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Corynebacterium ulcerans in humans and cattle in North Devon

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SUMMARY

A case of *Corynebacterium ulcerans* sore throat in a community that drank raw milk from its own farm led to the discovery of another symptomless human infection. Eight cows in the herd were found to be infected and the intermittent pattern of excretion was demonstrated in another cow followed through its lactation. Further evidence of milk infected by *C. ulcerans* was found by examining all raw milk samples submitted to the laboratory. Two other human cases were diagnosed in Devon during the period of this investigation.

INTRODUCTION

Since Gilbert & Stewart (1927) reported the isolation from human throat lesions of corynebacteria possessing the toxins of both *Corynebacterium diphtheriae* and *Corynebacterium pseudotuberculosis* (*ovis*), which they called *Corynebacterium ulcerans*, cases of human infection have been reported only occasionally, usually associated with the consumption of raw milk. Meers (1979) reviewed these reports, added some cases of his own and commented that although one of them presented as severe diphtheria, the infection generally causes only mild disease. *C. ulcerans* produces the exotoxins of both *C. diphtheriae* and *C. ovis* and its taxonomic position has been the subject of much discussion (Maximescu *et al.* 1974); it did not appear in the approved list of bacterial names (Skerman, McGowan & Sneath, 1980). Carne & Onon (1982) recorded observations on 125 strains isolated from man and animals and reported considerable variation in morphological and biochemical reactions. They stated that the majority of human strains produce predominantly diphtheria toxin. Sulea, Pollice & Barksdale (1980) reported that *C. diphtheriae*, *C. ulcerans* and *C. ovis* differed from all other species of corynebacteria in their inability to deaminate pyrazinamide, and proposed the interesting hypothesis that these three species evolved from a common ancestor which parasitized ungulates in pre-human times. This report is principally concerned with the incidence of infection by *C. ulcerans* in a religious community and the herd of cattle kept there to provide them with raw milk. Two other human cases are reported, and the results of the examination of raw milk from herds belonging to producer-retailers are presented and discussed.

MATERIALS AND METHODS

A young woman from a religious community presented to her general practitioner complaining of a sore throat. He took a throat swab from which *C. ulcerans* was isolated. The community occupies an isolated position near the North Devon coast. It consists of a population of about 60 living and working together in a large house and its associated farm. The older members of the community tend to stay for years but some of the younger ones come for quite short periods. Visitors come for courses or holidays between a day and a fortnight in length. On the farm is a herd of cattle with approximately 30 in milk at any one time. Heifer calves are reared and eventually join the herd, so that buying-in is unnecessary.

Throat swabs from cases of sore throat are routinely plated on to a tellurite medium, usually Hoyle's. When the first case was diagnosed, nose and throat swabs were taken from all the inhabitants of the community; a bulk milk sample from the herd was examined. After the organism had been isolated from milk, routine sampling was carried out. Weekly bulk samples were taken from the herd and individual cow samples were collected to identify the carriers and to demonstrate the regularity or otherwise of excretion. The examination of milk from cows coming into the milking herd again after calving was carried out as a routine. All raw milk samples submitted to the laboratory for a period of 6 months, were examined for *C. ulcerans*, and 30 ml of milk was centrifuged. The deposit and cream were mixed and plated on Hoyle's medium. Isolates of *C. ulcerans* were identified by picking colonies on to blood agar for film, biochemical examination and subculture to Loeffler's medium for toxigenicity tests subcutaneously in guinea-pigs. Antibiotic sensitivity tests were carried out.

