Necrotising enterocolitis as an infectious disease — evidence from an outbreak of invasive disease due to extended-spectrum beta-lactamase-producing Klebsiella pneumoniae

To the Editor: Necrotising enterocolitis (NEC) is a severe gastro-intestinal disorder, predominantly seen in hospitalised low-birth-weight newborn infants. It is associated with significant morbidity and mortality. Infants with NEC require parental nutrition and intravenous antibiotics with prolongation of hospitalisation. Severe cases require surgical resection of necrotic bowel wall with the attendant problems of prolonged hospitalisation. Severe cases require surgical resection of necrotic bowel wall with the attendant problems of prolonged hospitalisation. Necrotising enterocolitis places an enormous burden on resource-poor institutions.

We recently documented an outbreak of invasive disease due to extended-spectrum beta-lactamase-producing Klebsiella pneumoniae (ESKP). The majority of patients had concomitant NEC. Rotavirus, a well-described risk factor for NEC, and endemic in the neonatal wards, was also implicated.

The aims of this study were twofold: firstly to investigate the relationship between ESKP, rotavirus and NEC in a cross sectional study, and thereafter to determine whether the implementation of improved infection control measures was associated with a reduction in the incidence of NEC.

Diagnosis of necrotising enterocolitis. The presence of any of the following clinical criteria: mild abdominal distension, feeding intolerance or vomiting were regarded as 'suspected NEC'. Dilated 'sausage-shaped' bowel loops or thickened bowel loops seen on abdominal radiography were regarded as supportive evidence for suspected NEC. For 'confirmed NEC' any of the following clinical criteria were diagnostic: severe abdominal distension, occult blood in stool, bile-stained vomiting, persistent ileus, pneumatosis intestinalis or bowel perforation requiring surgical intervention.4

Survey for rotavirus and ESKP. Stool specimens from all patients in both intermediate care wards were submitted for rotavirus detection in a cross-sectional survey. Bi-weekly rectal swabs from all patients were submitted for ESKP culture as part of the infection control strategy.

Microbiology and virology. Rectal swabs were taken on dry, cotton-tipped swabs. Stool samples were collected in sterile containers. All swabs were cultured on McConkey medium. Rectal swabs were assayed for rotavirus and adenovirus 40 and 41 by enzyme-linked immunosorbent assay (Rotoclone and Adenoclone, Cambridge Biotech, Worcester, UK).

Statistical analysis. Chi-square analysis and odds ratio (OR) were calculated using Epi Info version 6.03, Center for Diseases Control, Atlanta, Georgia, USA.
DISCUSSION

The present study provides strong evidence that NEC is, in part, an infectious disease. NEC has been shown to occur in clusters, often associated with outbreaks of nosocomial disease. We demonstrated an extremely high incidence of stool colonisation with both ESKP and rotavirus in our cross-sectional survey and a reduction in ESKP colonisation a year later, thus demonstrating poor compliance with handwashing and other infection control practices and subsequent improvement. The high prevalence of dual colonisation in patients with NEC suggests either a causal relationship or that another unidentified hand-transmissible agent might be implicated.

As a further analysis of the extent of ESKP colonisation in the intermediate care wards, a comparison was made for first month of initial intervention and the same month a year later, once infection control practices were perceived to be well implemented. In August 1996, 39% of admissions to the intermediate care wards became colonised with ESKP. In August 1997 only 20% of admissions became colonised (OR 2.92, \( P = 0.000006 \)), suggesting that colonisation during the outbreak was excessive and that infection control practices had been at least partially effective.

Improved infection control associated with a reduction in NEC. From 1 January to 30 September 1996, 35 (12.8%) of 239 infants were admitted from the intermediate care wards for management of severe NEC. From the beginning of October 1996 through April 1997, 18 (6%) of 298 admissions were for NEC. This represents a decline of more than 50% (\( P = 0.0085 \)) (Table II). A comparative analysis of ICU admissions for NEC from January through September 1994 and October through April 1995 showed incidences of 2.9% and 3.9% respectively (OR 0.75, \( P = 0.5 \)).

<table>
<thead>
<tr>
<th>Period of study</th>
<th>Admissions to the neonatal intensive care unit (N)</th>
<th>Patients with NEC admitted to the intensive care unit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>January - September 1996</td>
<td>239</td>
<td>35 (12.8)</td>
</tr>
<tr>
<td>October 1996 - April 1997</td>
<td>298</td>
<td>18 (6)</td>
</tr>
<tr>
<td>Odds ratio 2.28 (1.21 - 4.31), ( P = 0.0085 )</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table II. The influence of improved infection control practice on patients with confirmed NEC admitted to the neonatal intensive care unit.

In conclusion, infection control measures that include adequate hand hygiene are potent factors in prevention of NEC.

