International activities:
 - **European Network on Carbapenemases** with some reference labs:
 - ESCMID Consensus Conference on Carbapenamases Production in *Enterobacteriaceae*, *P. aeruginosa* and *A. baumannii*, Paris 2011
 - epidemiology, detection, surveillance
 - significant reviews

REVIEW

10.1111/j.1469-0691.2012.03815.x

Identification and screening of carbapenemase-producing *Enterobacteriaceae*

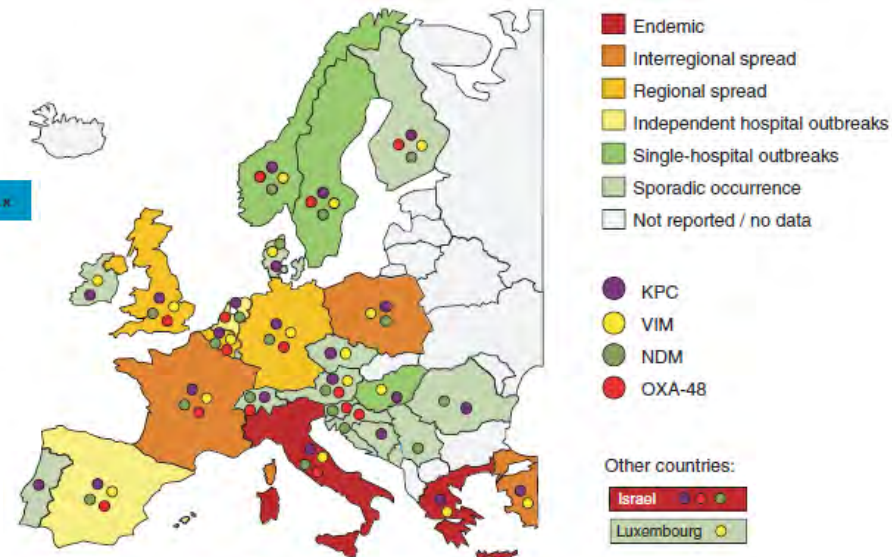
P. Nordmann¹, M. Gniadkowski², C. G. Giske³, L. Poirel¹, N. Woodford⁴, V. Miriagou⁵ and the European Network on Carbapenemases⁶

REVIEW

10.1111/j.1469-0691.2012.03821.x

Rapid evolution and spread of carbapenemases among *Enterobacteriaceae* in Europe

R. Cantón^{1,2}, M. Akóva³, Y. Carmeli⁴, C. G. Giske⁵, Y. Glupczynski⁶, M. Gniadkowski⁷, D. M. Livermore^{8,9}, V. Miriagou¹⁰, T. Naas¹¹, G. M. Rossolini¹², Ø. Samuelsen¹³, H. Seifert¹⁴, N. Woodford⁹ and P. Nordmann¹¹; the European Network on Carbapenemases⁶



CPE reference labs / units in Europe

• International activities:

- **Carbapenem Non-Susceptible Enterobacteriaceae (CNSE) Working Group** (incl. all European reference labs):
 - Meeting on Carbapenemase-Producing Klebsiella, Bilthoven 2010
 - epidemiology, detection, surveillance, infection control
 - position paper
- **ECDC & ECDC NARFPs & EARS-Net Contact Points** (reference labs):
 - European NDM-1 electronic survey, 2010
 - NDM epidemiology & surveillance

EUROROUNDUPS

Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts

H Grundmann (Hajo.Grundmann@rivm.nl)^{1,2}, D M Livermore³, C G Giske⁴, R Canton^{5,6}, G M Rossolini⁷, J Campos⁸, A Vatopoulos⁹, M Gniadkowski¹⁰, A Toth¹¹, Y Pfeifer¹², V Jarlier¹³, Y Carmell¹⁴, the CNSE Working Group¹⁵

RESEARCH ARTICLES

New Delhi metallo-beta-lactamase 1-producing Enterobacteriaceae: emergence and response in Europe

M. J. Struelens (marc.struelens@ecdc.europa.eu)¹, D L Monnet¹, A P Magiorakos¹, F Santos O'Connor¹, J Giesecke¹, the European NDM-1 Survey Participants²

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
2. The European NDM-1 Survey Participants are listed at the end of the article

