

## **A milk-borne outbreak of serious infection due to *Streptococcus zooepidemicus* (Lancefield Group C)**

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### SUMMARY

An outbreak of infection due to *Streptococcus zooepidemicus* (Lancefield Group C) is described. At least 11 patients were affected and the infection was responsible for, or contributed to, the deaths of seven of these. Clinical features included septicaemia, meningitis and endocarditis. The source of infection was unpasteurized milk from a dairy herd with mild intermittent mastitis.

### INTRODUCTION

Of the four recognized species of Lancefield Group C streptococci only one, *Streptococcus equisimilis* is regularly found in man; the others are primarily animal pathogens and have only occasionally been reported as causing disease in humans. However, isolated cases and, more recently, small outbreaks of severe infection due to *S. zooepidemicus* have been reported (Barnham, Thornton & Lange, 1983; Ghoneim & Cooke, 1980; Report, 1983). We report one more such outbreak, the largest and most serious yet seen in England, in which the vehicle of infection was unpasteurized cows' milk.

### THE OUTBREAK

*S. zooepidemicus* was isolated from 11 in-patients admitted between 31 March and 4 June 1984 to the two hospitals in a district in West Yorkshire. The organism was isolated from blood culture, CSF or mycotic aneurysm; nine of the isolates were from patients admitted before the end of April (see Table 1). Seven patients died, though the infection was not completely responsible in all of them. Nine of the patients were older than 70 years, one was aged 52 years and another was an infant of 1 day, born prematurely. A further fatal case was reported to us from a neighbouring district. The details of each patient are as follows:

*Case 1.* On 31 March a male aged 73 years was admitted to hospital stuporose, having been acutely ill for 1 week with a history of 'feeling the cold' for 5 weeks.

Table 1. *Details of infected patients*

Patient	Date of admission	Sex	Age (years)	Main disease features	Source of isolate	Outcome
1	31. 3. 84	M	73	Septicaemia, meningitis	Blood and CSF	Died
2	2. 4. 84	F	52	Septicaemia, bacterial endocarditis	Blood	Discharged
3	14. 4. 84	F	74	Septicaemia	Blood	Died
4	16. 4. 84	M	74	Septicaemia, mycotic aneurysm	Mycotic aneurysm	Discharged
5	17. 4. 84	M	1 day	Septicaemia	Lung and CSF	Died
6	20. 4. 84	M	72	Septicaemia	Blood	Died
7	27. 4. 84	M	71	Septicaemia	Blood	Died
8	27. 4. 84	M	75	Septicaemia	Blood	Discharged
9	29. 4. 84	M	73	Septicaemia, bacterial endocarditis, meningitis	Blood and CSF	Died
10	2. 5. 84	M	71	Septicaemia, meningitis	Blood and CSF	Discharged
11	4. 6. 84	M	79	Septicaemia, bacterial endocarditis	Blood	Died
12	12. 5. 84	F	80	Septicaemia, meningitis	Blood	Died

He died within 48 h of admission and the clinical diagnosis of septicaemia and pyogenic meningitis was confirmed by culture of *S. zooepidemicus* from blood and CSF. Permission for autopsy was not obtained.

*Case 2.* Two days later a female aged 52 years was admitted with pyrexia and a history of a 'flu-like illness for 3 weeks which had been treated with antibiotics by her general practitioner. A mitral valve lesion was detected and a clinical diagnosis of bacterial endocarditis confirmed by growth of *S. zooepidemicus* from blood. She was treated with penicillin and a cephalosporin, and after 4 weeks discharged from hospital. Although evidence of valvular involvement disappeared following treatment the patient has residual myocardial damage and impairment of peripheral circulation in one arm following an embolic episode in the acute illness. The patient's husband had been ill with a severe febrile illness at about the same time.

*Case 3.* On 14 April a female aged 74 years was admitted with fever and 'collapse'. *S. zooepidemicus* was cultured from blood the following day. The illness eventually responded after 4 weeks to intensive therapy with penicillin and a cephalosporin. Four months later, she died suddenly and at autopsy, death was found to be due to a large cardiac aneurysm complicating a myocardial infarct. The appearance of the infarct suggested that it had coincided with the febrile illness but culture from the large amounts of mural thrombus in the aneurysm were negative for *S. zooepidemicus*.

*Case 4.* On 16 April *S. zooepidemicus* was isolated from a swab taken from a mycotic aneurysm in a vein graft in a femoral artery of a male aged 74 years. The patient had been re-admitted for vascular surgery 2 days after discharge from a medical ward where he had been successfully treated for a severe febrile illness with penicillin and a cephalosporin. At that time, no blood culture had been performed. Following surgical replacement of the mycotic aneurysm by further graft, the patient recovered.

