Epidemic nephritis in Nova Serrana, Brazil

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Summary

Background Outbreaks of nephritis have been rare since the 1970s. From December, 1997, to July, 1998, 253 cases of acute nephritis were identified in Nova Serrana, Brazil. Seven patients required dialysis, and three patients died. We did a case-control study to investigate the cause of the outbreak.

Methods Using a matched cluster design, we examined seven recent patients, their family members (n=23), and members of neighbourhood-matched control households (n=22). We subsequently interviewed 50 patients and 50 matched controls about exposure to various dairy products. We also cultured dairy foods and took udder-swab and milk samples from cows.

Findings Throat cultures indicated that nephritis was associated with group C *Streptococcus equi* subspecies *zooepidemicus*, a cause of bovine mastitis. *S zooepidemicus* was detected in four of seven case households (six of 30 people) and no control households (p=0·09). Patients were more likely than matched controls to have consumed a locally produced cheese called *queijo fresco* (matched odds ratio 2·1, p=0·05). The nephritis attack rate was 4·5 per 1000 in Nova Serrana but 18 per 1000 in the village Quilombo do Gaia (p=0·003). The largest supplier of unpasteurised *queijo fresco* was a farm in Quilombo do Gaia. *S zooepidemicus* was not detected in food samples or in swabs collected from cows in August, 1998, although mastitis was evident among cows on the suspected farm. Throat cultures of the two women who prepared cheese on this farm yielded the outbreak strain of *S zooepidemicus*. After the cheese was removed from the distribution system, no further cases were reported.

Interpretation A large outbreak of glomerulonephritis was attributed to *S zooepidemicus* in unpasteurised cheese. This outbreak highlights the dangers of consuming unpasteurised dairy products and need for global efforts to promote food safety.

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Introduction

In the 1950s and 1960s, large outbreaks of post-streptococcal glomerulonephritis, which predominantly affected children, were reported in association with certain strains of group A *Streptococcus* spp.[1–4] Outbreaks of poststreptococcal nephritis are now rare.[5,6] This report describes the clinical and epidemiological features of a large epidemic of nephritis in Brazil in 1998.

Methods

Description of outbreak

From December, 1997, to July, 1998, 253 cases of glomerulonephritis were reported in the state of Minas Gerais, Brazil. Most patients resided in Nova Serrana (population 27 500). The clinical syndrome began with fever, headache, and myalgia, followed by cervical adenopathy. After 7–10 days, patients developed glomerulonephritis with oliguria, haematuria, generalised oedema, and hypertension. The local investigation by Directoria Regional de Saúde de Divinópolis indicated that most patients were over 20 years of age. In the previous year, the local nephrologists had seen no adults with nephritis. Histological examinations of renal biopsy samples were consistent with post-infectious glomerulonephritis. Serological assays for cytomegalovirus, Epstein-Barr virus, arboviruses (including dengue), coxsackieviruses B1-6, yellow fever, Rocio virus, Andes hantavirus, Puumula virus, and Sin Nombre virus were negative. No new cases were reported in June, 1998; however, in July, five new cases were reported and a new investigation was started.

Aetiology

To establish the cause of illness, we assessed seven recently identified patients, their household members, and neighbourhood-matched controls. We defined an outbreak-related case as nephritis with onset between December, 1997, and August, 1998, in residents of Minas Gerais with at least two of the following symptoms: systolic blood pressure higher than 140 mm Hg or diastolic blood pressure higher than 90 mm Hg for adults and blood pressure above the 95th percentile of the age-specific normal limit for children; oedema; and at least trace haematuria or 30 mg/dL proteinuria.

From July 18 to July 31, 1998, we assessed seven households of cases with illness onset from July 1 to July 28 (30 people, seven previously identified as patients) and seven neighbourhood-matched control households (22 people). Control households were located on the same neighbourhood street as case households and selected using random number generation. Two random numbers were generated in each case to determine the direction and distance from the case household. If no-one was home at that house we went to the next house. There were no refusals. For each member of a case or control household, we tested urine by a dipstick test, measured blood pressure, and collected swabs from the oropharynx and any skin lesions for microbiological culture.

