Nationwide study of haemolytic uremic syndrome: clinical, microbiological, and epidemiological features

E J Elliott, R M Robins-Browne, E V O’Loughlin, V Bennett-Wood, J Bourke, P Henning, G G Hogg, J Knight, H Powell, D Redmond, Contributors to the Australian Paediatric Surveillance Unit

Abstract

Aims—To establish the incidence and aetiology of haemolytic uremic syndrome (HUS) in Australia and compare clinical and microbial characteristics of sporadic and outbreak cases.

Methods—National active surveillance through the Australian Paediatric Surveillance Unit with monthly case notification from paediatricians, July 1994 to June 1998. Children under 15 years presenting with microangiopathic haemolytic anaemia, thrombocytopenia, and acute renal impairment were identified.

Results—Ninety-eight cases were identified (incidence 0.64 per 105 years/annum and 1.35 per 105 children <5 years/annum). Eighty-four were associated with diarrhoea (64 sporadic, 20 constituting an outbreak) and 14 were atypical. Shiga toxin producing Escherichia coli (STEC) O111:H− was the most common isolate in sporadic HUS and caused the outbreak. However O111:H− isolates from outbreak and sporadic cases differed in phage type and subtyping by DNA electrophoresis. STEC isolates from sporadic cases included O26:H−, O113:H21, O130:H11, OR:H9, O157:H−, ONT:H7, and ONT:H−. STEC O157:H7 was not isolated from any case. Only O111:H− isolates produced both Shiga toxins 1 and 2 and possessed genes encoding E coli attaching and effacing gene ( intimin) and enterohemolysin. Outbreak cases had worse gastrointestinal and renal disease at presentation and more extrarenal complications.

Conclusions—Linking national surveillance with a specialised laboratory service allowed estimation of HUS incidence and provided information on its aetiology. In contrast to North America and Japan, the British Isles, STEC O157:H7 is rare in Australia; however, non-O157:H7 STEC cause severe disease including outbreaks. Disease severity in outbreak cases may relate to yet unidentified virulence factors of the O111:H− strain isolated.

Keywords: Shiga toxin; E coli; haemolytic uremic syndrome; surveillance

Haemolytic uremic syndrome (HUS) is characterised by microangiopathic haemolytic anaemia, thrombocytopenia, and acute renal impairment. It is usually preceded by diarrhoea, often bloody. Karmali et al first identified the association between HUS and infection with Shiga toxin producing Escherichia coli (STEC) O157:H7 in children,1 2 which is now well established.3–7 STEC were previously known as verotoxin producing E coli. In North America and Europe most HUS is caused by STEC of serotype O157:H7 and major outbreaks have occurred following ingestion of contaminated food or drink, swimming in contaminated water, contact with farm animals, through environmental contamination, or person to person spread.4 5 While the major cause of infection in humans is STEC O157:H7, other serotypes also may cause diarrhoea and HUS.10–12 Differences in the occurrence of STEC serotypes appear to be geographic; data suggest non-O157:H7 STEC strains predominate in Australia.12–24 and contribute to disease in several other countries.18 20 21 25 Although typically associated with intestinal infection, HUS may also follow urinary tract infection with STEC26 or systemic infection with neuromedinase producing bacteria.27 HUS may be familial28 or associated with immunodeficiency, immunosuppression, and pregnancy.29

The epidemiology of HUS in the southern hemisphere is poorly described.30–32 Although diarrhoea associated HUS occurs in Australia, STEC O157:H7 has rarely been implicated. This may reflect the fact that diagnostic laboratories do not routinely test for this STEC in patients with diarrhoea or may indicate that HUS in Australia is caused by different STEC than are commonly implicated in Europe and North America. The frequency of STEC associated diseases in Australia is unknown. We undertook nationwide surveillance of HUS, as a marker of STEC related disease, through the Australian Paediatric Surveillance Unit (APSU).

