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Hospital outbreak control requires joint efforts from hospital management, microbiology and infection control

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SUMMARY

An outbreak of multidrug-resistant *Klebsiella pneumoniae* producing the extended-spectrum β-lactamase CTX-M15 affected 247 mainly elderly patients in more than 30 wards in a 1000-bedded swedish teaching hospital between May 2005 and August 2007. A manual search of the hospital administrative records for possible contacts between cases in wards and outpatient settings revealed a complex chain of transmission. Faecal screening identified twice as many cases as cultures from clinical samples. Transmission occurred by direct and indirect patient-to-patient contact, facilitated by patient overcrowding. Interventions included formation of a steering group with economic power, increased bed numbers, better compliance with alcohol hand disinfection and hospital dress code, better hand hygiene for patients and improved cleaning. The cost of the interventions was estimated to be €3 million. Special infection control policies were not necessary, but resources were needed to make existing policies possible to follow, and for educational efforts to improve compliance.

Introduction

Extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae* has caused many hospital outbreaks, mainly in intensive care and neonatal units.[1,2] In 2005, multidrug-resistant (MDR) *K. pneumoniae* isolates were isolated from urinary samples from Uppsala University Hospital, Sweden, in increasing numbers. Affected patients were located in many different wards with no obvious connections between them. Genotyping of isolates from clinical specimens suggested an outbreak with a CTX-M-15-producing clone.[3] Frequent movements of patients within the hospital provided many potential points of contact between elderly and disabled patients. The aim of this report is to describe the complex chain of transmission between patients and the interventions undertaken to curb the outbreak.[4]

Methods

Setting

Uppsala University Hospital is a 1000-bedded, highly specialised public hospital with about 80 wards each housing 20–25 patients in 1–4-bedded rooms, and five intensive care units (ICUs). About 10% of beds are in single rooms with en-suite bathrooms. The Infection Control (IC) team consisted of one, and sometimes two, full time physicians, three IC nurses for the hospital and one for the community. The hospital microbiology laboratory reported any isolation of MDR bacteria such as meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci and ESBL-producing *Klebsiella* spp. daily to the IC team. The Infection Control Committee (ICC), chaired by the chief physician of the hospital, included representatives from IC, the Departments of Infectious Diseases, Occupational Health, Microbiology, and Public Health; hospital administration, hospital information and hospital service suppliers. One nurse and one auxiliary nurse from each ward were appointed as link nurses, and joined together to form hygiene groups in each clinical department. These groups met monthly, supervised by their designated IC nurse.

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The hospital uniform code stipulated short-sleeved working clothes for all categories of staff, with no rings or wristwatches permitted. An alcohol-based hand disinfectant was to be used before and after tending to a patient, before donning and after removing gloves, and when entering or leaving a patient room. Hand washing with ordinary soap was used before disinfection only when hands were visibly dirty. Gloves were used when touching secretions, excretions, and contaminated or dirty equipment. Gowns or aprons were used only for close contact with a patient or a patient's bed. Doctors' white coats were removed before close patient contact. The precautions were the same for patients nursed in single or isolation rooms. Masks, caps and overshoes were not used in wards.

Ward cleaning was performed by external contractors, and included weekday cleaning of floors and bathrooms and toilets. Moist microfibre mops were used, one per room. The mops were washed at 85 °C with detergent, rinsed with a preservative and dried in a tumble dryer, stored and used within 24 h. Nursing staff took care of spills, etc., using an alcohol + detergent surface disinfectant (DAX ytdesinfektion plus®, Opus Health Care AB, Malmö, Sweden).

The hospital antibiotic policy was communicated to doctors through policy documents, lectures and direct contact from specialists from the Department of Infectious Diseases. In 2004, the year before the outbreak, an average of 45.9 defined daily doses (DDD) of antibacterial drugs were used in the hospital per 100 patient-days. Cephalosporins accounted for 20% of total antimicrobial use and quinolones 12%.

Study design

The study was conducted over a 28 month period between May 2005 to September 2007. All patients with confirmed ESBL-producing *K. pneumoniae* isolated from any site were included. A patient was defined as a case when the isolate was identified by pulsed-field gel electrophoresis (PFGE) as belonging to the outbreak clone. Cases identified through samples taken at the discretion of the clinician were called 'clinical' cases.

Patients sharing a room with a known case during the week preceding the detection of the case were called contacts, and had stool, urine, wound and respiratory tract samples sent for culture. The hospital patient registration system allowed daily tracing of patient admissions, discharges and movements between wards. This information was collected for each case prospectively from March 2006 onwards, and retrospectively back to December 2004 and manually transferred to a data sheet.