We reviewed inpatient charts for patients at the Hospital São José in Nova Serrana with discharge codes for nephritis from January to July, 1998, and inpatient and outpatient charts for the same period for patients examined by nephrologists at Hospital São João de Deus in Divinópolis. Cases with onset after Aug 1, 1998, were identified prospectively from health department notification. We interviewed patients in the Quilombo do Gaia neighbourhood in the nearby town of São Gonçalo do Pará (figure 1).

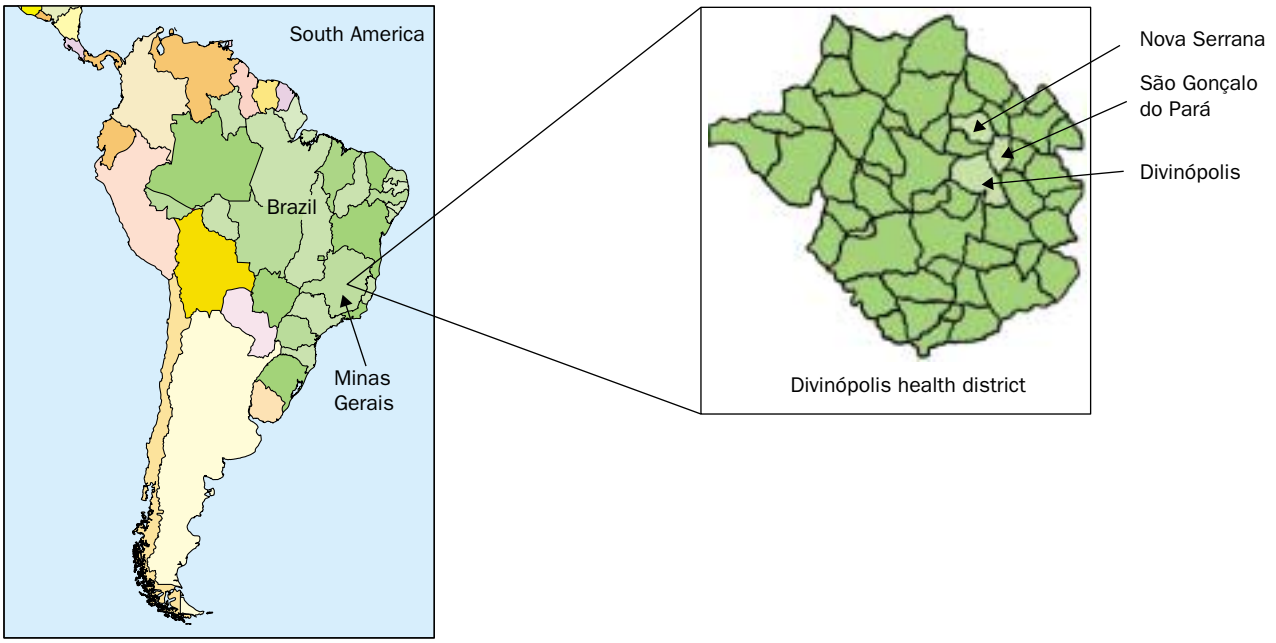

Figure 1: **Map of Divinópolis regional health district, Minas Gerais, Brazil**

Case-control study of risk factors

From Aug 15 to Aug 18, 1998, we carried out a telephone-based case-control study to determine risk factors for nephritis. For each patient with a telephone number, we sought a control matched for age (>15 years or <15 years) and sex, by systematic telephone dialing. We were aware that the organism suspected of being the cause of illness had previously been associated with unpasteurised milk products, so we focused our questions on exposure to animals and consumption of dairy products. We asked individuals about their food preferences during the previous 6 months. Trained personnel interviewed the participants in Portuguese.

Environmental and laboratory investigations

We collected available milk products, including yoghurt, milk, and cheese, from the homes of four recent patients and selected samples from supermarkets and from a local fair. We obtained information about origins of pasteurised and unpasteurised dairy products from the Nova Serrana Agriculture Secretary and local supermarkets.

