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Antimicrobial resistance

Carbapenem resistance: implementation of an enhanced surveillance system

This article describes the background to the planned implementation of an electronic reporting system for the enhanced surveillance of carbapenem resistance in Gram-negative bacteria.

Increasing carbapenem resistance among Gram-negative bacteria is a major public health concern in the UK and worldwide [1,2]. Carbapenems have become the antibiotics of last resort for many serious bacterial infections, especially in the healthcare setting. Therefore it is crucial to prevent the spread of carbapenem-resistant bacteria, to identify emerging resistance mechanisms and to monitor changing resistance patterns. This imperative was highlighted in the recently published UK Five Year Antimicrobial Resistance Strategy 2013 to 2018 [3].

In Gram-negative bacteria, carbapenem resistance results from one or more of several different mechanisms, including the production of acquired carbapenemases. Acquired carbapenemases are included in Ambler β-lactamase classes A, B and D. Ambler class A β-lactamases include the *Klebsiella pneumoniae* carbapenemases (KPC), one of the most frequently isolated carbapenemase families [4,5]. New Delhi metallo-β-lactamases (NDM) belong to the Ambler class B carbapenemases, as also do the Verona integron-encoded metallo-β-lactamase (VIM) and IMP (named after their affinity for imipenem) families of carbapenemases. The final class of carbapenemases, known as the carbapenem-hydrolysing class D β-lactamases (CHDLs), are most frequently found in *Acinetobacter* spp., but recently there has been increasing detection of OXA-48 and OXA-48-like enzymes among Enterobacteriaceae [6].

Data from PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit shows that many carbapenemase-producing Enterobacteriaceae are resistant not only to carbapenem antibiotics, but to many classes of antibiotics (table 1). Only colistin remained active against >90% of all carbapenemase-producing Enterobacteriaceae confirmed by AMRHAI in 2014 (table 1). However, colistin-resistant isolates have been referred to AMRHAI from UK laboratories.

Table 1. Antibiotic susceptibilities of carbapenemase-producing Enterobacteriaceae isolates from the UK, submitted to the AMRHAI Reference Unit in 2014

Antibiotic	Proportion of susceptibility, % [a]					
	Metallo-enzyme producers (NDM, VIM, IMP) (n=c. 400)			Non-metallo-enzyme producers (KPC, OXA-48, GES, IMI) (n=c. 1250)		
	E. coli	*Klebsiella*	*Enterobacter / Citrobacter*	*E. coli*	*Klebsiella*	*Enterobacter / Citrobacter*
Imipenem (IPM)	3	2	3	48	7	40
IPM-EDTA [b]	100	88	94	69	17	42
Meropenem	6	5	8	73	12	51
Ertapenem	3	0	3	4	0	1
Ampicillin	0	0	0	0	0	0
Co-amoxiclav	1	0	0	1	0	0
Piperacillin (PIP)	0	0	1	0	0	1
PIP-tazobactam	2	0	1	1	0	1
Cefotaxime	1	0	0	10	3	13
Ceftazidime	1	0	0	25	7	34
Aztreonam	13	13	23	15	7	34
Ciprofloxacin	17	6	20	61	30	68
Gentamicin	31	24	24	51	56	66
Tobramycin	22	7	8	51	47	59
Amikacin	49	33	62	92	82	96
Colistin	100	93	93	100	94	100
Tigecycline	99	52	73	98	59	80

a. Susceptibility defined using BSAC v. 13 (June 2014) breakpoints

b. Diagnostic test to distinguish metallo- from non-metallo- enzymes; not for therapeutic use

Active in vitro against <50% isolates
Active in vitro against 50-90% isolates
Active in vitro against >90% isolates

Evidence of transmission of genes conferring carbapenem resistance between bacterial species has been well documented and this poses challenges in the surveillance, management and control of antimicrobial resistance [7]. In December 2013, Public Health England (PHE) published the “Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae”, including a risk assessment matrix, to support efforts in the management and control of carbapenem resistance [8]. Although the toolkit is focussed on Enterobacteriaceae, it is recognised that carbapenem resistance is also of concern in other Gram-negative organisms, including *Pseudomonas* spp. and *Acinetobacter* spp. [9]. A national enhanced surveillance programme for carbapenem resistance, with a focus on Gram-negative bacteria expressing *acquired* carbapenemases, is in development and will help to provide improved understanding of the current situation across England.