Country	Stage	Epidemiological scale	Documented introduction from abroad	Dominant class	Underreporting			
Greece	5	Endemic	Yes	KPC/VIM				
Israel*				KPC				
Italy	4	Interregional spread	Yes	KPC				
Poland					Likely			
France	3	Regional spread	Yes	KPC				
Germany				OXA-48/VIM	Likely			
Hungary				KPC	Likely			
Belgium				VIM	Likely			
Spain	2b	Independent hospital outbreaks	Yes	KPC/VIM/IMP	Likely			
England and Wales				NDM				
Cyprus	2a	Single hospital outbreak		VIM				
Netherlands				Yes	KPC			
Norway				Yes	KPC			
Scotland					KPC			
Sweden				Yes	KPC			
Bosnia Herzegovina				Yes	KPC			
Denmark					KPC/VIM			
Finland				Yes	KPC			
Croatia		VIM						
Czech Republic	1	Sporadic occurrence	Yes	VIM/KPC				
Ireland				KPC	Likely			
Lithuania				?	Likely			
Latvia				?	Likely			
Malta				?				
Portugal					KPC	Likely		
Romania					?	Likely		
Switzerland					KPC			
Austria				0	Not reported			
Bulgaria								Likely
Estonia		Likely						
Iceland								
Slovenia								

CPE reference labs / units in Europe

- International activities:
 - European Survey on CPE (EuSCAPE):
 - partial ECDC funding
 - Scientific Advisory Board (SAB) (group of European experts)
 - National Experts (NEs): EARS-Net Contact Points (reference labs)
 - sentinel laboratories (in proportion to the country size)
 - aimed at revealing actual rates of carba-NS and CPE in Europe
 - electronic questionnaire survey on CPE by all NEs, February 2013
 - baseline survey paper, June 2013
 - laboratory structured survey, November 2013 – April 2014
 - paper in preparation



RAPID COMMUNICATIONS

Carbapenemase-producing *Enterobacteriaceae* in Europe: a survey among national experts from 39 countries, February 2013

C Glasner¹, B Albigler², G Bulst¹, A Tambić Andrašević³, R Canton^{4,5}, Y Carmell⁶, A W Friedrich¹, C G Giske^{7,8}, Y Glupczynski⁹, M Gniadkowski¹⁰, D M Livermore^{11,12}, P Nordmann^{13,14}, L Polret^{13,14}, G M Rossolini¹⁵, H Selfert¹⁶, A Vatopoulos¹⁷, T Walsh¹², N Woodford¹⁸, T Donker¹, D L Monnet², H Grundmann (h.grundmann@umcg.nl)¹, the European Survey on Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group¹⁹

AMR monitoring and research in Poland

- **The National Medicines Institute:**
 - **The National Reference Centre for Susceptibility Testing:**
 - guidelines for AST and AMR mechanism detection
 - postgraduate education in AST performance
 - reference ID & AST diagnostics
 - AMR monitoring (national & international)
 - passive within EARS-Net (data collection & processing)
 - active by continuous surveillance or specific projects
 - » isolates & data collection; state-of-the-art basic laboratory analysis
 - » alert AMR pathogens, *e. g.* MRSA, VI/RSA, VRE, CPE, CRAB, MBL-PA
 - **Research groups:**
 - large- & small-scale molecular epidemiology projects on APs
 - clonality & AMR mechanisms
 - national or international collaborative studies
 - typing for local outbreak investigations





