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Clinical Audits/Service Improvements

Recommendations for detection and rapid management of carbapenemase-producing Enterobacterales outbreaks

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SUMMARY

There is large heterogeneity in approaches to tackling nosocomial outbreaks caused by carbapenemase-producing Enterobacterales (CPE), however there is limited guidance on how to approach their management. Rapid and robust infection prevention and control interventions can be effective in preventing and reducing the impact of outbreaks in healthcare environments. We present a stepwise approach to aspects of CPE outbreak management, including the development of an action plan, engagement and communication with key stakeholders, developing a dynamic risk assessment, and staff education. These can provide a blueprint for organisations to create templates and checklists to inform their own outbreak response.

Introduction

Carbapenem antibiotics are widely used for treating Gram-negative infections that have developed resistance to other, previously effective, classes of antibiotics. The emergence of resistance to these 'last resort' antibiotics poses a threat to the provision of healthcare to individual patients and to the wider system. Reports of outbreaks of colonisation or infection with carbapenemase-producing Enterobacterales (CPE) are increasing globally and in the UK. Many are probably missed, particularly where testing for resistance mechanisms is not routine;

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additionally plasmids carrying resistance mechanisms can easily spread between genera making outbreaks more challenging to identify [1]. Given the associated morbidity and mortality, health systems must take robust steps to prevent, detect and control CPE outbreaks [2]. Endemicity within healthcare settings is the likely consequence of a failure to curtail CPE spread, with associated disruption to services and impact on patients.

Conventionally an outbreak is described as 'a similar illness or infection in two or more people linked in time and space'. However, a single occurrence of CPE (in a colonised or infected patient) may indicate an unrecognised outbreak; if the patient was not identified as high risk on admission, transmission may have already occurred in the absence of infection prevention and control (IPC) interventions [3,4].

While the evidence base for the prevention and control of outbreaks of CPE is still emerging, when robust infection prevention and control interventions are applied, transmission can be controlled. Fundamentally, the steps to prevent or interrupt outbreaks are simple, however the implementation is difficult but necessary as these organisms are unforgiving of any lapse in IPC. The steps to prevent or interrupt transmission and therefore prevent outbreaks can be summarised through the "source > pathway > receptor" model, as seen in Figure 1.

Providers should consider the steps of care pathways with this model to determine where transmission events may occur and take steps to mitigate them. Using the logic that separation of any of these three components breaks the chain of transmission, the following recommendations have been developed to prevent and control clusters or outbreaks of CPE in healthcare settings. Full guidance on the management of CPE in health and social settings can be accessed at https://www.gov.uk/health-and-social-care/antimicrobial-resistance.

These recommendations were developed through expert consensus by a working group convened to inform the production of national guidelines and were informed by clinical and public health experience and published scientific literature.

Key aspects of CPE outbreak control

Robust planning, effective leadership, collaboration and communications (including the provision of clear explanations and information for patients) are key to the control of CPE. We detail key recommendations in subsequent sections.

Engage senior management

Engaging organisational and local health and social care senior management is vital; senior management should make it their business to be involved as they are best-placed to champion IPC work and retain ownership of the delivery of health services [5]. A recent review of the implementation of the English guidance 'Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae' (hereafter 'CPE toolkit'), noted that senior management engagement resulted in easier and better resourced response planning [6].

Develop a CPE management and outbreak plan

Healthcare providers should develop and regularly review and test (exercise) a local CPE outbreak management plan for responding to a general increase in cases, a local cluster or wider outbreak. Key components of the plan should include activities to increase engagement and understanding, as well as the optimisation of processes and practices; these are further set out in Box A.

Box A

Components of a CPE Management and Outbreak Plan

- Develop local arrangements for an outbreak control team, including involvement of senior management
- Conduct dynamic risk assessments that account for the evolution of outbreak scenarios:
  - Review current epidemiology in the hospital and locality in IPC meetings, incident meetings and other relevant fora
  - Ensure robust and rapid detection of colonised or infected cases through optimised laboratory methods [7] and surveillance, including the scrutiny of data relating to unusual isolates and trends
  - Develop and implement isolation approaches for single cases and larger cluster/outbreak situations
  - Optimise IPC practice and cleaning approaches, including audits
  - Monitor and manage antibiotic pressures through embedded antimicrobial stewardship programmes
  - Determine and implement staffing requirements to manage an outbreak situation
  - Ensure approaches to internal and external patient transfers are optimised to minimise the risk of infection transmission
- Develop an outbreak communications plan for internal and external communications, including information for patients
- Identify, develop and test effective cascade methods to provide rapid reminders of the need for strict adherence to the 'CPE Management and Outbreak Plan' and standard IPC operating procedures to relevant staff
- Develop education programmes for all staff to ensure that there is good understanding of CPE and that staff are clear of their role(s) in the management of an outbreak situation.