Cross-sectional survey. The cross-sectional survey for rotavirus was conducted over a 4-day period from 19 to 24 August 1996, and results are shown in Table I. Rotavirus was detected in 35 of 44 samples (79.5%) and adenovirus type 40/41 in none. Thirty-one infants (70.5%) were colonised with both rotavirus and ESKP simultaneously. Thirteen infants (29.5%) of the 44 surveyed had either confirmed or suspected NEC. Ten of the 13 (77%) had isolation of both ESKP and rotavirus.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus-positive</td>
<td>35</td>
<td>79.5</td>
</tr>
<tr>
<td>ESKP-positive</td>
<td>35</td>
<td>79.5</td>
</tr>
<tr>
<td>Rotavirus- and ESKP-positive</td>
<td>31</td>
<td>88.6</td>
</tr>
<tr>
<td>Patients with NEC*</td>
<td>13</td>
<td>29.5</td>
</tr>
<tr>
<td>Patients with NEC and positive for rotavirus and ESKP</td>
<td>10</td>
<td>77</td>
</tr>
</tbody>
</table>

* Four patients had suspected and 9 confirmed NEC.

ESKP = extended-spectrum beta-lactamase-producing Klebsiella pneumoniae; NEC = necrotising enterocolitis.
We thank Dr Wilhelm Steyn for assistance with data analysis. The study was supported by the Medical Research Council of South Africa. We also thank colleagues from the neonatal and obstetric services of the University of Cape Town for accommodating extra patients during the outbreak. We acknowledge the help of Tanya Stander from the Department of Medical Virology, University of Stellenbosch for virological studies.

M F Cotton C H Pieper G F Kirsten

Department of Paediatrics and Child Health University of Stellenbosch and Tygerberg Children's Hospital Tygerberg, W Cape

H Orth

Department of Medical Microbiology University of Stellenbosch and Tygerberg Hospital Tygerberg, W Cape

D C Theron

Department of Community Medicine University of Stellenbosch and Tygerberg Hospital Tygerberg, W Cape


**CHILDHOOD ACUTE VIRAL HEPATITIS IN CAPE TOWN**

To the Editor: Most episodes of acute viral hepatitis (AVH) are easily recognised. Of the hepatitis viruses hepatitis A, hepatitis B and hepatitis E (HA, HB, HE) are most likely to cause the typical syndrome. In South Africa, serological surveys have suggested that HA infection occurs in early childhood in poor communities, but that many adults in wealthier communities remain susceptible.12 HB is mainly acquired in childhood.3 The epidemiology of HE is only partly known.4

In childhood, AVH is usually uncomplicated and self-limited and no therapy is required. It is not possible to identify the agent responsible without serological or virological tests. It is also not possible to predict which child will run a complicated course.

In the light of this, the policy of the Red Cross War Memorial Children's Hospital (RCCH) Medical Outpatients' Department (MOPD), which largely serves children from poor Cape Town communities, has been to perform liver function and serological tests only on children attending with AVH who have special epidemiological circumstances (such as the institutionalised child) or suspected complications.

A number of factors led to a review of this policy. The options for HA and HB prophylaxis for contacts have changed with the advent of vaccines. Since 1995 all infants have been immunised against HB.3

This study represents part of an attempt to arrive at an appropriate policy on the management of children with AVH in this and similar settings. The study aimed to examine the demography and pattern of diagnosis, referral, complications, and notification of children with AVH.

Patients with AVH attending the RCCH during 1996 (the last complete year during which unreferred non-urgent patients were seen at the hospital) were studied. Data were assembled from computerised records of visits to the MOPD by patients with viral hepatitis (using the International Classification of Diseases 9 (ICD 9), Code 070.0), patients with a discharge diagnosis of viral hepatitis or hepatic coma (ICD 9 Code 572.2), patients with positive HA immunoglobulin M (IgM) tests (identified from laboratory results) and the hospital register of notifications. Patients with chronic HB were excluded after reviewing the clinical records of patients with HB (ICD 9 Codes 070.2 and 070.3). Serious complications were explored by examining the clinical records or discharge summaries of inpatients. A notification rate was calculated by comparing the notification register with the whole data set.

Table I shows the race, sex and age composition of the 326 patients. The median age was 70 months and the maximum 14 years. Two hundred and seventy-two of the outpatients (83.4%) were self-referred. Analysis of postal codes showed that the areas that patients came from reflected the usual drainage areas for the MOPD, but formerly 'black' areas were underrepresented compared with formerly 'coloured' areas (ratio 1:6). The ratio for all patients who attended the MOPD in 1996 was 1:2. Whether this indicates differing patterns of self-referral for jaundice or a genuinely lower rate of symptomatic AVH among black children cannot be ascertained from these data.