*Case 5.* On 17 April, an autopsy was performed on a 23-hour-old male infant of 32 weeks gestation. Although the cause of death was considered to be respiratory distress due to prematurity, culture of body organs produced a growth of *S. zooepidemicus*. The mother, father and brother of this infant had a febrile illness before the mother was admitted to hospital and her illness was thought to have precipitated premature labour. These illnesses were not investigated but may have been caused by *S. zooepidemicus* infection.

*Case 6.* On 20 April, a man aged 72 years admitted to a psychiatric unit because of exacerbation of depression and confusion was found to have a fever. There was no clinical evidence of meningitis. He was transferred to a medical ward. Blood culture produced a growth of *S. zooepidemicus*. The fever resolved after treatment with penicillin, a cephalosporin and other wide-spectrum antibiotics, but his general condition remained poor and he died 4 months later of cerebro-vascular disease and myocardial ischaemia. At autopsy, no bacterial growth was obtained but there was evidence of recent endocarditis with peripheral embolism and it was considered that the septicaemia had accelerated the decline in his health.

*Case 7.* A male aged 71 years was admitted to hospital on 27 April with clinical deep vein thrombosis and a 4-week history of backache. He had a fever and blood culture yielded *S. zooepidemicus*. While being treated with antibiotics, he died

suddenly and the cause of death was certified as massive pulmonary embolism. Permission for autopsy was not obtained.

*Case 8.* Also on 27 April, a male aged 75 years was admitted with a 4-week history of rigors. *S. zooepidemicus* was grown from blood. After a protracted illness, he responded to prolonged antibiotic therapy which included penicillin and a cephalosporin.

*Case 9.* A male aged 73 years was admitted on 21 April with a suspected leaking abdominal aortic aneurysm. He had pyrexia and evidence of ischaemic heart disease, became increasingly confused, and eventually developed meningitis. Lumbar puncture confirmed presence of pyogenic meningitis and *S. zooepidemicus* was cultured from blood and CSF. He did not respond to treatment and died. At autopsy the cause of death was found to be ruptured abdominal aortic aneurysm, but meningitis and bacterial endocarditis were confirmed. The organism was isolated from the valve vegetations and, although it was not isolated from the aorta, it seems possible that the aortic aneurysm was due to or affected by the septicaemia as described by Perkins & McRae (1974).

*Case 10.* On 2 May, a male aged 71 years was admitted to hospital with a deep vein thrombosis, having felt 'off colour' with intermittent pyrexia for 2 weeks. He became increasingly confused, and on 15 May acute meningitis was confirmed by lumbar puncture; *S. zooepidemicus* was grown from blood and CSF. He recovered after treatment with wide-spectrum antibiotics and returned home after 6 weeks in hospital.

*Case 11.* On 4 June, a male aged 79 years was admitted to hospital with septicaemia, and *S. zooepidemicus* was isolated from blood culture on 8 June. His illness began on 16 April with a 'flu-like illness which affected two other members of his family at the same time. His fever persisted and was complicated by chest infection which failed to respond to a 5 day course of Augmentin prescribed by his general practitioner. In hospital antibiotic treatment with cephalosporins, ampicillin and metronidazole produced no improvement and he died on 19 June when autopsy confirmed the presence of septicaemia associated with bacterial endocarditis.

*Case 12.* Colleagues in an adjacent Health District 20 miles away informed us of an elderly woman aged 80 years who had died on 13 May of meningitis and septicaemia. She died 14 h after admission to hospital but blood culture yielded a growth of haemolytic streptococcus Group C not fully identified as *S. zooepidemicus*. Because of the clinical and bacteriological similarities, relatives of the deceased were questioned and it was found that, on a visit to relatives early in April, she spent a few days in a flat which received a regular supply of unpasteurized milk (from farm A).

### *Treatment*

Most of the patients were treated with intravenous cefotaxime 1 g 6-hourly supplemented by intramuscular benzyl penicillin 3 mega units 6-hourly when the results of cultures became known. In those surviving, the cephalosporin was discontinued after 2 weeks but oral penicillin continued for up to 1 month, particularly in those with evidence of endocarditis. In patients not moribund on admission, meningitis seemed to respond well to this treatment and blood cultures

were quickly rendered sterile. However, in endocarditis and aneurysm where bacteria were probably shielded within valve vegetations and mural thrombi, the infection proved more difficult to eradicate.

