

## More and more third generation cephalosporin-resistant enteric bacteria everywhere?

## Molecular profiling of beta-lactam-resistant Enterobacteriaceae collected as part of the Tigecycline European Surveillance Trial (TEST) in 2012-2013

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**Objectives:** TEST monitors the *in vitro* activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally. This study reports the  $\beta$ -lactamase content of a subset of TEST isolates collected in 15 European countries in 2012-2013.

**Methods:** Non-duplicate clinical isolates were collected from defined infection sites. Susceptibility testing was performed by CLSI broth microdilution by the local laboratory using supplied panels and interpreted using EUCAST breakpoints. Confirmation of meropenem non-susceptibility and extended-spectrum  $\beta$ -lactamase (ESBL) phenotypes was performed at IHMA, Inc. A subset of isolates that were meropenem non-susceptible (MIC > 2 mg/L) and/ or positive for ESBL production using the CLSI disk diffusion confirmatory test were molecularly characterised for genes encoding ESBLs, serine carbapenemases (KPC, OXA-48), metallo- $\beta$ -lactamases (MBLs; NDM, VIM, IMP) and AmpC  $\beta$ -lactamases.

**Results:** 15,690 *Enterobacteriaceae* were collected from Belgium (965), Bulgaria (29), Croatia (94), Denmark (167) Finland (171), France (2488), Germany (3093), Ireland (398), Italy (2734), Poland (91), Portugal (866), Romania (18), Spain (3833), Sweden (296), and the United Kingdom (447) in 2012-2013. The overall collection was 68.1% susceptible to ceftazidime, 97.1% susceptible to meropenem, and 92.4% susceptible to tigecycline. A subset of 1626 isolates (48 *Enterobacter* spp., 718 *Escherichia coli*, 831 *Klebsiella* spp., and 29 other *Enterobacteriaceae*) were molecularly characterised. The  $\beta$ -lactamase content of isolates are shown below.

Enzyme Groups (n=1626) <sup>1</sup>	Great Britain (70) <sup>2</sup>	Nordic (34)	Portugal (112)	Spain (319)	France (226)	Belgium (86)	Germany (213)	Italy (523)	East (43)
ESBL (1246)	67; 95.7%	32; 94.1%	101; 90.2%	256; 80.3%	208; 92.0%	73; 84.9%	187; 87.8%	287; 54.9%	35; 81.4%
AmpC (27)				11; 3.4%	4; 1.8%	2; 2.3%	2; 0.9%	7; 1.3%	1; 2.3%
ESBL+AmpC (13)		1; 2.9%		5; 1.6%	2; 0.9%		2; 0.9%	2; 0.4%	1; 2.3%
KPC (165)			6; 5.4%	4; 1.3%			1; 0.5%	154; 29.4%	
KPC+ESBL/AmpC (32)				1; 0.3%			1; 0.5%	30; 5.7%	
OXA-48 (4)				3; 0.9%		1; 1.2%			
OXA-48+ESBL/AmpC (21)	1; 1.4%			13; 4.1%	1; 0.4%	2; 2.3%	2; 0.9%	1; 0.2%	1; 2.3%
VIM (9)				6; 1.9%				3; 0.6%	
VIM+ESBL/AmpC (30)				3; 0.9%			5; 2.3%	20; 3.8%	2; 4.7%
NDM+ESBL+AmpC (3)				2; 0.6%					1; 2.3%
NDM+OXA-48 (1)						1; 1.2%			
No ESBL, AmpC, or Cp/ase identified (75) <sup>3</sup>	2; 2.9%	1; 2.9%	5; 4.4%	15; 4.7%	11; 4.9%	7; 8.1%	13; 6.1%	19; 3.6%	2; 4.7%

<sup>1</sup>Includes original/ broad-spectrum  $\beta$ -lactamases in addition to the indicated enzymes.

<sup>2</sup>Great Britain (n): Ireland (40), United Kingdom (30); Nordic: Denmark (6), Finland (23), Sweden (5); East: Bulgaria (5), Croatia (15), Poland (17), Romania (6).

<sup>3</sup>Stable derepression of chromosomally-encoded  $\beta$ -lactamases was not assayed.

**Conclusions:** Country-to-country differences in the incidence of  $\beta$ -lactamases, especially serine carbapenemases and MBLs, were observed. No IMP MBLs were detected among characterized isolates.