The enhanced surveillance of carbapenem-resistant Gram-negative bacteria will use a web-based electronic reporting system (ERS). The ERS will serve two main functions: (i) as a system for laboratories to request confirmation and characterisation of carbapenem-resistant Gram-negative bacteria where expression of an acquired carbapenemase is suspected and; (ii)

as a system for laboratories to report bacteraemias caused by carbapenem-resistant Gram-negative bacteria. The ERS will collect information on patient demographics, submitting laboratory (including specimen and Trust details), healthcare setting and risk factors. Some of this information must be provided at the time of isolate referral or bacteraemia reporting (core dataset). All other information should be provided within seven days of the isolate referral or bacteraemia report (enhanced dataset).

Laboratories will be requested to refer and report organisms suspected of producing acquired carbapenemases as detailed in the most recent version of the "UK Standards for Microbiology Investigations: Laboratory Detection and Reporting of Bacteria with Carbapenem-Hydrolysing β-lactamases (Carbapenemases)" (10). Furthermore, laboratories will be requested to report all cases of bacteraemia caused by carbapenem-resistant Gram-negative bacteria, irrespective of suspected resistance mechanism.

The ERS will be implemented in spring/summer 2015. User guides for laboratories and Infection Prevention and Control Teams will be prepared and circulated prior to the system going live.

The enhanced surveillance of carbapenem resistance in Gram-negative bacteria will help stakeholders develop a greater understanding of the epidemiology of carbapenem resistance in England through the regular analysis and feedback of results. Analysis of data at the regional and national levels will allow identification of patient groups that may be more affected by carbapenem-resistant organisms, monitoring of changes in the epidemiology of carbapenemase-producing bacteria and the evaluation of interventions introduced to prevent the spread of carbapenem resistance. Furthermore, Trusts and laboratories will be able to access and manage their data locally, providing an opportunity for local-level data analysis.

The enhanced surveillance programme is one of many activities initiated by PHE, in collaboration with the NHS, that aims to tackle the emergence of carbapenem resistance in England. The collection and analysis of enhanced surveillance data will be crucial in informing and refining policy and guidelines around the prevention and management of patients infected with or colonised by carbapenem-resistant Gram-negative bacteria.

References

1. DH (2013). Annual Report of the Chief Medical Officer (Volume Two): infections and the rise of antimicrobial resistance.

2. WHO (2104). Antimicrobial Resistance: Global Report on Surveillance.

3. DH (2013). UK Five Year Antimicrobial Resistance Strategy 2013 to 2018.

4. Nordmann P, Cuzon G, Naas T (2009). The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria. *Lancet Infect Dis* **9**:228-36.

5. Woodford N, Turton JF, Livermore DM (2011). Multiresistant Gram-negative bacteria: the role of high-risk clones in the dissemination of antibiotic resistance. *FEMS Microbiol Rev* **35**: 736-55.

6. Mathers AJ, Hazen KC, Carroll J, Yeh AJ, Cox HL, Bonomo RA, et al (2013). First clinical cases of OXA-48-producing carbapenem-resistant *Klebsiella pneumoniae* in the United States: the "menace" arrives in the new world. *J Clin Microbiol* **51**: 680-3.

7. Goren MG, Carmeli Y, Schwaber MJ, Chmelnitsky I, Schechner V, Navon-Venezia S (2010). Transfer of carbapenem-resistant plasmid from Klebsiella pneumoniae ST258 to Escherichia coli in patient. *Emerg Infect Dis* **16**: 1014-7.8.

8. PHE (2013). Acute Trust toolkit for the early detection, management and control of Carbapenemase-Producing Enterobacteriaceae.

9. Freeman R, Moore LSP, Charlett A, Donaldson H, Holmes AH (2014). Exploring the epidemiology of carbapenem-resistant Gram-negative bacteria in west London and the utility of routinely collected hospital microbiology data. *J Antimicrob Chemother*.

10. PHE. UK Standards for Microbiology Investigations: Laboratory Detection and Reporting of Bacteria with Carbapenem-Hydrolysing b-Lactamases (Carbapenemases).