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Editorial

Carbapenemase-producing Enterobacterales: a challenge for healthcare now and for the next decade

One of the greatest antimicrobial resistance challenges for the safe provision of healthcare and infection prevention control professionals is from carbapenemase-producing Enterobacterales (CPE). Acquired carbapenemases have been described in many Gram-negative species, the most prevalent in England being OXA-48-like, NDM, KPC, VIM, IMP [1,2].

The acquisition of acquired carbapenemases by successful Enterobacterales clones has led to the global spread of CPE [3], with uncontrolled transmission resulting in endemic situations in some countries [4] and in regions of England [5]. The spread of carbapenemases may also be due to dissemination of successful plasmids within diverse strain types, as has been observed with OXA-48 [6]. Further, species producing multiple acquired carbapenemases have been reported, with combinations of OXA-48-like plus NDM being the most common in England [1].

Treatment options for infections caused by CPE are challenging and for some CPE (particularly NDM-producers) options are extremely limited. In their study, Lim *et al.*, highlight the empiric use of ceftazidime/avibactam for OXA-48 producers [7]. In England, the 30-day all-cause case fatality rate of invasive CPE infections is 23.8% [1].

Although decolonisation is not recommended for the clearance of resistant Gram-negative bacteria [8], active screening of high-risk patients on admission to hospital is advised to allow early detection of colonisation and early implementation of interventions and control measures. In their paper within this special edition, Corless *et al.*, provide evidence of the benefits of a rapid screening strategy through using rapid PCR-based methods, with the authors finding resulting reductions in bed days lost to CPE [9].

Outbreaks can occur when colonised patients remain undetected or infection prevention control measures are breached. Given the breadth of transmission routes and reservoirs involved [10], such outbreaks are difficult to manage, detrimental to patient outcome, disruptive to the delivery of clinical services, and prolonged and costly to control [11,12]. Previous studies have reported that robust multimodal approaches are required to curtail outbreaks in healthcare institutions [13–15].

Lim *et al.* describe an outbreak of OXA-48-producing *Klebsiella pneumoniae* discovered only upon culture from a patient with no known risk factors, with subsequent widespread screening then yielding positive samples from 60 patients [7]. Similarly, Sivaramakrishnan *et al.* describe how increasing the sensitivity of their hospital screening protocol led to identification of positive samples from 96 patients, enabling containment of this uncovered CPE outbreak using 'ward based' approaches [16].

Both of the OXA-48-like outbreaks reported in this issue highlight the importance of screening, with the occult transmission events requiring extensive case finding, widening screening and follow up of potential contacts. Although in these instances infections with CPE were limited, the prolonged nature of both outbreaks demonstrates the widespread dissemination of the pathogens, the disruption to services, and the unnecessary expenditure of human and financial resources.

Also in this special edition, Puleston *et al.*, put forward recommendations for detection and rapid management of carbapenemase-producing Enterobacterales outbreaks, outlining components of a 'CPE Management and Outbreak Plan' and thus providing a template from which organisations can develop their own outbreak response [17].

Some countries have achieved success in implementing policies and keeping these pathogens under control [18,15], with a national approach being key. Surveillance is a crucial element of national prevention and control strategies. Several countries have systems in place to monitor the reporting of acquired carbapenem resistance, with some mandating reporting [19]. The approach in England, and findings from it, are described in Freeman *et al.* [2]. To further strengthen the surveillance of acquired carbapenemase producers in England, the Health Protection (Notifications) Regulations 2010 have been amended to include acquired carbapenemase producers. Therefore, from 1st October 2020, diagnostic laboratories in England will have the duty to report acquired carbapenemase-producing Gram-negative bacteria isolated from human samples to the national surveillance authority (currently Public Health England).

Not all CPE are resistant to carbapenems based on clinical breakpoints, making them difficult to detect using any single laboratory screening strategy. Sivaramakrishnan *et al.* highlight the importance of robust diagnostic methods to identify CPE [16]; this aspect of a control strategy cannot be underestimated and is a feature of several reported outbreaks in the global literature. As such, PHE strongly recommend that diagnostic laboratories have the capacity to definitively identify at least the 'big 4' carbapenemases.

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Given the threat CPE infections pose, the multi-faceted elements of surveillance and infection prevention and control required, and the fact that evidence on effectiveness of interventions is lacking, it is important for organisations to share their experiences to inform practices to best tackle the threat. This special edition aims to provide examples of screening and infection, prevention and control practices that were successful in real-world, including outbreak, settings [7,9,16]. Alongside these shared experiences from NHS organisations, epidemiological insights gained from an enhanced surveillance system in England are described [2], and finally, building on the previous papers, recommendations that bring together the elements and principles of outbreak control [17].

Conflict of interest statement

None declared.

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