A cluster of cases of haemolytic uraemic syndrome in north Queensland associated with a novel Shiga-like toxin-producing *Escherichia coli*

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Introduction

The Tropical Public Health Unit (TPHU) in Townsville was alerted on 16 March 2004 to the possibility of a cluster of cases of haemolytic uraemic syndrome (HUS). This followed the admission of an 18-month-old female from a small regional hospital to a hospital in Townsville. At the time of this child's admission, a report was also made (from the same hospital in Townsville) of another case of HUS, from the same small regional town, two months previously. Very few details were initially available on the previous case.

The public health responses comprised epidemiological and environmental investigations. The implications of the delay in notification of the previous case (hereafter referred to as the first case) on these investigations are discussed. In addition, this report describes the organism causing the HUS as a type of *Escherichia coli* not previously known to elaborate Shiga-like toxin (SLT) in human populations.

Method

Initial investigations by the TPHU included a follow-up of both cases. Identification of the first case was made through interviews with staff of the regional hospital, then following the clinical referral pathway to locate the case. After identification and location of the first case (a 10-year-old male), telephone interviews were conducted with the parents of both children using a standard questionnaire. The questionnaire included questions on symptoms, details of hospitalisation, attendance at school and educational facilities, identification of unwell siblings, travel, environmental exposures, and a food history for 10 days preceding the onset of the illness. In addition, the case report required information on laboratory criteria for the diagnosis of HUS as well as information on clinical presentations.

On identification of the original case and completion of a case report, it was noted that an incomplete examination of faecal samples had been undertaken during the original admission. Therefore, repeat samples from the case were collected, with a specific request for examination for Shiga-like toxins and SLT-producing organisms. At the same time, identification of a recent dysenteric illness in a sibling of the first case was noted, and faecal samples were also collected for this child.

A site visit was made to a remote cattle property, identified as a possible source of infection in the first case. Environmental samples (water, cattle faeces, cattle feed) were taken and referred to the Queensland Health Scientific Services, Brisbane, for testing.

A face-to-face meeting was arranged between the mothers of both cases in order to facilitate identification of any links between the two families. At this point the working hypothesis, based on interviews conducted, was that the first case had acquired his infection on the cattle station visited, with person-to-person transmission leading to the second case.

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Results

Epidemiological investigation

Interviews and case report questionnaires were carried out with the two families involved. The first case of HUS, the 10-year-old male, became unwell on 28 January 2004 and the second, the 18-month-old female, on 9 March 2004. Faecal samples taken at the time of admission of the second case were positive for a Shiga-like toxin in both faeces and culture, and an entero-haemorrhagic *E. coli* (EHEC), or Shiga-like toxin producing *E. coli* (STEC), 086:H27 was eventually identified.

Faecal samples taken from the first case during his admission were not specifically tested for the presence of a SLT, with an infection with *Salmonella* the only organism identified. Repeat samples, taken two months after the onset of the illness, were positive for the same SLT (*stx*-2) and the same STEC (*E. coli* 086:H27) as in the 18-month-old child.

In addition, from the histories taken it was noted the 5-year-old sibling of the first case had had a dysenteric illness (consistent with a haemorrhagic colitis) in February 2004, and had been admitted to another Queensland Hospital. Unlike his sibling, he did not develop HUS; he also did not have a complete faecal examination at the time of his admission. A repeat faecal sample collected from this child in late March was SLT (*stx*-2) positive and *E. coli* 086:H27 was isolated.

Similarly, the 18-month-old child with HUS had a 6-year-old sibling who had a recent vague history of abdominal pain. A faecal sample from this child was also SLT (stx-2) and *E. coli* 086:H27 positive.

Food histories taken from all family members did not identify any obvious potentially contaminated food items, and did not reveal any specific food items common to the two families. The first family affected had spent most of the month before the onset of illness in the first case at a remote cattle station in North Queensland. This stay involved working on a daily basis in close contact with cattle on the property, and included drinking untreated water from the property's supply. The second family had no link with the property and did not report close contact with any domestic animals.

However the face-to-face meeting between parents of both families revealed a common link between the families. The two siblings (who had tested positive for the SLT and *E. coli* 086:H27) of the HUS cases both attended the same class in the same pre-school.

Following these investigations, the working hypothesis was further refined. It appeared likely that the STEC had been acquired at the remote cattle station by the first HUS case, who then transmitted it during household contact to his sibling (who in turn developed a dysenteric illness). Transmission then probably occurred to the second family through the pre-school contact, then through household contact on to the 18-month-old (who developed HUS) from her sibling.