Microbiology

Clinical samples were cultured and organisms identified with routine laboratory methods.[5] Isolates of ESBL-producing *K. pneumoniae* were stored at −70 °C from 1 May 2005 onwards, strains of ESBL-producing *K. pneumoniae* previously stored from January 2004 to 1 May 2005 were thawed and re-examined.

Antibiotic susceptibility testing was performed by disc diffusion as recommended by the Swedish Reference Group for Antibiotics (SRGA, www.srga.org). First-step ESBL detection criteria were resistance to cefadroxil (≤13 mm) and/or resistance/reduced susceptibility to ceftazidime (<24 mm). Phenotypic confirmation of ESBL production was performed by a disc diffusion synergy test.

Surveillance specimens were plated onto McConkey agar with 5 μg cefotaxime and 10 μg ceftazidime discs (Oxoid Ltd, Basingstoke, UK). Colonies growing within the expected zones of cefotaxime and/or ceftazidime were identified to species level. The sensitivity of stool screening was found to be 95% compared to 47% for urine samples, hence screening was limited to faecal samples only. Real-time polymerase chain reaction (PCR) was used from March 2007 to detect faecal organisms with the *bla*CTX-M phylogenetic group 1 gene.[6]

Molecular typing was performed by PFGE with *Xba*I (Life Technology, Invitrogen, Carlsbad, CA, USA).[3] Isolates showing indistinguishable or closely related band patterns (≤6 band differences, >80% similarity) were regarded as clonally related.[7]

About 400 environmental cultures were taken in the months of February and November 2006 from frequently touched items or surfaces in wards with suspected transmission, using Rodac contact plates (Biotrace®, Runcorn, UK) and incubated at 30 °C for 5 days. Isolates were typed with standard methods.[5]

Interventions

For details of case finding and interventions, see Table I.

A steering group was formed, with the power to make financial decisions and chaired by the chief physician of the hospital. The ICC met weekly to report on the course of the outbreak and the implementation of interventions.

An IC team visited wards the same day as a new case was found. Contacts were sampled within two working days if still in the hospital at the time. Cases who shared rooms with other patients were moved to single rooms if they had diarrhoea, urinary incontinence or a discharging wound.

An IC audit was conducted in wards where new cases had been found. The level of staffing and staff training, the availability of hand disinfectant to staff and patients, and the number of single rooms and bathrooms were recorded and reported to the steering group.

The frequency of cleaning was increased to include weekends and cleaning of bathrooms and toilets twice daily. Cleaning procedures were not changed.

The IC team provided education about ESBL-producing organisms and hygiene precautions, and delivered training sessions in hand-disinfection to doctors, nurses and auxiliary staff in all departments with cases, as well as to all cleaners and janitors and to temporary staff covering holiday periods. Information was also given to patients and their families, and to media.

Patients were encouraged and helped to disinfect their hands before meals and after toilet visits. Breakfast buffets were abandoned in favour of individual patient meals distributed on trays.

A point prevalence survey in February 2006 had demonstrated bed occupancies in geriatric wards and the transplant ward of between 100% and 113%. Patient rooms in geriatric and surgical wards that had been used as offices were re-allocated. More toilets were installed in the geriatric wards to make it possible to allocate separate toilets to patients in single rooms. A new admission ward was opened. Transplant patients moved to a newly reopened ward. In the same year, extra staff members were employed in the summer to avoid the usual reduction in numbers of beds during holiday periods.

Results

Outbreak strain

The outbreak strain was first grown from a clinical specimen submitted in December 2004. During the study period, the outbreak strain was isolated from 247 patients. The first positive isolate was grown from a clinical sample in 172 cases (urine 131, secretions 24, blood 11, and six from respiratory specimens). Of these, 139 were taken before contact tracing or screening had started.

The outbreak strain was resistant to the penicillins, the cephalosporins including cefepime, ciprofloxacin, monobactams,

