Outbreak of extended spectrum β-lactamase producing *Klebsiella pneumoniae* in a neonatal unit

Jennifer Royle, Sharon Halasz, Gillian Eagles, Gwendolyn Gilbert, Dianne Dalton, Peter Jelfs, David Isaacs

**Abstract**

An outbreak of extended spectrum β-lactamase producing *Klebsiella pneumoniae* (ESBLKp) in a neonatal unit was controlled using simple measures. Normally, the control of such infections can be time consuming and expensive. Seven cases of septicaemia resulted in two deaths. ESBLKp isolates were subtyped by pulsed field gel electrophoresis, and four of the five isolates typed were identical. Control of the outbreak was achieved by altered empiric antibiotic treatment for late onset sepsis and prevention of cross infection by strict attention to hand washing. Widespread colonisation of babies in the unit was presumed, so initial surveillance cultures were not performed. No further episodes of sepsis occurred.

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Keywords: β-lactamase producing *Klebsiella pneumoniae*; antibiotic resistance; hygiene; sepsis

Gram negative bacillary sepsis is a common nosocomial problem in neonatal units. Australian data from 1992–3 revealed coagulase negative staphylococcus as the pathogen in about 1% of cases. Routinely associated with widespread colonisation of babies, systemic infections, and death.

Reports of recent outbreaks highlight the problem of multiresistant strains of *Klebsiella*. The presence of *Klebsiella* in high numbers in the stool provides a reservoir for spread from baby to baby, with transfer on the hands of staff, and, indeed, positive culture results from staff members’ hands have been obtained. The problem of multiresistant strains of *Klebsiella*. The presence of *Klebsiella* in high numbers in the stool provides a reservoir for spread from baby to baby, with transfer on the hands of staff, and, indeed, positive culture results from staff members’ hands have been obtained.

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for necrotising enterocolitis, and not known to be colonised with ESBLKp, developed septicaemia. Treatment with cefotaxime and gentamicin was started, as Gram negative sepsis was suspected. After ESBLKp had been isolated amikacin was substituted and the baby recovered.

Cases 3 and 4 occurred after a further 10 weeks, and cases 5 and 6 another five weeks later. Two babies died; in each case empirical antibiotic treatment was begun to which the ESBLKp subsequently proved resistant. Case 7 occurred one week after cases 5 and 6, by which time the empiric antibiotic choice had been changed in view of the outbreak. The organisms in cases 1 and 2 were sensitive to amikacin and imipenem. Cases 3 to 6 grew organisms resistant to amikacin and sensitive only to imipenem.

One other unit baby developed endotracheal tube colonisation with the ESBLKp strain on 2 March 1996. This baby died on 4 March from causes other than sepsis. In March 1996 an urgent meeting was held with the infection control team and the neonatologists to decide strategies to prevent further cases, and to decide how the unit antibiotic policy should be changed.

**INTERVENTION**

The infectious diseases team and neonatologists decided on strategies to deal with the outbreak. The empirical antibiotic policy for suspected late onset sepsis was changed to imipenem and vancomycin. Surveillance cultures of babies or of the environment were not performed immediately, as negative cultures would not reliably exclude colonisation or contamination. The primary source of infection was presumed to be colonised infants, with gut colonisation as the major reservoir.

All babies in the unit at the time of the outbreak were presumed to be colonised. Case 6 was placed in one of the two isolation rooms, as she was known to be colonised. All babies were to be regarded as potential reservoirs for further spread. New (presumably uncolonised) babies admitted to the unit were nursed in areas within the two main rooms of the nursery with the colonised babies.

The primary focus for preventing cross contamination was hand washing. In-service education sessions explaining the outbreak to the nursing staff and unit nursing educators were conducted. The importance of hand washing to prevent baby to baby spread of gut colonising organisms was stressed. The wearing of disposable gloves for nappy changing, a policy previously only variably practised, was reinforced.