Environmental sampling

A visit to the remote cattle station, where the first case's family had spent most of the month preceding his illness, was undertaken by the TPHU team. Interviews were conducted with the station owner, and his family, in an attempt to identify particular high risk activities (for example, contact with cattle, drinking untreated water) undertaken by the first case during his stay, and to identify any other illness in contacts. Environmental samples were collected for testing from areas on the property where the first case had either spent some time or engaged in potentially risky activities.

No other individuals with a recent enteric illness of any sort were identified on the station. Because of his contact with cattle at the property, faecal samples were collected from the father of the first case; which was positive for a SLT (*stx*-1), but not the same STEC type as seen in the cases.

Samples taken from a number of water supplies (bore water at cattle yard, house kitchen, and shed bore supply) were negative for the SLT and the organism under investigation. In addition, samples of cattle faeces, chicken and duck faeces, cattle feed (molasses and coconut husk meal) were all also negative for the SLT and organism under investigation. One of the cattle had SLT-1 and, like the father, was eliminated from this investigation.

Discussion

An association between infection with Shiga-like producing *Escherichia coli* (so named because of their similarity to toxins produced by *Shigella*) and the post diarrhoeal haemolytic uraemic syndrome (HUS) was first described in 1983.[1] HUS is defined as a clinical syndrome made up of acute renal injury, thrombocytopenia and microangiopathic haemolytic anaemia.[1,2] The organism most commonly associated with this illness is *E. coli* 0157.[1] The epidemiology of *E. coli* O157 is now well described, although the pathophysiology of HUS is less well understood.[2] Since the initial descriptions of *E. coli* O157, other serotypes of Shiga-like toxin producing *E. coli* (STEC) have been noted to cause similar disease in humans.[3]

Infections with STEC have been described associated with the ingestion of both food and water contaminated with the organisms. Contaminated meat, particularly ground beef used in hamburgers, has resulted in multiple outbreaks of disease.[2] In South Australia in 1995, a large outbreak of HUS was linked to the consumption of contaminated sausage.[4] In this outbreak, the organism concerned was *E. coli* 0111:NM and a total of 23 cases of HUS, and 30 cases of haemorrhagic colitis, were described. Of the 23 cases of HUS one child died. A recent study in South Australia, in contrast, noted that ingestion of berries was a significant risk factor in the development of sporadic STEC infection.[5] Similarly, outbreaks have been described in relation to contaminated fresh produce including, for example, radish sprouts, lettuce, alfalfa sprouts, and unpasteurised apple juice.[1]

Reservoirs of infection in animals, particularly in cattle, have also been well described.[1] In Australia; up to 118 serotypes of STEC have been found in healthy cattle[6] though the importance of the diversity of serotypes described, in terms of human disease, is not clear.

Outbreaks of STEC infections following exposure to buildings contaminated with the organism after an agricultural show and following exposures in petting zoos, highlight the importance of these animal reservoirs as a source of infection.[7] In the United Kingdom a strong association between sporadic infections with STEC and contact with a farm environment has been demonstrated.[8]

In the cases detailed above, infection with a novel EHEC/STEC (O86:H27) is described. This is the first report of an O86 serotype producing SLT in humans (personal communication, Denise Murphy). In the four cases with proven STEC (with the serotype O86:H27) infection, two developed HUS, the most serious complication of such an infection (STEC are estimated to result in HUS in 5–8% of cases[2]). Whether this high rate of disease is the result of enhanced virulence of the organism, or a consequence of undetected mild or asymptomatic cases, is not clear.

Despite the negative findings of the environmental sampling, it remains likely that infection with STEC in the first case was the result of exposure to the organism on the cattle property visited, with person-to-person transmission leading to subsequent cases. The rate of person-to-person transmission of STEC is likely to be high, as only low numbers of the organism are required to cause disease.[2] The majority of family contacts of cases of HUS, for example, have evidence of infection with STEC as indicated by antibodies to the toxin.[2]

The delay in the notification of the first case of HUS meant that there was a delay in the public health response. These delays were the result of incomplete microbiological investigations of the first case's faecal sample, and the lack of awareness among the case's clinicians that HUS is a notifiable disease in Queensland. The *Salmonella* Chester, a non Shiga-like toxin-producing organism, isolated from the first case was almost certainly an incidental finding and in the context of HUS, should have raised the suspicion of a concurrent undetected infection with a SLT-producing organism.[9] If the first case had been promptly notified it is possible that further person-to-person transmission of the implicated STEC might have been prevented.

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