# Methods

CASE ASCERTAINMENT, CASE DEFINITION, AND CASE CLASSIFICATION

Cases were ascertained prospectively through the APSU by active, national surveillance between July 1994 and June 1998 inclusive.30

www.archdischild.com

Correspondence to: A/Prof E Elliott, Dept of Paediatrics and Child Health, University of Sydney, c/o The Children’s Hospital at Westmead, Locked Bag 4001, Westmead, NSW, 2145, Australia elizabe2@chw.edu.au

Accepted 28 March 2001
All paediatric specialists in Australia were sent a monthly, reply paid report card and asked to indicate whether they had seen any child under 15 years of age in the previous month with any of the conditions listed on the card, including HUS. HUS was defined as “microangiopathic haemolytic anaemia (haemoglobin <100 g/l with microscopic evidence of fragmented red blood cells), thrombocytopenia (platelet count <100 000 x 10^9), and acute renal impairment (oliguria or anuria with increased serum urea and creatinine)”. During the study period over 900 clinicians were mailed and over 93% report cards were returned to the APSU each month. The APSU notified study investigators of reported cases of HUS each month. Investigators obtained further information on individual cases (clinical presentation, outcome, demographics, and laboratory results) from clinicians notifying cases by standardised postal questionnaire (96% of questionnaires were returned). Data provided was de-identified to maintain patient anonymity. Diarrhoea associated cases of HUS were classified as “sporadic” or “outbreak” cases. The single outbreak consisted of cases occurring in South Australia in January and February 1995 and in whom a common causative organism was subsequently confirmed. Cases with no significant gastrointestinal disease or isolation of STEC in the stool and with a family history of HUS, with an atypical or relapsing course or with confirmed systemic infection with a neuraminidase producing organism, were classified as “atypical”. The ethics committee of the Children’s Hospital at Westmead, Sydney approved the study.

MICROBIOLOGY
Clinicians reporting cases were asked to send paired serum samples and a stool sample or rectal swab and Ecoli isolates from faeces or implicated food, if available, to a centralised laboratory for isolation and characterisation of STEC isolates. Colonies from stool specimens, obtained as soon as possible after the diagnosis of HUS and cultured on MacConkey agar, were tested for production of Shiga toxin (Stx) using HeLa cells. Stx1 or Stx2 was identified by neutralisation with monoclonal antibodies. Colony and Southern blotting was used to probe STEC isolates for genes encoding virulence associated factors, namely Stx1, Stx2, Ecoli attaching and effacing gene (eae, intimin), and enterohemolysin. Serotyping of STEC strains was performed at the Victorian Infectious Diseases Reference Laboratory. The relatedness of O111:H– isolates from outbreak and sporadic cases was investigated by pulsed field gel electrophoresis (PFGE) as described previously. The DNA patterns obtained were aligned with the aid of Gel Compar software (Applied Maths, Kortrijk, Belgium) to form a composite image, and were analysed as recommended by Tenover and colleagues. Paired serum samples (acute and convalescent, collected approximately two weeks apart) were tested for agglutinating antibodies to O antigens 26, 111, and 157. Detailed microbiological data on outbreak cases have been reported elsewhere.

ANALYSIS OF DATA
Incidence estimates and confidence intervals were calculated using Stat-Exact. Comparison of outbreak and sporadic groups was made using Student’s t test, Mann–Whitney U test, and χ² or Fisher’s exact tests. Incidence trends were analysed using the Cochran–Armitage trend.

Results
CATEGORISATION OF CASES, INCIDENCE, SEASONAL, AND GEOGRAPHIC DISTRIBUTION
In a 48 month period, 98 cases of HUS were identified, of which 84 (86%) were associated with gastrointestinal symptoms. Sixty four were sporadic cases and 20 comprised a single outbreak in South Australia occurring in January and February 1995. Fourteen “atypical” cases were identified, of whom five had an atypical or relapsing course, four were familial, three were associated with pneumococcal infection, one was associated with immunodeficiency, and one had an STEC associated urinary tract infection. The median age of cases at diagnosis was 31 months (interquartile range 16–70 months) and 70/98 (71%) children were under 5 years of age. Ninety one (92%) children were hospitalised for a median (interquartile range) of 14 (7–21) days.