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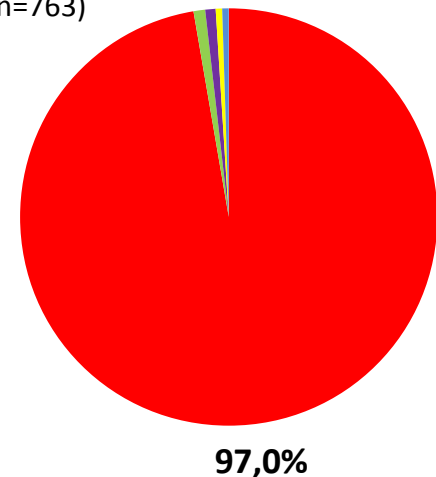
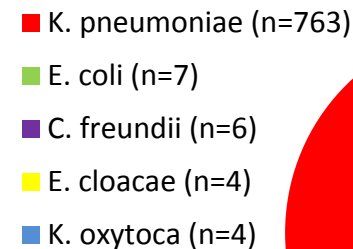
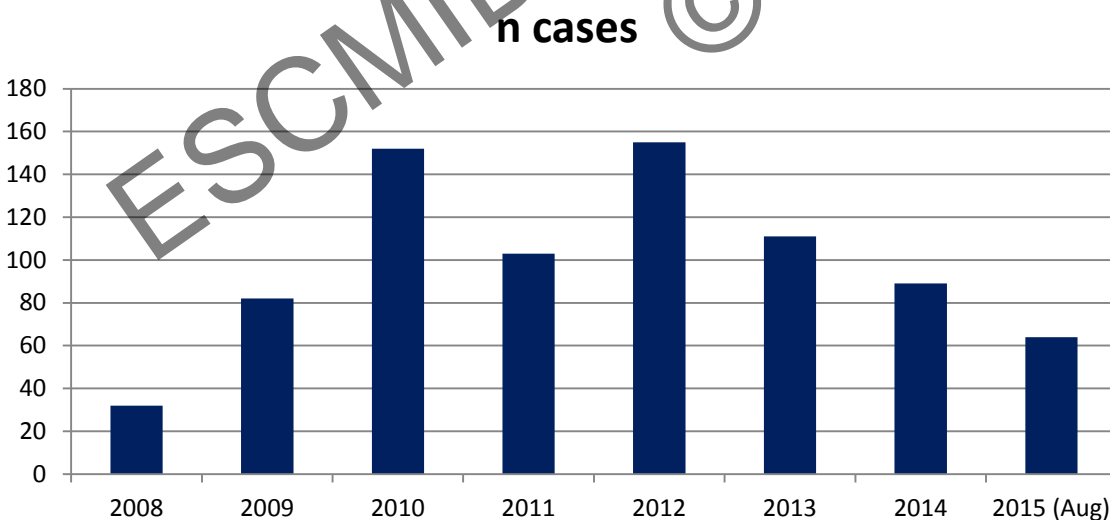
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KPCs in Poland

KPCs in Poland:

- 1st case reported: May 2008, Warsaw, patient with no travelling history
- rapid dissemination: CPE problem No. 1 by the end of 2012
- clusters of cases in 5 administrative regions
- scattered cases in other sites; several imports (USA, Italy, Greece, Ukraine)

year	2008	2009	2010	2011	2012	2013	2014	2015 (Aug)	total
n cases	32	82	152	103	155	111	89	64	788
n hospitals	5	18 (13)	34 (23)	30 (18)	36 (15)	23 (6)	30 (12)	25 (5)	97





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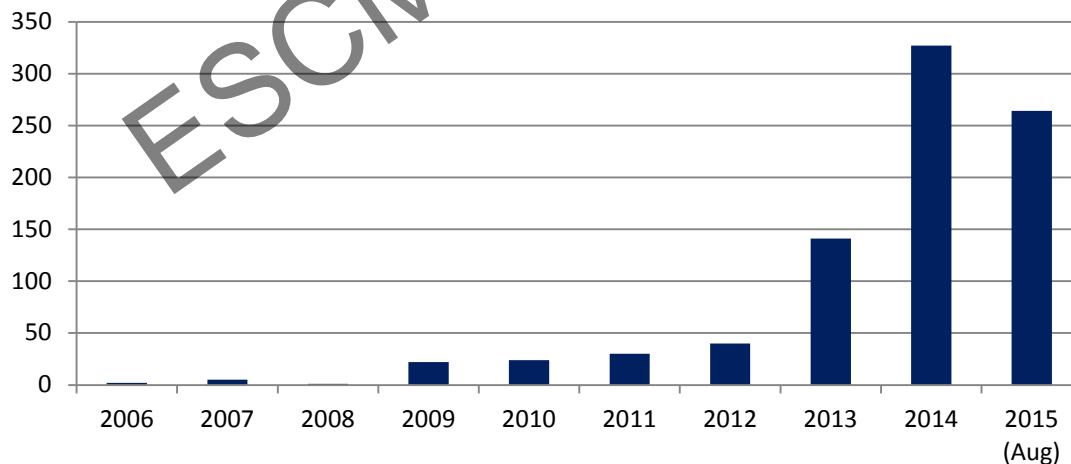
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MBLs in Poland (CPE)