Table I
Case-finding strategies and interventions

Time period	Intervention	Case-finding policy	'Clinical' cases	Screening cases	Screening cultures	Screening samples per new case
2005 May–Dec	IC contact with wards with more than one case.	Samples taken at the discretion of the physician.	65	0	0	
2005 Nov	In neurological rehabilitation ward resulting in improved hand hygiene of patients and staff. ICC extra meeting. Alert on hospital intranet. Letter to all hospital doctors.	No screening cultures.				
2006 Jan–Apr	Case–control study initiated. Environmental sampling in surgical ward.		10			
2006 May–Aug	Attempts to place cases with risk factors in single rooms. Overcrowding in geriatric and surgical wards reported.		64			
2006 late Sep	Steering group formed, weekly meetings. Laboratory search system improved.					
2006 Oct	ICC to meet weekly. 37-point action plan launched. Policy document on intranet. Case records forms introduced. Report to National Board of Health and Welfare.	Contact tracing.	8	10	58	6
2006 late Oct–Nov	IC team (nurse and doctor) visits to wards with new cases. Cases with risk factors moved to single rooms. Contacts sampled within 2 days. Audits in affected wards. Environmental sampling in geriatric ward.	All wards: in- and outscreen stool, urine, wound, CVC.	9	22	8896	404
2006 Nov–Dec	Kitchen aids employed, to avoid simultaneous food handling and patient care. Hand disinfection for patients. New antibiotic policy programme promoted.	All wards: in- and outscreen. Stool only.	4	6	3522	587
2006 Dec–2007 Jan	Information leaflets on hand hygiene to patients and visitors. Stickers about hand hygiene above all washstands. Dress code campaign. Bathroom cleaning increased to twice daily, 7 days/week. Visit by National Board of Health and Welfare.	All wards: in- and outscreen. Weekly screen in geriatric ward. Stool only.	3	17	8182	481
2007 Feb	Transplant ward moved.	Weekly screen in surgical, geriatric and medical wards. Stool only.	1	2	1682	841
2007 Mar–Aug	New admission ward opened. A few new toilets and single rooms. More beds open during summer months.	Weekly screen and outscreen of all patients moved from surgical, geriatric and medical wards. Stool only.	9	18	12 570	629
2007 Sep	Final report to National Board of Health and Welfare.					
		Total	172	75	34 910	2948

IC, infection control; ICC, Infection Control Committee; CVC, central venous catheter.

cotrimoxazole, nitrofurantoin, and tobramycin. It showed intermediate susceptibility to tigecycline, but remained fully sensitive to gentamicin, amikacin, the carbapenems, colistin and fosfomycin.

Fourteen isolates of ESBL-producing *K. pneumoniae* did not belong to the epidemic clone. Each had a unique PFGE pattern and none caused cross-infections.

Case characteristics

The source patient was a 41-year-old man colonised with the outbreak strain and MRSA, who was treated in the departments of oncology, dermatology and general medicine during week 51, 2004. Of the other 247 cases identified during the study period, 113 were female, and 134 male, with a median age of 78 years (range: 4–100). From October 2006 to June 2007 a simplified case record was used prospectively, covering 93 consecutive clinical and screening cases. Sixty-five (70%) of this group had received antimicrobial therapy before the first positive ESBL *K. pneumoniae* culture. Ten patients (11%) had a central venous catheter. Thirty-four (37%) had a permanent urinary catheter and 37 (40%) had incontinence pads. Nineteen (20%) had diarrhoea, defined as three or more loose stools per day. Fifty-six (62%) needed some help with their personal hygiene and/or with feeding.

Course of the outbreak

There was a four-month gap between the source patient and identification of the first outbreak case. Numbers of new cases

peaked during the summer of 2006 and when contact and screening sampling started in October 2006. A steady decline in cases was seen from mid-January 2007, although 30–40 known cases were present in the hospital each week (Figure 1). Six screening samples were needed to find one new case in contact tracing, and more than 400 in the other screening exercises (Table I).

Seventy-six percent (187/247) of the cases had been nursed in one or more of 12 wards housing geriatric, infectious diseases, orthopaedic, vascular surgery, urology, transplant, oncology and dermatology patients.

No transmission could be demonstrated in the ICUs.

Two of the early cases had visited the dermatology department during the same week as the source patient. Of the 20 first diagnosed cases, all but one had been in the same hospital location as another early or later case; 16 in wards and outpatient settings, two in wards only and one in an outpatient setting only.

Chains of transmission for 20 consecutive cases diagnosed when screening had been in operation for a month were followed. These cases were diagnosed in 3 weeks. One case was diagnosed at autopsy and had had no known contact with the hospital. The remaining 19 cases had visited or been admitted to the hospital on a median of 19 (range: 2–37) occasions after the admission of the source patient. On a median of 3 occasions (range: 1–13) they were admitted to wards in the same weeks as in all 49 known (possible source) cases. The shortest possible incubation time was a median of 2 weeks (range: 1–61). They had visited a median of 7 different wards (range: 1–22) and the emergency department a median of once (range: 0–6). Three of them visited dermatology or dialysis departments regularly.

Interventions

Infection control audits revealed no reasons to change the existing IC guidelines used in the hospital, but identified several obstacles to compliance, including patient beds in corridors and treatment rooms, and lack of hand disinfectant dispensers. Staff shortages frequently caused patients to help each other with personal hygiene.