Nurses were declared to be the advocates for the babies. Each nurse was given the responsibility to act on behalf of the babies under his or her care, and to insist that all attending personnel wash hands before and after handling the baby. Any medical or paramedical staff refusing to wash his or her hands after being asked to do so by the attending sister was to be reported to the infection control team. A high level of motivation emerged among the nursing staff: “nurse power” advocacy was well received by visiting staff.

Attendance of at least one of the infectious disease team at a weekly neonatal ward round was routine. However, on each occasion during the subsequent 10 weeks, the outbreak was discussed and the importance of hand washing reiterated.

### Results

No further episodes of sepsis occurred after case 7. Ten weeks after the antibiotic policy was changed, fecal or rectal swab cultures from all the babies in the unit were taken to assess the point prevalence of colonisation.

Fecal culture from case 6 was positive for ESBLKp but only one other baby, admitted two weeks earlier, was positive. This baby was placed in the isolation room with case 6. Apart from case 6, all babies on the unit had been admitted after the epidemic intervention had started. Repeat surveillance cultures performed one week later on all babies on the unit confirmed positive cultures only in the same two babies in the isolation room.

The empirical antibiotic policy for suspected late onset sepsis was changed back to vancomycin and gentamicin for all unit babies, other than for the two babies in isolation who were to be treated empirically with vancomycin and imipenem if they became clinically septic.

Subtyping of the ESBLKp isolates was performed on cases 3–7. The isolates from the earlier two cases were not available for testing.

### Table 1  Cases of ESBLKp sepsis

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sex</th>
<th>Gestation (weeks)</th>
<th>Birthweight (kg)</th>
<th>Underlying problems</th>
<th>Antibiotics before ESBLKp sepsis and days of use</th>
<th>Date of ESBLKp sepsis</th>
<th>Sites of positive cultures</th>
<th>Empiric antibiotics</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>41</td>
<td>3.5</td>
<td>Bladder exostrophy</td>
<td>A2, G2, Am(oral)5</td>
<td>30/7/95</td>
<td>Blood, urine</td>
<td>Ami, F</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>40</td>
<td>3.7</td>
<td>NEC (day 3)</td>
<td>A9, G9, M9</td>
<td>29/10/95</td>
<td>Blood</td>
<td>Ctx, G then Ami (at 24 hours)</td>
<td>Survived</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>34</td>
<td>2.0</td>
<td>Malrotation; volvulus; NEC (day 25)</td>
<td>CI 12, G14, A7, M4</td>
<td>19/1/96</td>
<td>Blood</td>
<td>Ctx, G then Imi (at 24 hours)</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>35</td>
<td>2.4</td>
<td>Gastroschisis</td>
<td>Ami1, Ami11, M5, G5</td>
<td>27/1/96</td>
<td>Blood</td>
<td>V, G then Ctx, G (at 24 hours) then Imi (1 dose)</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>29</td>
<td>1.2</td>
<td>HMD</td>
<td>Nil</td>
<td>3/3/96</td>
<td>Blood</td>
<td>V, G</td>
<td>Died</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>25</td>
<td>0.6</td>
<td>CLD, FT; NEC, multiple gut resections</td>
<td>Multiple</td>
<td>3/3/96</td>
<td>Blood</td>
<td>A, G then Imi (at 48 hours)</td>
<td>Survived</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>37</td>
<td>2.82</td>
<td>Cloacal exostrophy; lipomyelo-meningocele</td>
<td>A6, G6, M4</td>
<td>11/3/96</td>
<td>Blood, urine</td>
<td>Imi</td>
<td>Survived</td>
</tr>
</tbody>
</table>

HMD = hyaline membrane disease; CLD = chronic lung disease; FT = failure to thrive; NEC = necrotising enterocolitis; ESBLKp = extended spectrum β-lactamase producing *Klebsiella pneumoniae*; A = ampicillin; G = gentamicin; Ctx = cefotaxime; M = metronidazole; Ami = amikacin; F = flucloxacillin; V = vancomycin; G = gentamicin.
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nated Klebsiella SHV-2. More than 27 species were first reported in Germany due to a plasmid mediated resistance to the third generation cephalosporins, nor prolonged courses of other antibiotics. However, as we do not perform surveillance cultures on admission to the unit, we are unable to say whether the first baby was already colonised before admission.