Cultures and first-morning samples of milk were obtained from each cow on the two farms that supplied the supermarkets in the region (other farms sold their produce door-to-door). Oropharyngeal swabs from patients and udder swabs from all cows on the two suspect farms were sent to the US Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) for culture. All food samples and milk samples from farm X (n=38) and the neighbouring farm Z (n=14) were sent to the Instituto de Microbiologia, Universidade Federal do Rio de Janeiro, in Brazil.

Streptococci in the samples were identified at CDC by standard methods for species identification.[7] Pulsed-field gel electrophoresis was done on all *S zooepidemicus* isolates,[8] which were also tested at CDC for antibiotic susceptibility by the National Committee of Clinical Laboratory Standards broth microdilution method.[9]

Food samples were tested by transferring about 20 g of cheese from different parts of the sample to plastic zip bags containing 100 mL sterile 2% sodium citrate solution at 40°C. After manual emulsification of the samples, 10 mL suspension were inoculated into 5 mL Todd-Hewitt broth (BBL Microbiology Systems, Cockeysville, MD, USA) supplemented with nalidixic acid (15 mg/L) and colistin (10 mg/L). For milk and yoghurt samples, 10 mL were inoculated directly into 5 mL of the supplemented broth. Inoculated broth was incubated at 37°C for 18–24 h and then streaked onto trypticase soy 5% sheep-blood agar plates. Suspect streptococcal colonies were then identified by standard methods.[7]

A double selective-enrichment procedure was also used on 81 of 101 samples. After emulsification of the cheese as described, 50 mL of the suspension were inoculated into 100 mL supplemented broth. For milk samples, 50 mL were inoculated directly into 100 mL supplemented broth. After incubation at 37°C for 18–24 h, 1 mL of each culture was inoculated in 5 mL supplemented broth. After growth at 37°C, cultures were streaked onto blood-agar plates, and assessment for streptococcal colonies and identification of isolates were done.

Statistical analysis

For aetiology, data were recorded by the investigators and entered and validated in EpiInfo version 6.01. Individuals in case and control households were compared after controlling for clustering within a household and stratifying by each pair of matched households. To allow for the complex design and provide appropriate variance estimates, we analysed the data with Sudaan software (version 7.5). For the case-control study of risk factors for disease, matched univariate analysis was done.

Results

Of throat specimens collected from a total of 52 individuals in the household aetiology study, six yielded group C *Streptococcus* sp, confirmed as *S zooepidemicus*. The six isolates came from four of the seven previously known patients and from two children of one patient who yielded positive isolates. Although these two children were not previously recognised as having nephritis, both had haematuria, proteinuria, and hypertension. No *S zooepidemicus* was isolated from samples taken from the 21 symptom-free household contacts of patients or the 22 control-household members (p=0·09). Throat cultures from four additional people diagnosed with nephritis after completion of the household study identified *S zooepidemicus* in one individual. Renal biopsy tissue from all eight patients showed proliferative and crescentic glomerular disease of varying severity, consistent with post-streptococcal glomerulonephritis.

Of 152 possible cases of outbreak-related illness indicated by the diagnostic coding of the local physicians, 18 did not meet our strict case definition. Of the 134 confirmed cases (table 1), 99 (74%) occurred from February to April, 1998 (figure 2). The median age of

	Number affected	Attack rate (cases per 1000)
Adults	120 (90%)	4·3
Children <15 years	9 (7%)*	0·9
Females	86 (65%)	3·9
Males	48 (35%)	3·4
Region†		
Nova Serrana (population 27 500)	123 (92%)	4·5
Quilombo do Gaia (population 400)	7 (55)	18
Boa Vista‡ (population 944)	1 (<1%)	1
Divinópolis (population 171 600)	3 (2%)	0·17

*For five patients, no data on age were available. †p<0·0001. ‡Village on the outskirts of Nova Serrana.

Table 1: **Demography and attack rates of 134 nephritis patients**

patients was 37 years (range 6–81). Patients from Nova Serrana came from all neighbourhoods, and although no geographic clustering was evident, attack rates differed by area within the Divinópolis health district (table 1). Clinical and laboratory data from the patients with nephritis subsequently identified by physicians are shown in table 2. 97 (72%) patients were admitted to hospital, and the median length of hospital stay was 3 days (range 1–128).