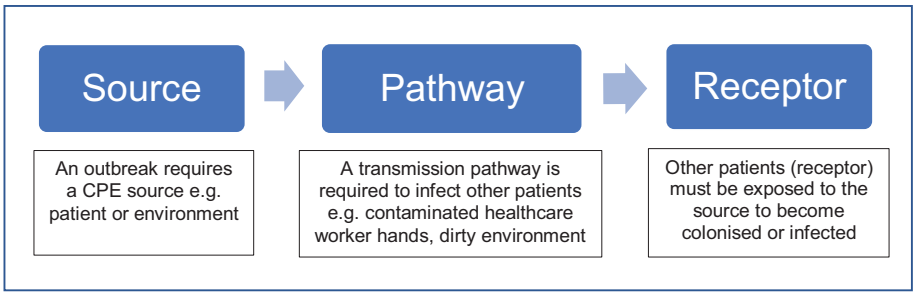

Figure 1. Transmission model.

Local arrangements for an outbreak control team

An outbreak or incident control team (OCT) is required to risk assess, coordinate and manage the response to an outbreak, cluster or an increase in cases above the usual baseline.

OCT meetings should follow a standard, minuted agenda to ensure all aspects of outbreak control are considered and actioned. A dynamic risk assessment of the outbreak should be developed along with an action plan identifying roles and responsibilities (regularly revised as an outbreak evolves) to guide the required response and control measures.

Dynamic risk assessment and action plan

A dynamic risk assessment (adapted from Lepelletier [8]) and action plan should address the points detailed in Table 1.

Table 1
Aspects for inclusion and consideration when conducting a dynamic risk assessment to contain and control CPE in healthcare settings

Component	Considerations
Type of patients	- Transmission is more likely with high dependency patients and patients unable to maintain personal hygiene (e.g. diarrhoea or draining wounds).
Identification of colonised and infected patients, including surveillance	- Early detection of colonised patients on the ward or unit through screening supports the implementation of the IPC activities required to achieve control. - Disease surveillance systems are important for the identification and control of healthcare-associated infections and for understanding the impact of IPC activities [9]. - Consideration should be given to widening screening to assess the degree of spread including through the screening of contacts e.g. patients in the same bay or ward, or those known to have been in contact with the case(s) including those transferred to other wards or units. - The frequency and scope of screening will need to be informed by local expertise, resources and local risk assessments. - Other body screening sites, additional to rectal sampling, may be considered to increase detections, including the axilla and groin [10]. - Patients that initially screened negative, who then require transfer to a high-risk ward (e.g. intensive care), may warrant an additional screen at transfer and isolation pending the result of the screen [11]. - High-risk clinical areas, such as critical care units, should consider weekly or monthly screening to ensure early detection of cases of CPE. - The implementation of a case (colonised or infected) and contacts dynamic registry can help identify (otherwise unrecognisable) epidemiological links leading to the identification, and remediation of an environmental reservoir [12]. - Decolonisation of patients is not recommended and may induce resistance to decolonisation agents [13]. - Screening of patients already discharged from an outbreak ward to their usual home setting is not generally recommended; however, tagging the patient record that the patient has been on an outbreak ward should be considered, so ~~that~~ if readmitted they can be screened and pre-emptively isolated pending the rescreening results. - Screening in community care settings is not generally recommended, however decisions should be risk assessed based on local circumstances, such as if transmission is suspected [14—16].
Laboratories and IPC teams should implement systems for tracking patients with key infections	- Systems should identify and track potential cases (based on phenotypic antibiotic sensitivities) and monitor laboratory confirmed cases. The data require skilled interrogation as these analyses will inform the management of the outbreak. - Systems should take account of the potential for resistance mechanisms to spread to other Gram-negative bacteria. - Line lists of cases are required (including patient demographics, locations, specimen dates and risk factors) for tracking patient risks and movements. - Laboratories should consider adopting assays for the rapid identification of acquired carbapenemases [7]. - Laboratories must ensure that isolates confirmed as carbapenemase producers are reported to public health authority surveillance systems. - Diagnostic laboratories are well placed to support local non-hospital healthcare providers in the rapid identification of clusters or outbreaks in their locations; consideration should be given to how to identify and proactively communicate abnormal findings to these settings.