- *P. aeruginosa* from 1998
- **Enterobacteriaceae:**
 - 2006: *K. pneumoniae* VIM-4, Bydgoszcz, unknown origin
 - 2009: *Serratia marcescens* IMP-19, Mielec, unknown origin
 - 2011: *E. coli* NDM-1, Warsaw, from the Congo
- **Dramatic increase from 2013** – more than KPCs

MBL cases in total: n=856

MBL	2006-08	2009	2010	2011	2012	2013	2014	2015 (Aug)	total
No. cases	8	22	24	30	40	141	327	264	856





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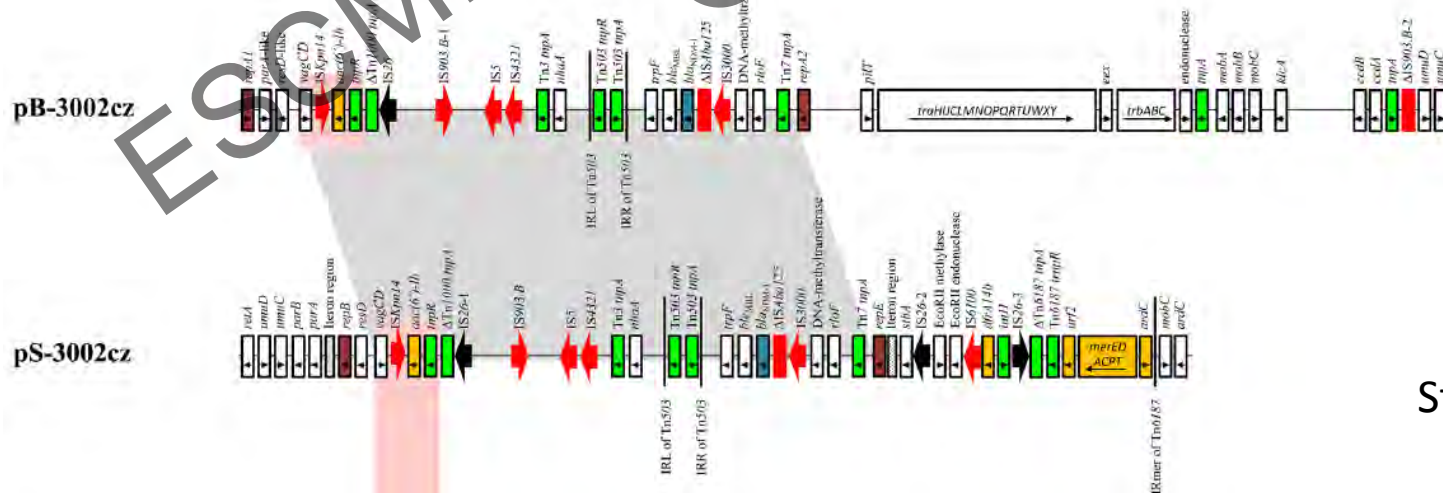
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NDM interregional outbreak

- **Molecular study:**
 - detailed on 56 isolates from 12 centres from 2012-2013
 - partial on 10 isolates from 6 centres from 2014
 - *K. pneumoniae* ST11 subclone of high microheterogeneity
 - similar to a Czech isolate from 2013 of Slovak origin in 2012 (Studentova 2015)
 - two NDM-1-encoding plasmids of low or no self-transmissibility potential
 - plasmid rearrangements
 - often co-production of the ESBL CTX-M-15



Studentova et al. 2015;
Baraniak et al. 2015

NDM imports

- **NDM-1 sporadic cases:**

Centre	Date	Organism	NDM	Origin
Warsaw 1	07.2011	<i>E. coli</i> ST410	NDM-1	Congo
Warsaw 1	08.2013	<i>K. oxytoca</i> ST164	NDM-1	Montenegro
Gdynia	09.2013	<i>E. coli</i> ST448	NDM-5	India
Bydgoszcz	12.2013	<i>P. mirabilis</i>	NDM-1	Afghanistan
Nowa Sól	12.2013	<i>K. pneumoniae</i> ST45	NDM-1	???
Sosnowiec	02.2015	<i>E. coli</i>	NDM-?	India
Warsaw 1	03.2015	<i>K. pneumoniae</i> ST147	NDM-1	Tunisia
Warsaw 2	03.2015	<i>K. pneumoniae</i> ST147, <i>E. coli</i> ST410	NDM-1	Tunisia



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 - Małgorzata Herda
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 - Waleria Hryniewicz
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