#### *Management of the outbreak*

The investigation was undertaken by a team consisting of the consultant pathologist (hospital control of infection officer), the chief environmental health officer, the community physician (environmental health) and the divisional veterinary officer. The team communicated or met daily and visited two local farms (A and B) on several occasions. Liaison was made with the regional Public Health Laboratory and with the PHLS Communicable Disease Surveillance Centre. Isolates were sent to the Streptococcus Reference Laboratory of the Central Public Health Laboratory, Colindale for full identification. General practitioners in the district were informed by letter of the situation and doctors responsible for hospital admissions were alerted to elderly patients presenting with characteristic symptoms, but no further cases (except case 12) were reported. The outbreak caused great interest from the 'media' and enquiries were dealt with mainly by the chief environmental health officer and the community physician.

#### *Investigation of the outbreak*

The investigation started with a search for a common causative factor. Patients 1–9 and 11 lived within an area of about one and a half mile radius and all 11 victims drank unpasteurized green-top bottled milk.

Although two retailers supplied the milk to patients 1–9 and 11 the supply came from one dairy farm (farm A) with a herd of 17 cows. Milk from the cows was pooled, filtered and bottled on the farm after cooling. From 3 May Environmental Health officers obtained daily samples of milk, specimens from milk filters and swabs from farm environment and workers. These were persistently negative until 18 May when *S. zooepidemicus* was isolated from a bottle of raw milk offered for sale on 14 May and originating from farm A.

Patient 10 also drank unpasteurized milk but apparently from a different supplier. This finding led to an intensive investigation of milk, environment and workers in a larger and more modern dairy farm in the area with a herd of 60 cows (farm B). Occasionally, this farm would supply milk to farm A, but always in pasteurized (bottled) form. This made farm B an unlikely source of the infection, supported by the evidence that all the previous cases had been in the distribution area of farm A with none observed among consumers of milk from farm B. Eventually, relatives of patient 10 confirmed that occasionally their green-top bottles would carry the name of a different farm stamped on the foil. It was then established that milk roundsmen from the two farms would meet in the course of their deliveries and sometimes exchange bottles to make good shortages. In this way, unpasteurized milk from farm A could certainly have been consumed by this patient on more than one occasion.

#### *Veterinary investigations*

Following the isolation of *S. zooepidemicus* from the bottled raw milk, veterinary officers of the Ministry of Agriculture visited farms A and B and took milk samples

for culture from individual cows. The organism was not isolated from samples or animals on farm B. Although the 17 cows in the herd of farm A appeared healthy, *S. zooepidemicus* was recovered from one cow, from one quarter of the udder. Subsequently, two other healthy cows were found to be excreting the organism intermittently in their milk. The animals were considered to be suffering from a subclinical mastitis and were slaughtered outside the area. Unfortunately, material saved from the udders was inadequate for histological and bacteriological examination. The source of infection in the cows was unclear but an indistinguishable isolate of *S. zooepidemicus* (see Barnham *et al.* 1987; Skjold *et al.* 1987) was recovered from the vaginal swab of a mare, the only horse on the farm; it was not known to have grazed in the same field as the milk herd.

#### *Control measures*

On the day (18 May) that the Regional Public Health Laboratory reported a positive culture from a bottle of milk originating from farm A, a heat treatment order of indefinite duration was served on the farmer, although no milk was subsequently sold for human consumption and the farmer has since ceased milk production. Following this no further cases were identified; although patient 11 was admitted on 4 June, the onset of his illness clearly preceded the cessation of milk distribution from farm A. Following local press publicity of the incident, there has been a 10–30% drop in demand for raw milk and a greater number of queries concerning installation of on-farm pasteurization plants.

#### DISCUSSION

There are four identified species of Lancefield's Group C streptococci; *S. equi*, *S. dysgalactiae*, *S. equisimilis* and *S. zooepidemicus*. The host range varies among members of the species *S. equi* appears to be restricted to equids and is the commonest cause of equine strangles, and *S. dysgalactiae* is a pathogen in lambs and in the mammary gland of the cow.

*S. equisimilis* has been isolated from carriage and infection, particularly in pigs and humans. *S. zooepidemicus* is commonly found in a number of animals, particularly the horse, and is an occasional cause of mastitis in cows.

Until recently, only very few cases of human infection have been reported with *S. zooepidemicus*. The fact that until recently only a few diagnostic laboratories have identified the species in Group C streptococcal infections may explain this. All cultures of the organisms isolated from the first 11 cases were  $\beta$ -haemolytic streptococcus Group C (*S. zooepidemicus*) with an AP120 strep. profile 4463607. These cultural characteristics were confirmed by the Streptococcus Reference Laboratory, Colindale, and found identical to those of the streptococci isolated from milk specimens.