(*continued on next page*)

Table 1 (*continued*)

Component	Considerations
Staff-patient ratios and IPC expertise	- Transmission events are more likely where staff are looking after more patients than can be safely managed or where ward occupancy is greater than the designed capacity. - OCTs should ensure staff-patient ratios on outbreak wards/units are adequate and address deficiencies. The optimal staff-patient ratios will vary depending on the type of patients and the intensity of care they require [5,17—19]. - It is critical that providers have sufficient IPC expertise and staff experienced in outbreak management [9].
IPC guidelines and standards	- Adherence to IPC guidelines and cleaning standards is vital during CPE outbreaks. Combined antimicrobial stewardship, environmental cleaning and source control through the application of robust IPC practice with standard care (including isolation or cohorting) has been found to be the most effective bundle of interventions to prevent acquisition [20]. - Experienced representatives of the OCT should visit the affected areas to determine that there is robust adherence to IPC guidelines and cleaning standards [21—23]. - Contamination of cleaning equipment (e.g. mops) may occur; consideration should be given to investigating such potential sources [24]. - Healthcare providers should ensure single use patient equipment is used or where equipment must be reused, that appropriate disinfection/decontamination is ensured. - It is vital that patient spaces that have been occupied by patients harbouring CPE are robustly cleaned and decontaminated, particularly after the patient has been discharged; inadequate decontamination can lead to transmission events [25].
Environment	- Environmental microbiological sampling to detect environmental reservoirs guided by microbiological advice on suitable sites and sampling methods may be considered. - Positive environmental samples provide powerful evidence of cleaning deficiencies and can guide improvements, however negative results can provide false reassurance [26,27]. - Staff, patients and visitors must understand that hand hygiene sinks are for the sole purpose of hand-washing, not for disposing of food, drink or waste [28]. - CPE can be carried in the gut and are therefore easily spread through poor hygiene practice, by patients, relatives and staff. Fomites e.g. bedding contaminated with faecal soiling are therefore potential vectors. Providers need to have robust processes in place for diarrhoea management/faecal contamination mitigation. - The frequency of cleaning of toilets should be increased on outbreak wards. - Consideration should be given to staff clothing as a vector and whether additional measures are needed to reduce the transmission potential from the contaminated clothing [29—32]. - Sink and shower waster-traps can harbour high numbers of bacteria which can persist despite cleaning and decontamination efforts due to their protective biofilms. There is some evidence that CPE in waste traps and/or drainage biofilms can transmit to patients [33,34]. Physical removal of biofilm from drains is unlikely to be successful and interventions should aim to reduce transmission from these sites to patients.
Isolation capacity on the ward or unit	- The OCT should be satisfied that that the isolation capacity and approach to cohorting (if adopted) on the ward or unit includes access to en-suite facilities to minimise onwards transmission. - Decisions around isolating or cohorting patients should consider patient safety, ensuring that there is no increased risk of harm to patients; providers should risk assess the decision and monitor for harmful outcomes. - Although the isolation of high risk patients is recommended, this recommendation is not always feasible or followed which may increase the risk of transmission [35]. - Providers should understand what risk mitigation activity has been undertaken since the admission of known cases (e.g. to ascertain if there were delays in identification and isolation of cases) to help determine the potential scale of transmission [8] and to inform further actions. - Cohorting of patients and staff into separate streams may reduce transmission events; the decision to implement cohorting must be led by local risk assessment and can include the following categories in Box B. - Cohorting should NOT be undertaken where patients have differing mechanisms of carbapenem resistance as this risks plasmid transmission between genera and the development of greater antimicrobial resistance.

Table 1 (*continued*)

Component	Considerations
Manage antibiotic pressures in the healthcare facility	- Cohorting or isolation decisions should be informed by the colonisation pressure on the ward/unit i.e. the likelihood of a patient encountering a colonised patient [36]. Nosocomial transmission is more likely where the number of colonised patients is high. - Decisions around cohorting should be made with the advice of a microbiologist, to avoid inadvertently increasing harm by mixing patients with different resistance mechanisms. - Prescribing formulary changes may be required to minimise patient or environmental exposures to broad spectrum antibiotics, especially carbapenems and third-generation cephalosporins, whilst ensuring access to these where they are truly indicated. - Monitoring of antibiotic usage can help inform changes required.

Box B
Cohort groups

The following discrete groups can be considered for cohorting [8,11]:

1. Patients and healthcare staff for colonised or infected patients.
2. Contacts of colonised or infected patients (i.e. contacts of colonised or infected patients and the staff that have looked after them).
3. Newly admitted patients and healthcare staff.
4. Screen negative patients and healthcare staff.

Other containment measures

Restriction of colonised or infected inpatient movements to other departments should be considered to reduce transmission risks. Known colonised or infected patients should be put at the end of the day's list of work for a department (e.g. X ray, other clinic appointment, operating list), providing it is clinically safe to do so and clinical outcomes are not compromised, so that terminal cleaning can be undertaken after the case has left that department.

Ward or unit closures may be required, to try to contain onward transmission (e.g. to allow for a systematic deep clean), however efforts to contain an outbreak or cluster should be balanced against the wider safety of patients as there may be the potential for greater harm if patients are delayed in receiving their treatments.