With education, information and training, the use of alcohol hand disinfectant increased from 31 mL per patient day in 2005 to 82 mL in 2007. Overall compliance with the dress code was 94–96%, but physicians' compliance improved from 74% to 90%.

ESBL-producing *K. pneumoniae* were found only twice from environmental samples, one colony on a private telephone and four colonies on a toilet seat in a bathroom, both used by a case only.

The number of patient beds was increased from 215 to 245 in geriatric/medical wards. During the summer of 2007 more wards were kept open, increasing the number of available patient beds per day by about 25 in geriatric and 20 in surgical wards.

In 2007 the total antibiotic use had increased to an average of 49 DDD per 100 patient-days. Cephalosporin usage decreased from 20% of all antimicrobials used in 2004 to 9.4% in 2007; similarly, the proportion of quinolones used decreased from 12% of the total in 2004 to 8.7%. Details of antibiotic policies and use will be reported elsewhere.

Direct hospital costs for increased lengths of stay or attributable mortality were not calculated for the outbreak. In 2007, the hospital budgeted €3 million for the curbing of the outbreak. The funding was used for screening cultures, fewer ward closures during the summer months, employment and education of vacancy staff, more alcohol hand disinfectant and more clean laundry, renovation of fixtures in surgical and geriatric wards, more single rooms, reclaiming of patient rooms that had been converted to offices, and increased frequency of cleaning.

Discussion

Patients with ESBL-producing *K. pneumoniae* appeared sporadically in the hospital over a year or so before a major outbreak was

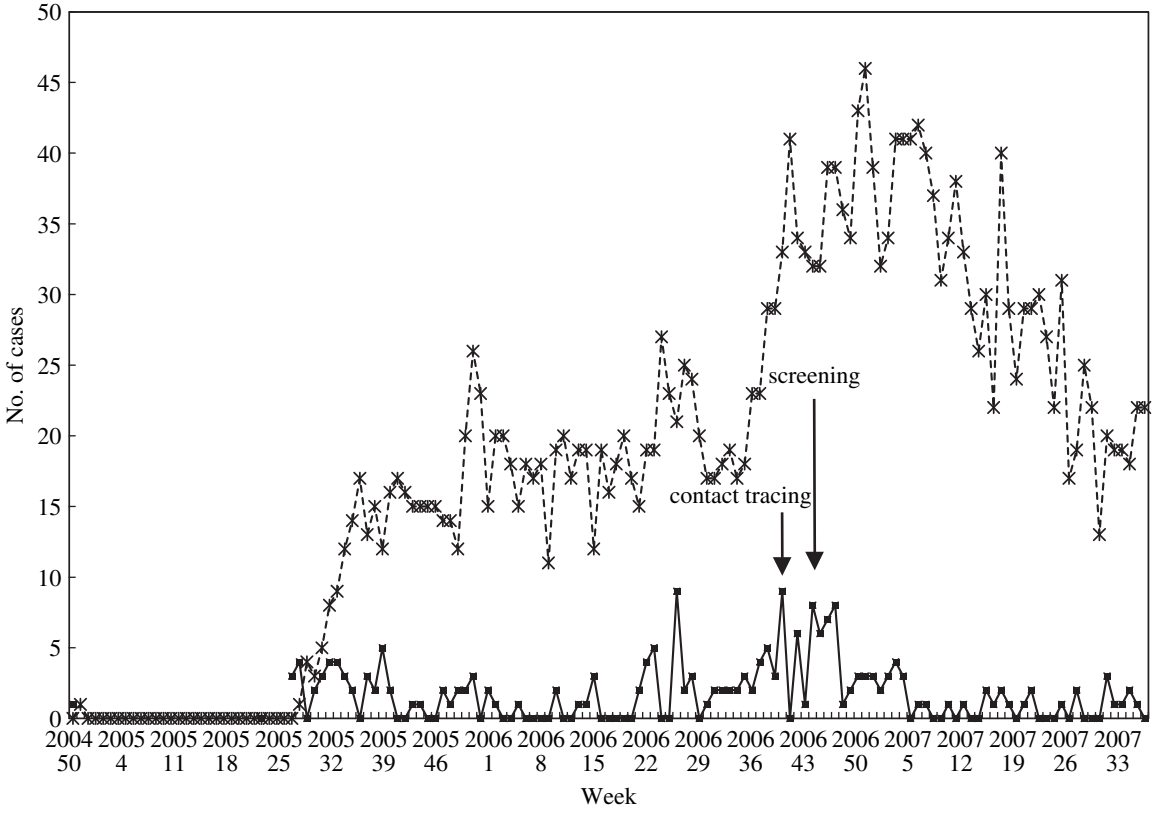

Figure 1. Known (dashed line) and new (solid line) cases present in the hospital each week.

suspected. Interventions during that time focused on IC in wards with cases, and antibiotic stewardship. There was an alert posted on the hospital intranet but no coordinated efforts to cope with patient overcrowding or lack of resources for screening cultures and typing. After a steering group, with administrative and financial power, mandated by the hospital management, was formed at the end of September and resources made available the outbreak was under control in less than four months (Figure 1).