Case-control study

Of 85 patients with telephone numbers, 33 could not be reached after systematic attempts, two patients refused to participate, and 50 (60%) were interviewed with matched controls. Patients were more likely than controls to eat *queijo fresco* and mozzarella from family farms, and brand A yoghurt (table 3). Of these foods, *queijo fresco* from family farms was the only food to have been consumed by most of the patients with nephritis. 36% of patients who ate *queijo fresco* reported buying it at a supermarket. Because mozzarella was commonly purchased in slices from the supermarket delicatessen counter, interviewees were often unaware of whether the mozzarella had been produced on a family farm. Individuals consumed a mean of four different milk products (range 0–9). The frequency of *queijo fresco* consumption was the same for patients and controls. Three individuals (two patients and one control) denied eating any dairy products on a regular basis.

Use of several different analgesics and non-steroidal anti-inflammatory drugs was associated with an increased risk of developing nephritis (data not shown). However, information on when patients took medications in relation to their illness onset was not available.

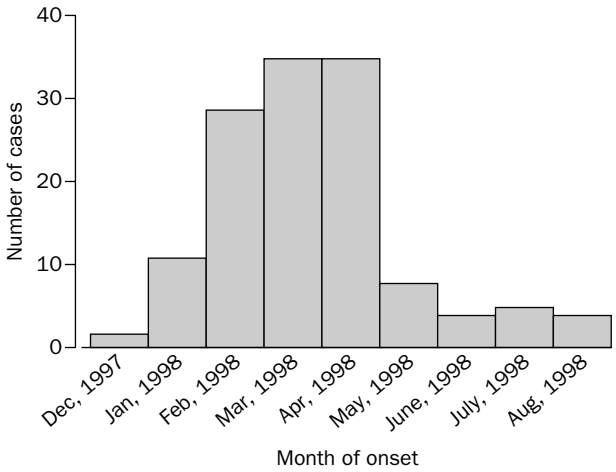

Figure 2: **Cases of nephritis in Minas Gerais, Brazil, by month of onset**

Finding	Number positive/patients for whom finding was reported in chart*
Dialysis	7/134 (5%)
Hypertensive encephalopathy (children)	2/9 (22%)
Death	3/134 (2%)
Oedema	124/126 (98%)
Cervical adenopathy	46/60 (77%)
Temperature >38·5°C†	12/122 (10%)
Creatinine >106 μmol/L	57/98 (58%)
Length of hospital stay >4 days	18/133 (14%)
Peak systolic blood pressure	
⩾140 mm Hg	103/125 (82%)
⩾170 mm Hg	40/125 (32%)
Peak diastolic blood pressure	
⩾90 mm Hg	106/125 (85%)
⩾110 mm Hg	32/125 (26%)
Low concentration of C3 complement	10/12 (83%)
Antistreptoptolysin O >200 Todd units	1/8 (12%)

*Denominators exclude patients for whom the finding was not recorded in the medical chart (either positive or negative) and thus is unknown. †Documented in the medical chart either during hospital stay or at time of outpatient visit.

Table 2: **Clinical and laboratory findings**

Trace-back investigation

We determined sources of locally produced *queijo fresco*, mozzarella, and brand A yoghurt distributed in Nova Serrana. Brand A yoghurt came from a large commercial source and was distributed throughout Minas Gerais. Mozzarella sold at one of the supermarket chains was from a small, family farm; mozzarella sold at the other supermarket chain was from two commercial sources that distribute widely in the area. *Queijo fresco* was regularly supplied to both supermarket chains by one family farm, farm X in Quilombo do Gaia, which was the largest supplier of *queijo fresco* in Nova Serrana. *Queijo fresco* was also supplied to one of the supermarket chains by a salesman who distributed cheeses from many small farms in the nearby area of Araxá. One supermarket chain also bought *queijo fresco* from a commercial source. Farm X also made *requeijão*, which was prepared from boiled milk.