Closure of wards/units clearly has an impact on healthcare operational capacity and may impact on the availability of scarce facilities e.g. specialised units; nonetheless closure can be a valuable intervention tool. Providers need to have thought through and developed standard operating procedures prior to CPE incidents that describe the situations when closure should be considered, the steps to be taken, including mitigation of risk to patients from loss of specialist services and the procedures for planned re-opening.

The risk of transmission from patients who are currently or previously CPE colonised attending outpatient clinics is unclear, but it is generally considered that provided they can exercise good hand hygiene and toileting practice and have any wounds covered, they should not need to be restricted in their movements. Some have adopted a precautionary approach and cohorted these patients [37]. Providers will need to make their own risk assessed judgement based on the local context.

Communication

Effective communication is key when transferring patients colonised or infected with CPE to other units or wards in the healthcare facility, or to other sites (e.g. care homes or other hospitals).

Relevant information should be cascaded to all cadres if healthcare and allied staff who need to be aware of the scale of the outbreak, including any remedial measures or changes to routine practice they should be aware of. Managerial oversight of the incident response needs to be owned by a dedicated individual with regular reports to the Trust board and senior infection staff.

Outbreaks should be communicated to relevant bodies such as neighbouring trusts, commissioners, providers and the local PHE Health Protection Team. The sending unit should outline the nature of the colonisation or infection of the patient and the containment measures required to the receiving unit.

Individual patient-level information should be shared on discharge with all members of the patient's care team, such as their General Practitioner, district nursing team, other facilities involved in their care, and family and carers. Discharge information to the primary care provider should be clear, including treatment issues or difficulties with infection control in shared care environments such as care homes. These are new concepts to primary care and a detailed explanation may be required; an explanatory leaflet to primary care practitioners may help.

Describe and report outbreak features to stakeholders

A key step in an outbreak response is to describe the outbreak, which can inform hypothesis generation and associated investigations to identify the source of the outbreak. Resulting findings should inform the development and implementation of prevention and control measures. Case definitions for cases and contacts should be established and the outbreak data used to determine epidemiological links and potential sources including environmental reservoirs. A report summarising these findings should be produced, updated and shared regularly, including an outbreak curve, patient movement mapping, patient network analysis (who has been in contact with whom) and notes of procedures undertaken (e.g. surgery, vascular lines) to identify potential exposure risks.

An analytical study (case control or cohort study) may help to further identify causal risk factors for informing further control measures. It is important that the current

epidemiological situation is reviewed in organisational IPC, OCT and healthcare facility management meetings regularly so that the incident management can be adjusted in the light of the current position.

Develop educational programmes for all staff

A review of the implementation of the 'CPE toolkit' noted front line healthcare staff (i.e. not IPC experts) had little knowledge or understanding of the threat posed by CPE [6]. Improving staff knowledge is therefore an important element of outbreak preparation and may improve their involvement and compliance with the required IPC activities. Healthcare providers should ensure that education on IPC and staff roles in an outbreak response is provided in advance of and during an outbreak. Appropriate multimodal approaches, according to staff needs, should focus on educational outcomes and increasing awareness. The approach to educational programmes should acknowledge the difficulties operational pressures may pose to staff engagement [9,38]. Refresher training is important to maintain knowledge, and raising awareness is particularly important during outbreak situations.

Educational programmes should encompass as a minimum:

- Context and role-appropriate knowledge of IPC management (all staff)
- Context and role-appropriate basic microbiology (all staff)
- Current policy for patient screening, including how to take a screening swab and refer to microbiology services for testing (all staff)
- Current best practices for prescribing, administering and monitoring antimicrobial therapy (staff prescribing and administering medications to patients)
- Importance of antimicrobial stewardship; careful conservation of existing antimicrobials (staff prescribing and administering medications to patients)
- Effect on individual patients' mental and emotional health whilst in isolation and how to communicate effectively when giving patients factual information in a format that they will understand
- Awareness of current outbreak procedures and the response required of staff

Conclusions

CPE outbreaks have the potential to cause widespread disruption to clinical services, limit the ability to perform medical procedures, cause harm and emotional stress to individual patients, and have widespread financial and reputational consequences. Adequate surveillance must be maintained to detect, at an early stage, introduction of CPE into the hospital environment to contain any transmission. An advance plan is essential to ensure: that appropriate admission samples are taken from high-risk patients and from patients on high-risk units (e.g. burns, transplant units); that CPE isolates can be adequately detected by local laboratories; that information is regularly reviewed to determine if transmission has occurred, and; that outbreak management strategies are in place, appropriately stress tested and regularly updated, with education provided to key staff. Ultimately, local risk assessments looking at the type of facility (including isolation capacity — especially on high risk units), patients, and available control measures are key to ensuring that risk is appropriately identified and mitigated. Addressing the points contained in this paper we hope will help institutions in developing their own robust local strategies to combat the spread of CPE.

Conflict of interest statement

None declared.

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