The cultural and physiological characteristics of the isolates are discussed by Barnham *et al.* 1987 and Skjold *et al.* 1987 who confirmed the identical nature of the streptococci from the animal and human sources by bacteriocin, bacteriophage typing and DNA fingerprinting.

The streptococcus was sensitive to penicillin, co-trimoxazole, erythromycin and cephalosporins. The presenting clinical features were those of septicaemia,

bacterial endocarditis, meningitis, deep vein thrombophlebitis and mycotic aneurysm. It is probably significant that, with the exception of the premature infant and one adult aged 52 years, all the other confirmed cases including the seven adult deaths were over the age of 70 years. The full extent of the outbreak remains unknown, as no active case finding was undertaken. It appears that any young people affected experienced only a short 'flu-like illness which would not have come to the notice of general practitioners, particularly since the first cases coincided with the usual febrile illnesses of late winter and early spring. Since the milk from the herd was pooled, it seems likely that many bottles of milk were infected.

None of the cases presented features of post-streptococcal glomerulonephritis as described by Barnham, Thornton & Lange (1983) and immunological staining of the kidneys from three cases showed no evidence of immune complex mediated glomerulonephritis.

The severity of the illness in our cases was not apparently related to the amount of milk consumed. While some patients drank large amounts of milk, others only added it to tea, coffee or cereals. The characteristics of the infection are similar to those reported by Ghoneim & Cooke (1980) which were eventually considered to be due to consumption of unpasteurized milk (Barnham, Thornton & Lange, 1983). The most recent outbreak with similar characteristics occurred in New Mexico (Report, 1983) with 16 cases of infection and 2 deaths due to consumption of cheese made from unpasteurized cows milk.

Since 1963, only ten single cases of infection due to *S. zooepidemicus* (Perkins & McRae, 1974; Report, 1983; Hazenberg, 1963; Köhler & Cederberg, 1976; Rose, Allen & Witte, 1980; Low, Young & Harding, 1980; Martinez-Luengos *et al.* 1982; Mulder & Zanen, 1984; Barnham, Ljunggren & McIntyre, 1987) and four small outbreaks (Ghoneim & Cooke, 1980; Report, 1983; Barnham, Thornton & Lange, 1983; Duca *et al.* 1969) have been reported. In two outbreaks and one solitary case (Barnham, Ljunggren & McIntyre, 1987; Barnham, Thornton & Lange, 1983; Duca *et al.* 1969) the clinical features were of post-streptococcal glomerulonephritis. In the other cases, the features were of septicaemia often with meningitis and bacterial endocarditis, as in the outbreak described here. Most reported infections were associated with close domestic animal contact, particularly horses, or with the consumption of unpasteurized cows milk.

This outbreak highlights again the danger of consumption of unpasteurized cows milk which is still offered for sale in England and Wales. It has been pointed out (Howie, 1985) that although only 3% of milk sold in England and Wales is unpasteurized, half of this is produced in the North of England, where 70% of milk-borne infection outbreaks were reported in 1983–4. The unsuitability of the northern Pennine terrain for beef and cereal production has encouraged small farmers to produce farm-bottle milk and this has promoted consumption of raw cows milk by consumers who are sometimes unaware that the product is unpasteurized. An increased interest in health foods has also made the public more receptive to unpasteurized cows milk in the mistaken belief that it is healthier. The district in which the outbreaks occurred had, in 1984, a greater number of producers (85) of unpasteurized farm-bottle milk than producers (19) pasteurizing before sale. In 1987 the figures were not significantly different in that there were

79 producers of unpasteurized farm-bottle milk and 19 producers pasteurizing before sale.

Sharp, Paterson & Barrett (1985) and Howie (1985) have stressed the dangers of milk-borne infection and pointed to the reduced incidence of such infections in Scotland since the introduction in 1983 of legislation requiring heat treatment of cows milk for sale to the public. The introduction of legislation in England and Wales in 1985 to prevent the sale of unpasteurized cows milk to shops or as part of a meal or refreshment is unlikely to reduce consumption significantly. Outbreaks of infection due to unpasteurized cows milk continue to be reported in the weekly Communicable Disease Reports of the Public Health Laboratory Service.

This outbreak of infection with *S. zooepidemicus* has been described as the most notable event attributed to consumption of raw milk in recent years in England (Sharp, Paterson & Barrett, 1985). It serves as a clear example and reminder of the perils of drinking raw milk.

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