One patient who lived in the city of Divinópolis had never travelled to Nova Serrana or Quilombo do Gaia. However, she had received a gift of cheeses bought directly from farm X. She consumed these cheeses shortly before becoming ill. Three people who worked on farm X and four people from Quilombo do Gaia, who regularly ate the

	Patients exposed	Controls exposed	Matched odds ratio (95% CI)	p
Queijo fresco				
Family farm	32 (64%)	21 (42%)	2·10 (0·99–4·46)	0·05
Any	33 (66%)	25 (50%)	1·72 (0·82–3·63)	0·15
Mozzarella				
Family farm	18 (37%)	8 (17%)	3·25 (1·06–9·97)	0·04
Any	35 (71%)	29 (60%)	2·20 (0·76–6·33)	0·14
Yoghurt				
Family farm	5 (10%)	2 (4%)	2·50 (0·49–12·89)	0·27
Brand A	10 (21%)	2 (4%)	5·00 (1·09–22·8)	0·04
Brand C	7 (14%)	3 (6%)	3·00 (0·60–14·86)	0·18
Brand D	15 (31%)	12 (24%)	1·40 (0·62–3·15)	0·42
Requeijão				
Family farm	24 (48%)	14 (29%)	1·90 (0·88–4·09)	0·10
Brand B	16 (32%)	7 (15%)	2·40 (0·85–6·81)	0·10
Any	29 (58%)	24 (50%)	1·23 (0·59–2·56)	0·58
Milk				
Family farm	23 (47%)	21 (42%)	1·17 (0·54–2·52)	0·70
Brand E	23 (46%)	20 (40%)	1·23 (0·59–2·56)	0·58
Any	40 (80%)	39 (78%)	1·10 (0·47–2·59)	0·83

Denominators for number of patients and controls vary from 48 to 50 depending on the number of respondents.

Table 3: **Food exposure among patients with nephritis and age-matched neighbourhood controls**

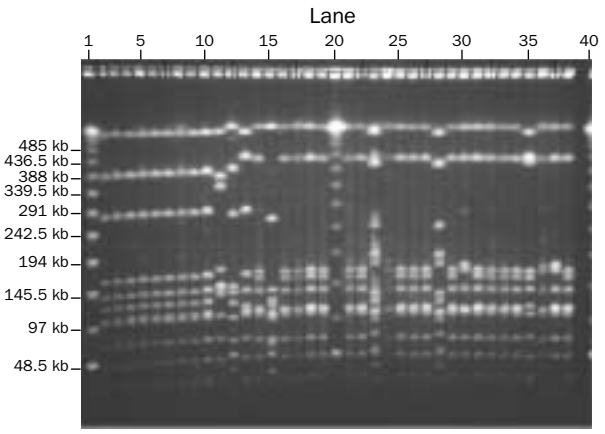

Figure 3: **Pulsed-field gel electrophoresis of isolates**
Lanes 1, 20, and 40, lambda ladder (size markers); lanes 2–10, outbreak isolates (this study); lane 11, animal group C *Streptococcus* sp; lane 12, Romania, 1968, human isolate; lane 13, England, 1982, human isolate; lane 14, New Mexico, 1983, human isolate; lane 15, ATCC 42079, *S equi zooepidemicus*; lanes 16–38, New Mexico, 1983, human isolates; lane 39, no sample.

cheese that the farm produced, were reported to have had nephritis as early as December, 1997, and January, 1998.

In August, 1998, *S zooepidemicus* was identified in throat cultures from three individuals associated with farm X: two of seven extended family members and one of three farm workers (not related to the family that owned the farm). Two of the three *S zooepidemicus* carriers were people who prepared the cheese. One of the foodhandlers had symptoms of nephritis in December, 1997; the other denied having symptoms of nephritis.

Of the 17 food samples (including ten of *queijo fresco*) collected from case households, none contained *S zooepidemicus*. Of 31 samples of cheese (20 of which were *queijo fresco*) from supermarkets and the local fair, including five cheese samples from farm X, and 52 samples of first-morning milk from cows, 23 yielded gram-positive, catalase-negative, group B haemolytic cocci. However, none of these were identified as *S zooepidemicus*.

Pulsed-field gel electrophoresis testing of all *S zooepidemicus* isolates from the outbreak revealed a single pattern that differed from historical isolates (figure 3). *S zooepidemicus* isolates were resistant to clindamycin (median inhibitory concentration 1·0), but were sensitive to all other agents tested.