The ESBLKp isolate from case 7 occurring at the height of the epidemic was not a genetic match with the other isolates. This highlights the benefits of subtyping organisms in an epidemic and raises further questions relating to the origins of different strains of ESBLKp.

Surgical patients were over represented in our outbreak—six of the seven patients having undergone recent surgical procedures. Because our unit is tertiary referral centre, several surgical patients are on the unit at any one time. Many non-surgical patients were colonised or presumed to be colonised, and only one became septic. This suggests that surgery may be a contributory factor. Gastrointestinal surgery, and in particular, ischaemic bowel, may be an important risk factor for sepsis.

Other outbreaks have also reported over representation of surgical patients. An outbreak of ESBLKp at Guy’s Hospital, London, was mostly seen in neonates recovering from cardiac surgery for congenital defects. The increased risk of clinical infection is probably associated with invasive procedures in general, and not restricted to major surgery. This highlights the relative likelihood of such an epidemic becoming a rapid clinical problem in a major surgical neonatal centre compared with smaller units where surgery is not performed on site.

Various outbreak management strategies have been described. The methods used address antibiotic policy, cohorting, hand washing, wearing of gloves and gowns, and environmental swabs. The expense of the management increases as the number of methods instituted rises. In some outbreaks short term antibiotic policy change has been reported as being adequate to prevent further spread of infection. Occasionally, an environmental source has been found and removal of the environmental source has led to rapid resolution of the outbreak.

Many outbreaks are managed with surveillance cultures and cohorting. If this approach is
Control of Klebsiella infection in a neonatal unit

levels of colonisation. Regardless of the level would add unnecessary cost. Klebsiella outbreaks are consistently associated with high levels of colonisation. Regardless of the level of colonisation we could not isolate large numbers of babies in the unit and would still have relied on increased hand washing to eradicate spread. Case 6 was isolated because persistent colonisation was assumed after confirmed infection, and because the increased awareness and discussion of the implications of multiresistant organisms, associated with nursing her in isolation, was felt to be advantageous.

In most Klebsiella epidemics, the primary source of infection is gut colonisation of infants. We began stage 1 management without searching for an environmental source and, as no further episodes of sepsis occurred, it is likely that none existed. If further cases had occurred we would have begun a second stage of management and surveyed the unit environment. One may question the possible continued risk to babies by not seeking out a possible external source, but with the change in antibiotic policy the risk to infants was reduced.

There is little published evidence to support the control of outbreaks by improved hand washing and the eventual discharge of colonised babies from the unit. Compliance with hand washing by staff has rarely been observed to occur on more than one third of occasions of patient contact, ranging from 28%–48%. Tibballs at the Royal Children's Hospital (RCH) in Melbourne recently reported baseline hand washing rates by Intensive Care Unit medical staff of only 12.4% before and 10.6% after patient contact, and only 4.3% of occasions both before and after patient contact. The RCH rates increased to about 1 in 3 occasions when the doctors knew they were being observed. However, with education, feedback reinforcement, and further observations the rates rose to 68.3% before, 64.8% after, and 55.2% both before and after patient contact. Rates after the study period ended were still well above 1 in 3, although they had fallen. How to maintain high long term rates of hand washing is unknown, but Tibballs' study confirms that short term hand washing improvement is possible. If this can be initiated at the time of an outbreak, it may prevent further cross contamination as the incentive to prevent further deaths in an epidemic is probably the best motivation for staff. However, most hand washing studies are not performed during epidemics.

We did not formally measure whether our educational approach to improved hand washing affected compliance. The rapid resolution of the outbreak may have been coincidental due to altering the antibiotic policy alone.

The methods for improving hand washing practices and their success are varied. Our approach to set up the nurse caring for each baby on a particular shift as the advocate has worked well, and discussion of the implications of multiresistant organisms was an advantage. Case 6 was isolated because persistent colonisation was assumed after confirmed infection, and because the increased awareness and discussion of the implications of multiresistant organisms, associated with nursing her in isolation, was felt to be advantageous.

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