The reported annual incidence of HUS (with 95% CI) was 0.64 (0.52 to 0.78) per 10⁵ children under 15 years. Incidence was significantly higher in children under 5 years (1.35 (1.06 to 1.72) per 10⁵) than in those aged 5–14 years (0.28 (0.18 to 0.39) per 10⁵; Fisher’s exact test, p < 0.0001). When outbreak cases were excluded from the analysis, the overall incidence was slightly, though not significantly lower.

Figure 1 shows the distribution of cases by type and month of presentation. During the entire study period there was a significantly higher incidence of cases during summer months (χ² test for trend, p < 0.001). This seasonal distribution persisted when outbreak and atypical cases were excluded. However, when the data were analysed by individual year of occurrence, a significant increase in sporadic cases in the summer only occurred in 1994–95, at the time of the outbreak. All sporadic cases

www.archdischild.com

Figure 1 Seasonal distribution of HUS cases by type; July 1994 to June 1998 (n = 98). Incidence of sporadic HUS decreased significantly over the study period (p < 0.001; Cochran–Armitage trend). Overall a seasonal (summer) peak in incidence was seen (p < 0.001).
Haemolytic uraemic syndrome

Table 1 Laboratory and clinical features of diarrhea associated HUS

<table>
<thead>
<tr>
<th>Laboratory features</th>
<th>Outbreak (n = 20)</th>
<th>Sporadic (n = 64)</th>
<th>p value (outbreak v sporadic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum haemoglobin (median; g/l)</td>
<td>73 (62–82)</td>
<td>62 (52–73)</td>
<td>0.06</td>
</tr>
<tr>
<td>Minimum platelet count (median; × 10^9/l)</td>
<td>29 (23–44)</td>
<td>56 (28–96)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Maximum neutrophil count (median; × 10^9/l)</td>
<td>9.3 (7.3–23.7)</td>
<td>8.6 (5.2–12.6)</td>
<td>0.05</td>
</tr>
<tr>
<td>Minimum serum sodium (mean; mmol/l)</td>
<td>128 (4)</td>
<td>131 (6)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Maximum creatinine (median; µmol/l)</td>
<td>463 (322–637)</td>
<td>280 (140–593)</td>
<td>&lt;0.05*</td>
</tr>
</tbody>
</table>

Clinical features

| Age (median; mth) | 63 (34–99) | 30 (18–57) | <0.05* |
| Age less than 5 years (n; %) | 9 (45%) | 49 (77%) | <0.05 |
| Duration hospital stay (median; days) | 17 (10–22) | 12 (7–17) | <0.01* |

Renal features

| Anuria (n; %) | 16 (80%) | 31 (48%) | <0.05 |
| Duration anuria (median; days) | 14 (10–20) | 5.0 (3–9) | <0.001* |
| Dialysis (n; %) | 18 (90%) | 35 (55%) | <0.01 |
| Duration dialysis (mean; days) | 14.8 (8.1) | 10.2 (6.3) | <0.05 |
| Acute hypertension (n; %) | 13 (65%) | 25 (40%) | 0.07 |
| Elevated creatinine at discharge (n; %) | 17 (85%) | 12 (19%) | <0.0001* |
| Hypertension at discharge (n; %) | 9 (45%) | 12 (20%) | <0.05 |

Gastrointestinal features

| Diarrhoea prodrome (n; %) | 20 (100%) | 64 (100%) | 0.001 |
| Duration diarrhoea (median; days) | 3.0 (2.0–4.3) | 5.0 (4.0–10.0) | 0.01* |
| Blood in stool (n; %) | 16 (84%) | 23 (36%) | <0.001* |
| Severe colitis (n; %) | 6 (27%) | 2 (3%) | <0.01 |
| Vomiting (n; %) | 17 (85%) | 50 (78%) | 0.75 |
| Acute pancreatitis (n; %) | 1 (5%) | 0 (0%) | 0.24 |