RESULTS

The isolate from the patient was identified as a toxigenic strain of *C. ulcerans*. She was treated with erythromycin and recovered. The swabs from the other members of the community yielded only one further isolate of *C. ulcerans*, from a person who was not ill and who cleared the organism without treatment. The bulk milk from the community farm grew a large number of colonies on Hoyle's medium and pasteurization was instituted. Eight cows were found to be excreting toxigenic strains of *C. ulcerans*. All these strains were resistant to cloxacillin, which was being used for routine prophylactic treatment at the time when the cows were dried off. After discussion with the veterinary adviser to the farm, cephalonium, a cephalosporin to which the organism was sensitive, was substituted. When each cow was dried off the cephalonium was injected into the udder. After the introduction of cephalonium treatment no cow reintroduced into the herd excreted *C. ulcerans* and no new heifer introduced into the herd excreted the organism. One cow, however, had been dried off just before the change of treatment and was excreting when she returned to the herd after calving. The results of weekly examination of milk from this cow throughout her lactation from May 1981 to January 1982 and of bulk specimens from the herd showed that although 14 out of 34 samples from the cow were positive, it was possible to demonstrate *C. ulcerans* in only two of 100 bulk milk samples taken over the same period.

Raw milk samples were examined from 52 other herds in North Devon. Five of them yielded *C. ulcerans*, four strains of which were toxigenic. In each of these herds *C. ulcerans* was only isolated on a single occasion out of at least eight samples. During the period of rather more than 2 years over which this examination was spread, one other human case occurred. This was in a 12-year-old boy in the same district who presented with a sore throat. His general practitioner took a throat swab, from which *C. ulcerans* was isolated, and instituted treatment with penicillin. The boy made a complete recovery and the organism was not isolated subsequently. Swabs from his parents and sibling were negative. The boy drank milk from one of the farms from which a toxigenic strain of *C. ulcerans* had been isolated. Re-examination of bulk milk samples, and on two occasions milk from each of the individual cows in the herd, failed to yield *C. ulcerans*. The boy had been immunized as an infant and had had his pre-school booster. Dr Gillian Churcher has told me of one other recent case of sore throat due to a toxigenic strain of *C. ulcerans* in south-west Devon. The patient drank pasteurized milk but was thought to have eaten unpasteurized cream. Inquiries of the other microbiologists in Devon revealed no other case.

DISCUSSION

Carne & Onon (1982) discussed the production of diphtheria toxin and *C. ovis* toxin in differing proportions by different strains of the organism. This may perhaps account for the comparative rarity of toxic symptoms as a result of infection. However, in all our cases there was a history of immunization and this, of course, would protect against the effect of diphtheria toxin. Wilson (1942) stated that 20 outbreaks of milk-borne diphtheria had been reported between 1912 and 1937. He considered that the infections were from human sources of *C. diphtheriae*, either directly into the milk by cough-spray, or by way of ulcerated teats of cows. In many of these outbreaks *C. diphtheriae* does not appear to have been grown from the milk, and it is interesting to speculate whether some of them may have been caused by *C. ulcerans*. Incidents of human infection by this organism are, however, rare. Galbraith, Forbes & Clifford (1982) recorded only four cases of *C. ulcerans* infection between 1951 and 1980 in England and Wales. These were the cases reported by Meers (1979). The lack of evidence of person-to-person spread of *C. ulcerans* suggests that an outbreak of diphtheria due to this organism would be epidemiologically different from one caused by *C. diphtheriae*.

Meers (1979) examined 197 samples of bulk milk received routinely from herds in South-West Devon and East Cornwall and found only one strain of *C. ulcerans*, which was non-toxigenic. The finding reported above of four toxigenic isolates from five strains from 52 herds may be evidence of a higher incidence of infection in cattle in North Devon. On the other hand, it could be explained by the fact that intermittent excretion appears to be the rule and that these herds were sampled repeatedly. The examination of samples from the community herd when only one cow was excreting the organism demonstrated the difficulty in isolating *C. ulcerans* from bulk samples. Repeated examination over a period of weeks or months would be required before it would be safe to conclude that *C. ulcerans* was not being excreted into raw milk sold by a producer-retailer. The treatment of infected cows by the injection of antibiotics to which the organism is sensitive appears to be

effective in eradicating *C. ulcerans* from a herd. However, so long as unpasteurized milk is consumed, the risk of human *C. ulcerans* infection will remain.

ADDENDUM

During the preparation of this paper there was another case of sore throat due to *C. ulcerans* in a member of staff of the community. The pasteurizing plant had broken down some days earlier. *C. ulcerans* was not isolated from bulk samples of milk taken from the herd on three occasions during the following month.

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