

HAEMOLYTIC URAEMIC SYNDROME: A CLUSTER OF CASES IN EARLY 1999

Haemolytic uraemic syndrome (HUS), an illness with potentially serious sequelae, is reported infrequently in Australia. This article summarises the limited NSW data available describing cases of HUS and outlines an investigation into an apparent increase in incidence of HUS in NSW in the first quarter of 1999.

BACKGROUND

HUS is characterised by microangiopathic haemolytic anaemia, thrombocytopenia and renal failure. HUS can be precipitated by a variety of factors including pregnancy, certain drugs, and infections associated with Epstein Barr Virus, *Shigella dysenteriae* type 1 and, most commonly, verocytotoxin-producing *Escherichia coli* (VTEC).^{1,2,3} There is also some evidence of a familial predisposition.^{4,5}

HUS is usually seen in children under four years of age,¹ and is the most common cause of renal failure in children.⁶ It follows a diarrhoeal illness in approximately 90 per cent of cases.⁴

VTEC-induced illness is characterised by bloody diarrhoea six to 48 hours after a non-specific gastrointestinal illness. Three to 10 days after the onset of disease, five to 15 per cent of infected persons may develop HUS.⁷ Mortality from HUS is about five per cent,^{6,7} and up to 50 per cent of survivors exhibit some degree of permanent renal damage.^{6,8}

VTEC infections have an incubation period of one to 12 days (typically three to four days) and produce a Shiga-like toxin (Shiga-like toxin I and II, or verocytotoxin I and II). Transmission frequently occurs after ingestion of beef contaminated with infected cattle faeces.^{6,9} The annual incidence of VTEC infection in industrialised countries ranges from one to 30 cases per 100,000 population.⁸

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TABLE 1

NOTIFICATIONS OF HAEMOLYTIC URAEMIC SYNDROME BY YEAR OF DISEASE, ONSET AND PLACE OF RESIDENCE BY PUBLIC HEALTH UNIT, NSW

Notifying Public Health Unit	Year of onset			Total
	1997	1998	1999*	
Central Sydney	–	–	1	1
Greater Murray	–	1	–	1
Hunter	–	2	–	2
Mid North Coast	1	–	–	1
New England	–	–	1	1
Northern Sydney	–	2	1	3
South Eastern Sydney	–	–	2	2
South Western Sydney	–	–	2	2
Total	1	5	7	13

* 1 January to 15 April 1999.
Source: Notifiable Diseases Database system, NSW Department of Health.

Only one outbreak of HUS has been reported in Australia. This involved 23 cases, all of whom were children under 14 years of age (mean age four years), and was linked to the consumption of mettwurst in South Australia in 1995. *E. coli* O111 was implicated in most of the cases and Shiga-like toxins were identified in the stools of 91 per cent of those affected.^{10,11}

Laboratories in NSW have been required to notify cases of VTEC (serotypes O157 or O111) infections since December 1996. Similarly, hospitals are required to notify of all cases of HUS, irrespective of aetiology.² The purpose of HUS surveillance is to:

- identify whether the case may be a potential source of infection for other people
- identify outbreaks and potential sources or sites of ongoing transmission
- better understand the epidemiology of this condition.²

Routine weekly review of case reports by the Health Protection Branch, NSW Department of Health, indicated an increase in notifications of HUS in the early part of 1999. The subsequent investigation is described below.

METHODS

Consistent with routine practice, all notifications of HUS were followed up by the respective public health units. Standardised information on food history, exposure to other people with a gastrointestinal illness, exposure to children in nappies, travel outside the case's area of residence, contact with livestock, and swimming activities was gathered. Where not already collected, the treating clinician was asked to obtain sera, stool or rectal swabs from the case.

The Health Protection Branch collated information on cases with an onset date after 1 January 1999 and, on the basis of preliminary evidence, coordinated identification

of the supplier and source abattoir of minced beef that had been consumed by the cases.

Historical data on reported HUS cases in NSW (1 January 1997 to 31 December 1998) were retrieved from the NSW Department of Health's Notifiable Diseases Database (NDD) system through the Health Outcomes Information & Statistical Toolkit (HOIST).

RESULTS

Case history and laboratory investigations

One HUS case was notified in NSW in 1997 and five in 1998. These cases lived predominantly in rural areas (67 per cent, $n = 4$).

Seven cases were notified between 1 January and 15 April 1999 and, of these, six (86 per cent) lived in the greater Sydney area (Table 1).