Other

| Seizures (n; %) | 5 (25%) | 7 (11%) | 0.18 |
| Central nervous system events* | 9 (45%) | 8 (13%) | <0.001* |
| Hyperglycaemia | 5 (25%) | 3 (5%) | <0.05* |
| Death <12 months after diagnosis | 1 (5%)† | 2 (3%)‡ | 0.42 |

Results are shown as n (%), mean (SD), or median (interquartile range). Comparison between outbreak and sporadic HUS was made using ‘Student’s t test; *Mann–Whitney U test; †χ² test; ‡Fisher’s exact test.

*Includes children with one or more of the following: seizure, intracranial haemorrhage or infarct, retinal haemorrhage, encephalopathy.

Death was due to: †multiple cerebral haemorrhagic infarction; ‡myocarditis with pericardial effusion; §complications of renal failure.

COMPARISON OF OUTBREAK AND SPORADIC CASES WITH DIARRHOEA

Table 1 shows laboratory and clinical features of children with diarrhea associated HUS. The outbreak group was significantly older than the sporadic group and the proportion of children under 5 years was lower. There was no gender bias. Duration of hospitalisation was significantly longer in the outbreak group.

The minimum haemoglobin and maximum neutrophil counts were not significantly different between groups (table 1). Maximum serum creatinine was significantly higher in the outbreak group and minimum platelet count and minimum serum sodium concentrations were significantly lower in the outbreak group.

EIGHTY per cent of outbreak and 48% of sporadic cases developed anuria; its duration was significantly longer in the outbreak group (table 1). Significantly more outbreak cases required dialysis and the duration of dialysis was significantly longer in the outbreak group.

The frequency of acute hypertension in groups did not differ. However, at discharge from hospital a significantly greater proportion of the outbreak group had persistent renal impairment (increased serum creatinine) and hypertension requiring treatment (table 1).

Although a diarrhoea prodrome was present in all 84 children, outbreak cases had a shorter prodrome and a much higher rate of macroscopic bloody diarrhoea (table 1). In outbreak cases the diarrhoea prodrome lasted between one and seven days and in sporadic cases, one to 30 days. Significantly more outbreak cases had severe haemorrhagic colitis. Left hemicolectomy was required in one outbreak case with ischaemic colon and partial colectomy in another. One sporadic case required appendectomy and omentectomy. Vomiting was reported in around 80% of both groups.

Acute pancreatitis occurred in one outbreak case and hyperglycaemia was significantly more frequent in the outbreak group (table 1). Insulin was required in two outbreak cases and one sporadic case. The proportion of children with central nervous system complications (intracranial bleed or infarct, retinal haemorrhage, encephalopathy, seizure) was higher in the outbreak group. One sporadic case had anterior compartment syndrome caused by rhabdomyolysis and required fasciotomy of the right leg. An iliac vein thrombosis occurred in one child in the outbreak group.

Three of 84 patients died (table 1). A 4 year old girl with outbreak HUS and acute renal failure, multiple cerebral haemorrhagic infarcts, and extensive colonic necrosis died two days after diagnosis. A 10 year old boy with sporadic HUS and STEC O111 in the stool died eight days after diagnosis, from cardiac complications (myocarditis with pericardial effusion and tamponade). A 1 year old boy with sporadic HUS died within 12 months of diagnosis with persistent hypertension and renal failure.

OUTCOME

Twelve month follow up data were available on all 19 survivors of the outbreak and 43 of 62 survivors of sporadic HUS. Six of 19 outbreak cases and four of 43 sporadic cases had chronic renal failure (persistent elevation of creatinine and/or glomerular filtration rate of <80 ml/min/1.73 m²) at follow up (p = 0.06). Hypertension persisted at 12 months in four sporadic but no outbreak cases. No survivors of the outbreak developed end stage renal failure, defined as requiring chronic dialysis (whether or not awaiting transplantation) or having had renal transplantation. Of the three sporadic cases that developed end stage renal failure by 12 months after diagnosis, one had had a kidney transplant, one was awaiting transplantation, and one had died. One sporadic case had persistent insulin dependent diabetes mellitus. Five children with sporadic HUS had seizures at follow up. Three of these developed seizures following discharge from hospital, so their aetiological relation to HUS is unclear.