Farm X had 38 dairy cows that grazed freely with horses. During the team's investigation visit in August, 1998, one cow had acute mastitis and two had chronic mastitis. No records about previous episodes of mastitis on the farm were available. Farmer X had been purchasing milk from nearby farm Z, which had 14 cows, since 1997. The milk from both farms was regularly used to make *queijo fresco* and *requeijão*, which were then sold to local supermarkets or directly to consumers at local fairs. Milking was done manually by farm personnel. Two workers on farm X prepared the cheese. The *queijo fresco* was made by mixing milk with a bovine coagulant containing 50% pig pepsin and allowing the mixture to sit for 40–60 min at room temperature until it coagulated. Excess liquid was removed and the cheese was placed in molds for refrigeration. The cheeses were then placed in bags for distribution. Farm X produced about 300 L milk and 40–45 kg cheese each day.

Local health authorities halted sale of the *queijo fresco* from farm X on Sept 1, 1998, and destroyed produce that was already in the retail distribution system. Farm X food handlers from whom *S zooepidemicus* was isolated were treated with penicillin, and repeat cultures were done. No further cases of nephritis were detected through December, 1999.

Discussion

S equi subspecies *zooepidemicus* is rare in human beings,[10,11] but is a well-known cause of disease in cows and horses.[12,13] In human beings, *S zooepidemicus* can cause post-streptococcal glomerulonephritis[14] and other syndromes.[14–21] Four previous outbreaks attributed to *S zooepidemicus* have been reported, with illness presenting as post-streptococcal glomerulonephritis in two[22,23] and as sepsis or meningitis in the other two.[24,25] Consumption of unpasteurised milk or milk products was implicated or suspected as the source of the infection in all four outbreaks. In one outbreak of sepsis, *S zooepidemicus* was isolated from the milk of three cows and from cheese samples.[24]

Unlike the more common post-streptococcal glomerulonephritis attributed to group A streptococcus, which affects children, outbreaks of glomerulonephritis due to *S zooepidemicus* have predominately affected adults.[22,23] There is no explanation for the unusual age distribution seen in glomerulonephritis caused by *S zooepidemicus*. We doubt that a difference in patterns of food consumption accounts for the higher attack rates among adults, because *queijo fresco* was popular among all ages (data not shown). The age distribution might represent a diagnostic bias if children with mild symptoms were less likely to come to medical attention. Host factors may also account for a difference in risk.

Of the foods associated with increased risk of nephritis in our case-control study, *queijo fresco* was consumed by most patients. Brand A yoghurt and locally produced mozzarella had higher odds ratios, but fewer than half the affected patients reported consuming these products. Because the outbreak lasted over 8 months, we asked the individuals about their regular food habits rather than the foods they had eaten during a specific period. Intermittent contamination of *queijo fresco* probably occurred; thus our method may have led to misclassification of exposures for the relevant period of risk for a given patient. Determination of the distribution sources of all foods associated with disease in the case-control study showed that only *queijo fresco* from farm X was widely distributed in Nova Serrana but not elsewhere in the state of Minas Gerais. There were many suppliers of mozzarella and brand A yoghurt was distributed throughout the state, so these products were unlikely to have caused a localised outbreak. Although food samples, first-morning milk, and swabs from cows on farm X did not yield *S zooepidemicus*, the high attack rate of clinical illness in Quilombo do Gaia, the history of direct purchase of food from farmer X by a patient residing in Divinópolis, and the identification of the outbreak strain of *S zooepidemicus* in samples from two cheesemakers support the conclusion that *queijo fresco* from farm X caused a continuing common-source outbreak of nephritis in Nova Serrana.

The cheese implicated in this investigation was prepared without boiling or other pasteurisation steps. The consumption of foods from unpasteurised milk products is intrinsically risky.[26] If present in raw milk from animals with clinical or subclinical mastitis, pathogens can easily enter the food distribution system. To prevent a recurrence of

this outbreak or illness caused by other zoonotic organisms, adequate boiling or pasteurisation of raw milk is needed. In regions where it is common for people to buy milk directly from farms or to prepare their own dairy products, heightened awareness of the dangers of consuming raw milk and of the importance of boiling and pasteurisation is necessary. Even with adequate pasteurisation, careful attention to avoid contamination after pasteurisation is also required.