Males and females were equally represented in the 1997 and 1998 cohorts and cases were predominantly under four years of age. On the other hand, the 1999 cases were more likely to be female, and older children or adults (Table 2). All cases survived the illness.

Five of the seven cases notified in 1999 had a history of a precedent gastrointestinal illness, three with bloody diarrhoea. One case (case number seven), who presented with ankle oedema and hypertension at 28 weeks gestation and anaemia, thrombocytopaenia and renal failure at 33 weeks, was considered by treating physicians to be experiencing complications of her pregnancy. No gastrointestinal illness was reported by this case. However, VTEC serology requested by the Health Protection Branch indicated a high positive titre for antibodies against *E. coli* O157.

Identifying VTEC from clinical specimens requires specialised procedures and must be specifically requested

TABLE 2

NOTIFICATIONS OF HAEMOLYTIC URAEMIC SYNDROME BY AGE, SEX AND YEAR OF DISEASE ONSET, NSW, 1997-98 AND 1999

Age group (years)	Sex			
	1997-1998		1999*	
	Male	Female	Male	Female
0 to < 2	-	2	-	2
2 to < 4	2	-	-	-
8 to < 14	-	-	1	1
20 to < 40	-	-	1	2
40 and over	1	1	-	-
Total	3	3	2	5

* 1 January to 15 April 1999.
Source: Notifiable Diseases Database system, NSW Department of Health.

by the clinician. Specimens taken at the onset of gastrointestinal illness generally were not examined for VTEC. Stool samples or rectal swabs taken after HUS diagnosis, where VTEC identification was requested, were collected on all but case number seven. A presumptive finding of VTEC was made on one specimen; however, serotyping identified the organism as *E. coli* O6H1 (non-Shiga toxin-producing).

Epidemiological investigation

The case histories and subsequent investigations failed to reveal a common exposure among cases. All except case seven had eaten minced beef in one form or another in the 12 days prior to the onset of symptoms.

Investigation of the source of the beef was completed for five of the six cases who consumed minced beef. A common supplier was identified in two cases (cases one and two, who experienced onset of symptoms in mid-January and early February). This supplier and another, linked to case two only, sourced beef from three abattoirs. No other commonalities were found.

DISCUSSION

The most obvious caveat in the interpretation of the figures presented in Tables 1 and 2 is the small numbers of cases. Statistical analysis of historical data was not attempted because of the small numbers.

However, accepting this limitation and using 1997 and 1998 NDD figures as a baseline, it appears that there was a cluster of cases, in time, in early 1999. The age and sex distribution of the recent cases differ somewhat from that predicted by the literature and those seen in NSW in 1997 and 1998. However, several overseas investigations have also found a predominance of HUS in females.¹² No epidemiological links were identified among the cases. The

source tracing of the minced beef consumed by the majority of cases failed to identify strong common features.

Another possible explanation of the findings is that routine notification for HUS in NSW is incomplete. This cluster of cases may then be due to improved reporting rather than to an increase in actual cases. Further, because the diagnosis of HUS in this cluster of cases was primarily clinical, without confirmation of a causative organism, increased awareness of the disease may also have played a role through improved clinical diagnostic sensitivity for the condition.

Surveillance by the Australian Paediatric Surveillance Unit in 1994 and 1995, identified 12 cases of HUS in NSW, all in children aged less than 16 years.⁴ If this figure is accepted as the true occurrence, rather than an aberration, the number of cases observed to April 1999 may indeed be an unremarkable seasonal occurrence.

Even when there is strong suspicion that VTEC is the causative agent, identifying the organism or Shiga-like toxins may be difficult. Recovery of *E. coli* O157 from the stools of infected persons has been observed to fall from 90 to 33 per cent over several days.⁹ However, detection of these parameters (along with serology) must be included in strategies for diagnosis and therapy. It is also important in identifying clusters of cases for further investigation.^{4,13} The falling likelihood, with time, of identifying a positive stool culture reinforces the importance of collecting specimens for VTEC identification as soon as HUS is suspected.

Difficulty in identifying the causative agent notwithstanding, the potential for preventing further cases necessitates a thorough investigation of all cases. Where possible, all cases should have blood taken for serological confirmation of VTEC infection and a stool sample or rectal

swab taken to identify VTEC or Shiga-like toxins. Routine investigation should include a detailed 12-day food history and identification of other relevant exposures.

Where VTEC identification is required, clinicians are advised to forward clinical specimens (stool, rectal swab, and serum) to their local pathology laboratory, emphasising the diagnosis of HUS.

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