MICROBIOLOGY

Stool and/or serum samples were available from all outbreak cases. STEC serotype O111:H– was isolated from 16/20 stools from...
Table 2  Characteristics of STEC isolates in diarrhoea associated HUS

<table>
<thead>
<tr>
<th>No. of isolates</th>
<th>Serotype</th>
<th>Sorbitol fermentation</th>
<th>Stx1†</th>
<th>Stx2†</th>
<th>eae</th>
<th>Enterohaemolysin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outbreak HUS*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>O111:H−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sporadic HUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>O111:H−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>1</td>
<td>O26:H−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>O113:H21</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O130:H11</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>O157:H−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>1</td>
<td>OR:H9</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

Specimens were investigated on 20/20 epidemic cases and 50/64 endemic cases.

*Paton et al.††

| O111:H− strains isolated from a patient who was also infected with a Shiga toxin 2 producing strain of Entero bacter cloacae.

§Obtained from a patient who was also infected with a Shiga toxin 2 producing strain of Enterobacter cloacae.

‡Virulence associated features not determined on this isolate.

†Obtained from a patient who was also infected with a Shiga toxin 2 producing strain of Enterobacter cloacae.

These children. Stool specimens or bacterial cultures were investigated from 50/64 children with sporadic HUS. STEC were isolated from 20/50 specimens (table 2). These included strains of serotypes O111:H−, O26:H−, O113:H21, O130:H11, O157:H−, O non-typeable:H−, O non-typeable:H7, and O rough (R):H9. All isolates fermented sorbitol except those of serogroup O157 (table 2). One child was infected with both STEC OR:H9 and an Stx2 producing strain of Enterobacter cloacae. STEC O111:H− was also isolated from the stool of the asymptomatic identical twin brother of a culture negative case of endemic HUS. The high number (30/50) of negative stool cultures in sporadic cases is not surprising in view of the long diarrhoea prodrome (up to 30 days) prior to diagnosis of some cases in this group.

Table 2 shows virulence associated characteristics of STEC isolates. All O111:H− strains from outbreak and sporadic cases produced Stx1 and Stx2 and carried the eae and enterohemolysin genes. However, PFGE analysis of the outbreak and sporadic O111:H− strains showed them to be different (fig 2). Furthermore, some O111:H− strains obtained from children with HUS in New South Wales around the time of the South Australian outbreak displayed a different phage type, colicin type and had different plasmid profiles compared to the epidemic strain. Of the non-O111:H− strains isolated and examined for the presence of virulence associated factors, all but three carried the enterohemolysin gene and produced enterohemolysin (table 2). Two of the strains that did not produce enterohemolysin were of indeterminate serotype and produced only Stx1 or Stx2. All non-O111 STEC produced either Stx1 or Stx2 but only one produced both. Five strains did not carry the eae gene. One sporadic case without STEC infection produced Stx1 and Stx2 and carried the gene for enterohemolysin but not that for eae.

Serum was available from 30 children with sporadic HUS, but as only one serum sample was available from most cases, we selected a high agglutinating antibody titre (≥1/640) to indicate recent infection with E coli strains of serogroups O26, O111, or O157. Five patients showed increased antibody to O157, one of whom was also culture positive for STEC O157:H−. All 25 other sera investigated for antibodies to serogroup O157 showed a titre of <1/80. Three patients who were culture positive for STEC O111: H−, had an antibody titre to O111 of >1/640. The other five O111 culture positive patients identified in this study did not undergo serological examination. One patient with negative stool culture had a titre of >1/2560 to O111. No patient showed increased antibody titres to O26.