The outbreak peaked in March, 1998. The subsequent decline in identified cases may have resulted from less frequent contamination of cheese, a change in hospital-admission practices for nephritis, less intensive case-finding, or an exhaustion of susceptible patients among consumers of *queijo fresco*. We speculate that the higher attack rate in February to April was caused by *S zooepidemicus* mastitis among cows on the implicated farm, which led to frequent contamination of the milk during that period. The relatively few cases that occurred later may be attributed to intermittent contamination during food preparation by the persistently colonised cheesemakers. The spread of *S zooepidemicus* by foodhandlers with pharyngeal colonisation is a possibility supported by reports of group A streptococcal outbreaks traced to foodhandlers who carried the organism in their throats or on their hands.[27–29] However, *S zooepidemicus* is difficult to culture from food. In an outbreak caused by *S zooepidemicus* in England, first morning milk was collected for 14 consecutive days before *S zooepidemicus* was isolated.[25] We may not have sampled enough milk to detect an organism that was intermittently present.

We estimated the minimum number of cases attributable to *S zooepidemicus* in this outbreak. Our case ascertainment methods would not have identified most illness that did not result in hospital admission or referral to a nephrologist. During our investigation, we identified two cases of unrecognised illness in case-household members (4% of our sample). During our telephone case-control study, we excluded potential controls who had symptoms consistent with outbreak-related disease. We identified one such individual during the telephone survey (2% of potential controls). Therefore, outbreak-related illness was probably much more common than we reported.

Contributors

Sharon Balter did the field investigation, analysed the data, and was responsible for drafting and writing the paper. Andrea Benin did the field investigation and analysed the data. Sergio Wynton Lima Pinto did the initial local field work on patients with renal disease and helped to design the study. Gladstone Alvim Grippe did the initial local field work in Nova Serrana and assisted in the design of the study. Expedito Luna did the initial field investigation, coordinated from a national level in Brazil, and assisted in the design of the study. Lucia Martins Texeira did the laboratory work involving the food samples. Delois Jackson, Leslye Leclaire, and John Elliott did the laboratory work involving human and animal samples. Richard Facklam helped to design the study and directed the laboratory efforts. Anne Schuchat was in charge of the investigation. All investigators helped to write the paper.

References

1 Kleinman H. Epidemic acute glomerulonephritis at Red Lake. *Minnesota Med* 1954; **37:** 479–83.

2 Poon-King T, Mohammed I, Cox R, et al. Recurrent epidemic nephritis in South Trinidad. *N Engl J Med* 1967; **277:** 728–33.

3 Kodama T, Miyamoto Y, Kotake I, Ochiai S. Epidemic nephritis in Japan. *Yokohama Med Bull* 1958; **9:** 105–18.

4 Stetson CA, Krause RM, Perry WD, Kohen RJ. Epidemic nephritis. *Trans Assoc Am Phys* 1954; lxvii: 276–82.

5 Roy S III, Stapleton FB. Changing perspectives in children hospitalized with poststreptococcal acute glomerulonephritis. *Pediatr Nephrol* 1990; **4:** 585–88.

6 Yap HK, Chia KS, Murugasu B, et al. Acute glomerulonephritis: changing patterns in Singapore children. *Pediatr Nephrol* 1990; **4:** 482–84.

7 Ruoff KL. Streptococcus. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of clinical microbiology, sixth edn. Washington, DC: American Society for Microbiology, 1995: 299–307.

8 Elliott JA, Farmer KD, Facklam RR. Sudden increase in isolation of group B streptococci, serotype V, not due to the emergence of a new pulsed-field gel electrophoresis. *J Clin Microbiol* 1998; **36:** 2115–16.

9 National Committee on Clinical Laboratory Standards. Performance standards for antimicrobial susceptibility testing, eighth informational supplement (M100-S8, 70-71). Pennsylvania: National Committee for Clinical Laboratory Standards, 1998.