Outbreaks such as this can become very large before being recognised, especially when most patients are colonised rather than infected, and identified cases are not obviously related in time and space. Colonised patients were at least twice as common as the infected 'clinical' cases. In addition, patients were moved, discharged and readmitted frequently due to shortage of beds, causing multiple patient-to-patient contacts. Only when adequate resources were allocated for contact tracing, screening cultures and typing, could a reliable epidemic curve, necessary for making decisions on intervention, be constructed.[8]

Visit to wards by the IC team and IC audits formed an important basis for choosing suitable interventions, which were then implemented following a decree from the steering group. The number of interventions means that there is no exact timeline for each of them and they cannot be individually assessed.

Interventions first implemented and continuing throughout the study period were those that did not involve large direct extra costs, such as tailor-made advice and education by the IC team, prioritising the isolation of risk patients to single rooms, a renewed focus on hand hygiene for patients as well as staff. The faecal–oral route was regarded as an important means of transmission, hence staff were reallocated in order to improve food handling and to avoid buffet meals. In addition it is likely that the hospital-wide alert improved the general compliance with the IC policy. No ward was closed as a means to control the outbreak.

In high risk wards, interventions incurring direct costs were necessary, such as increasing the availability of patient beds and of toilets. Patient-to-patient transmission in toilets, washrooms and when patients helped each other was documented through interviews and audits. Direct routes of transmission, such as contact via hands of patients, seem to have been important.[9] In geriatric and transplant wards, overcrowding was prohibited and patient transfers within wards were prevented. Overcrowding and understaffing, leading to frequent movements of patients and staff and to failure of IC practices, have caused the breakdown of control programmes for other MDR bacteria, even if patients are placed in single rooms after the identification of carriage of MDR bacteria.[10–12] Efforts to minimise overcrowding and understaffing during the summer of 2007 probably secured sustainable results.

The IC policy in the hospital was not changed and the outbreak was terminated without extra IC interventions such as environmental disinfection or contact precautions ad-modum Centers for Disease Control and Prevention, which suggests that such interventions may not always be necessary.[1,13,14]

Transmission of ESBL-producing *K. pneumoniae* from contaminated surfaces has been reported from The Netherlands.[15] Routine environmental cleaning has been shown to reduce transmission of resistant micro-organisms.[16] Increased frequency of cleaning of toilets may have had some impact in this outbreak. Increased frequency of cleaning of wards comprised only floors, which have not been demonstrated to be important in transmission of infection.[17,18]

No transmission was seen in the ICUs where no overcrowding was permitted, and patients remained in their beds. No MRSA transmission was observed during the study period. This implies that the standard of basic IC in the hospital was relatively high, although improvement was possible.[19]

Screening was used in order to identify wards and procedures carrying a risk for transmission, rather than to find new patient carriers.[20,21] The efficiency of screening exercises is difficult to evaluate, as the number of cases found per sample will always be highest initially. Screening could probably have been limited sooner to contact sampling and screening in risk wards.

Incubation period and attack rates were difficult to calculate as movements of cases were not logged and the case definition was based on colonisation rather than clinical infection. A detailed analysis of 20 cases during the screening period showed that in more than 50% of cases with a ward link to a known case, the calculated incubation period was as short as one to two weeks.

Risk factors for infection and colonisation with ESBL-producing *K. pneumoniae* were the same as those known from other studies.[22] The outbreak strain seems to have been highly transmissible, in contrast to other *Klebsiella* strains isolated during the study period. The strain may have had a high capacity to survive on skin, which could explain why improved hand disinfection of hospital staff and patients was probably the most important intervention.[23]

Repeated attempts had been made to decrease the use of cephalosporins and quinolones.[2,24] Despite this, the pattern of antibiotic usage did not change until a general awareness of the severity of the situation had been created.

Antimicrobial resistance has been reported to increase hospital costs, mainly by increasing hospital length of stay and attributable mortality.[25] This outbreak cost the hospital €3 million, used for interventions improving the standard of care. Not containing the outbreak, would have resulted in at least ten-fold losses through lost contracts for medical care.

Conflict of interest statement
None declared.

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