Discussion

The epidemiology of HUS in Australia has not been described previously. Four years of national surveillance through the APSU identified 98 patients under 15 years of age with HUS. Approximately 90% had diarrhoea associated HUS and 20 were affected during an outbreak of STEC O111:H− transmitted by contaminated mettwurst. Diarrhoea associated HUS was associated with at least eight different STEC serotypes. Although up to seven cases were associated with STEC O157, no strains of O157:H7 were isolated, indicating major geographical differences in strain prevalence...
Haemolytic uraemic syndrome

Comparison of clinical features of sporadic and outbreak cases of HUS suggests the outbreak strain caused more severe disease at presentation, although specific microbial factors accounting for these differences were not identified.

The active nature of the surveillance, high return rate of monthly report cards and questionnaires, and inclusion on our mailing list of all known paediatric specialists in Australia, suggest that we identified the majority of HUS cases. No other national data set is available for comparison. The incidence of HUS in children under 5 years (1.35 (95% CI 1.06 to 1.72) per 10^5) was lower than that reported in Canada (3.11 per 10^5 children <5 years) and the British Isles (3.3 per 10^5 children).

In Minnesota the incidence of HUS in children under 5 was 5.8 per 10^5 in 1988 and 2.1 per 10^5 in 1994–95. Overall, in the later study, one HUS case was reported for every 4.3–5.2 cases of STEC infection. This greatly overestimates the ratio of HUS to gastroenteritis as many cases of STEC induced gastroenteritis are unrecognised. This is borne out by a spate of recent outbreaks of STEC O157:H7 diarrhea associated HUS but that older children and elderly have increased susceptibility to diarrhea. STEC frequently produce enterohemolysin but the roles of this and other plasmid encoded factors in disease are unknown. The O111:H− strains, which caused the outbreak and those found to be associated with sporadic HUS, exhibited all the pathogenicity traits described above. However, comparison of outbreak O111:H− isolates with several O111:H− isolates from sporadic cases revealed differences in phage type and DNA restriction fragment length polymorphism, indicating that different O111:H− strains were responsible for outbreak and sporadic HUS. Genetic differences in the outbreak strain may contribute to differences in virulence by virtue of the presence of currently unknown virulence determinants or of different quantities of known determinants. A recent Minnesota study reported that molecular subtyping of strains isolated from the local community allowed the authors to identify mini outbreaks which would not have been recognised with standard microbial characterisation. Molecular subtyping is also useful for O111 STEC and may provide a mechanism to identify strains with different degrees of virulence.

In this study, several non-O157:H7 strains were identified in children with HUS, as previously recognised. Apart from O111, only one of these produced both Stx1 and Stx2. Three strains lacked the eae gene and two of these were negative for enterohemolysin. The aetiological role of such strains in HUS is open to question, given that Stx1 and Stx2 are encoded by somewhat promiscuous bacteriophages which are readily transmitted between different strains of E. coli. Thus, the ability to produce Stx may be acquired by a relatively harmless E. coli resident in the intestinal tract from a virulent STEC strain that was not detected when the stool sample was taken. In such cases serological investigation may shed light on the aetiological agent by permitting detection of antibodies to O antigens associated with the most frequent STEC O serogroups. This applied to four patients in this study who were culture negative, but displayed increased antibody titres to O157. Detection of antibodies to Stx1 and Stx2, as well as to intimin or functionally related, chromosomally encoded proteins, enterohemolysin, and flagella antigens may also provide useful retrospective information about the causative organism in culture negative patients. In this study, the relatively low isolation rate (40%) of STEC overall and of O157 strains in particular, from children with sporadic HUS may have been a result of an undue delay in obtaining samples for culture and transporting them to the laboratory. Isolation rates of O157 strains could conceivably have been improved by selective enrichment, for example, by using

www.archdischild.com
immunomagnetic enrichment of faecal samples. Such strategies, however, would probably have biased the data against non-O157 strains.