10 Vieira VV, Teixeira LM, Zahner V, et al. Genetic relationships among the different phenotypes of *Streptococcus dysgalactiae* strains. *Int J Systematic Bacteriol* 1998; **48:** 1231–43.

11 Vandamme P, Pot B, Falsen E, Kersters K, Devriese LA. Taxonomic study of Lancefield streptococcal groups C, G, and L (*Streptococcus dysgalactiae*) and proposal of *S dysgalactiae* subsp. *equisimilis* subsp. *nov*. *Int J Systematic Bacteriol* 1996; **46:** 774–81.

12 Bryans JT, Moore BO. Group C streptococcal infections of the horse. In: Wannamaker LW, Matsen JM, eds. Streptococci and streptococcal diseases: recognition, understanding and management. New York: Academic Press, 1972: 327–37.

13 Woolcock JB. Epidemiology of equine streptococci. *Res Vet Sci* 1975; **18:** 113–14.

14 Barham M, Ljunggren A, McIntyre M. Human infection with *Streptococcus zooepidemicus* (Lancefield group C): three case reports. *Epidemiol Infect* 1987; **98:** 183–90.

15 Ferrandiere M, Cattier B, Dequin PF, Hazouard E, Legras A, Perrotin D. Septicemia and meningitis due to *Streptococcus zooepidemicus*. *Eur J Clin Microbiol Infect Dis* 1998; **17:** 290–91.

16 McKeage MJ, Humble M, Morrison RBI. *Streptococcus zooepidemicus* cellulitis and bacteraemia in a renal transplant recipient. *Aust NZ J Med* 1990; **20:** 177–78.

17 Rose HD, Allen JR, Witte G. *Streptococcus zooepidemicus* (group C) pneumonia in a human. *J Clin Microbiol* 1980; **11:** 76–78.

18 Collazos J, Echevarria MJ, Ayarza R, Miguel J. *Streptococcus zooepidemicus* septic arthritis: case report and review of group C streptococcal arthritis. *Clin Infect Dis* 1992; **15:** 744–46.

19 Anonymous. Unpasteurised milk and *Streptococcus zooepidemicus*. *CDR Wkly* 1994; **4:** 241.

20 Martinez-Muengas F, Inclan GM, Pastor A, et al. Endocarditis due to *Streptococcus zooepidemicus*. *Can Med Assoc J* 1982; **127:** 13.

21 Francis AJ, Graeme R, Nimmo A, Galanis V, Nuttal N. Investigation of milk-borne *Streptococcus zooepidemicus* infection associated with glomerulonephritis in Australia. *Aust J Infect* 1993; **27:** 317–23.

22 Barham M, Thorton TJ, Lange K. Nephritis caused by *Streptococcus zooepidemicus* (Lancefield group C). *Lancet* 1983; i: 945–48.

23 Duca E, Teodorovici G, Radu C, et al. A new nephritogenic streptococcus. *J Hyg* 1969; **67:** 691–98.

24 CDC. Group C streptococcal infections associated with eating homemade cheese, New Mexico. *MMWR Morb Mortal Wkly Rep* 1983; **32:** 510–16.

25 Edwards AT, Roulson M, Ironside MJ. A milk-borne outbreak of serious infection due to *Streptococcus zooepidemicus* (Lancefield group C). *Epidemiol Infect* 1988; **101:** 43–51.

26 Headrick ML, Korangy S, Bean NH, et al. The epidemiology of raw milk: associated foodborne disease outbreaks reported in the United States, 1973 through 1992. *Am J Public Health* 1998; **88:** 1219–21.

27 Lossos IS, Felenstein I, Breuer R, Engelhard D. Foodborne outbreak of group A β-hemolytic streptococcal pharyngitis. *Arch Intern Med* 1992; **152:** 853–55.

28 Bar-Dayan Y, Klainbaum Y, Shemer J. Foodborne outbreak of streptococcal pharyngitis in an Israeli airforce base. *Scand J Infect Dis* 1996; *28:* 563–66.

29 Gallo G, Berzero R, Cattai N, Recchia S, Orefici G. An outbreak of group A foodborne streptococcal pharyngitis. *Eur J Epidemiol* 1992; **8:** 292–97.