Medium term prospective studies were supported by the National Health and Medical Research Council. Laboratory studies were carried out at the Laboratory for Australia and supported by the Australian and New Zealand Paediatric Nephrology Association and the Division of Paediatrics of the Royal Australasian College of Physicians. We thank the following clinicians, who provided clinical information on cases reported to this study: Drs Anderson, Andrews, Brown, Burke, Cheadle, Craig, Donaghy, Dung, Fenton, Frear, Fruen, Forrest, Ford, Frischman, Goldwater, Gadd, Gorton, Gray, Harris, Harding, Henning, Hewitt, Hill, Hodgen, Hodgson, James, James, Jaques, Jenkins, Jerdeni, Jones, Kelso, Kainer, Ketteridge, Knight, Lammi, Lewin, Lines, Lennon, McGinley, McLennan, Mulcahy, Munt, Neill, N’Ouahlin, Pearson, Prebble, Pellas, Petro, Rice, Roper, Ruben, Rosenberg, Roy, Shelton, Smith, Stuart, Sparnon, Taylor, Thesiger, Thomas, Tonge, Westphalen, White, and Wheaton. Laboratory assistance was provided by A Bigham, K Bettelheim, and D Lightbolk in Melbourne, and J Paton and P Goldwater in Adelaide. The APSU was funded by the Financial Markets Foundation for Children, the Commonwealth Department of Health and Aged Care, and the Clive and Vera Ramaciotti Foundation (administered by Perpetual Trustees). Laboratory studies were supported by the National Health and Medical Research Council of Australia.

We acknowledge all Australian paediatricians who contribute to the APSU, and the support of the Australian and New Zealand Paediatric Nephrology Association and the Division of Paediatrics of the Royal Australasian College of Physicians. We thank the following clinicians, who provided clinical information on cases reported to this study: Drs Anderson, Andrews, Brown, Burke, Cheadle, Craig, Donaghy, Dung, Fenton, Frear, Fruen, Forrest, Ford, Frischman, Goldwater, Gadd, Gorton, Gray, Harris, Harding, Henning, Hewitt, Hill, Hodgen, Hodgson, James, James, Jaques, Jenkins, Jerdeni, Jones, Kelso, Kainer, Ketteridge, Knight, Lammi, Lewin, Lines, Lennon, McGinley, McLennan, Mulcahy, Munt, Neill, N’Ouahlin, Pearson, Prebble, Pellas, Petro, Rice, Roper, Ruben, Rosenberg, Roy, Shelton, Smith, Stuart, Sparnon, Taylor, Thesiger, Thomas, Tonge, Westphalen, White, and Wheaton. Laboratory assistance was provided by A Bigham, K Bettelheim, and D Lightbolk in Melbourne, and J Paton and P Goldwater in Adelaide. The APSU was funded by the Financial Markets Foundation for Children, the Commonwealth Department of Health and Aged Care, and the Clive and Vera Ramaciotti Foundation (administered by Perpetual Trustees). Laboratory studies were supported by the National Health and Medical Research Council of Australia.


30 Elliott EL, Williams K. Communicable diseases and the Australian Paediatric Surveillance Unit. CDR (Lond Engl Rev) 1997;7:R14–16.


Nationwide study of haemolytic uraemic syndrome: clinical, microbiological, and epidemiological features

E J Elliott, R M Robins-Browne, E V O’Loughlin, V Bennett-Wood, J Bourke, P Henning, G G Hogg, J Knight, H Powell, D Redmond and Contributors to the Australian Paediatric Surveillance Unit

Arch Dis Child 2001 85: 125-131
doi: 10.1136/adc.85.2.125

Updated information and services can be found at: 
http://adc.bmj.com/content/85/2/125

These include:

References
This article cites 39 articles, 11 of which you can access for free at: http://adc.bmj.com/content/85/2/125#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Renal medicine (273)
Urology (446)
Child health (3922)
Diarrhoea (182)
Poisoning (165)

Notes

To request permissions go to: http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to: http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to: http://group.bmj.com/subscribe/