patient was receiving chemotherapy. Lung biopsy showed parenchymal, peribronchial and alveolar septal infiltration without any vascular congestion. Evidently the patient needed an alternative form of therapy, one directed specifically at the pulmonary lesions. Following the first course of radiotherapy, 200 rad to the entire lung field, a remarkable improvement was noted in the patient's respiratory status. A total of 600 rad was given over 3 days. The pulmonary capillary diffusion defect lessened dramatically, such that respiratory support was no longer necessary at the end of the radiotherapy. Chest roentgenograms then showed remarkable clearing of the infiltration, which had completely resolved 1 week later. There was no recurrence of the pulmonary problems for the subsequent 30 days that the patient lived.

We hope that this case helps to bring to light a seemingly forgotten complication of leukemia and a new dimension in therapy for leukemic lung infiltration. The response to this relatively simple treatment may be dramatic.

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Nosocomial outbreak caused by antibiotic-resistant strain of *Salmonella typhimurium* acquired from dairy cattle

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Salmonellosis is a persistent health problem in Canada.[1] It is widely accepted that the food chain is a major source of *Salmonella* infection in humans.[2,3] Yet few of the large number of foodborne salmonellosis outbreaks and individual cases regularly reported have been supported by microbiologic evidence confirming that a specific food item was responsible.[4,5] Epidemiologic evidence, derived from data based on the date of illness onset, symptoms, food histories and food-specific attack rates, is often the only tool available for establishing a link between an outbreak and a specific food. Here we provide epidemiologic, microbiologic and genetic eyidence implicating dairy cattle as the source of a recent outbreak in hospital of *S. typhimurium* infection among newborns. Raw milk appears to have been the vector for the transmission of the causative agent from bovine to human hosts.

In a 4-day period in the spring of 1982 several neonates in the nursery ward of a Quebec hospital became ill with *S. typhimurium* infection. The strain was phage-typed as type 772 (Laboratory Centre for Disease Control designation). Disc-diffusion assays revealed it to be resistant to ampicillin, chloramphenicol, kanamycin, streptomycin, sulfadiazine and tetracycline. Septicemia and meningitis developed in the index case, and the patient was still shedding the organism 5 weeks after the initial laboratory testing had been done.

Four days before the start of this outbreak another outbreak of *S. typhimurium* infection had been recognized among cattle on a dairy farm in the area served by this hospital. The illness had been in progress for some time: the first animal to be affected had become sick 2 weeks earlier. Initially the infected animals had been treated with chloramphenicol, but this therapy was stopped after several weeks when they failed to respond. Five months later 10 calves had died as a direct result of salmonellosis. The causative agent was also of phage type 772 and displayed the same resistance pattern as the agent in the hospital outbreak.

These microbiologic observations suggested that the isolates from the humans and the cattle had a common ancestry. To confirm this, *S. typhimurium* isolates from both outbreaks were subjected to conjugation analysis. Three isolates from the human and three from the cattle were mated with suitable *Escherichia coli* and *S. typhimurium* recipients. All six isolates transferred their antibiotic resistances from one strain to another, thus indicating that this phenotype was plasmid-determined. Isolates resistant to tetracycline or to ampicillin,

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chloramphenicol, kanamycin, streptomycin and sulfadiazine (ACKSSu) formed two separate transfer (plasmid) groups. Regardless of its source the ACKSSu plasmid produced an identical change in phage type upon its introduction into a second *S. typhimurium* strain. The ACKSSu plasmid from both sources displayed temperature-sensitive conjugal transfer in matings with the appropriate *E. coli* recipient.

Isolation of their deoxyribonucleic acid content followed by its analysis by agarose gel electrophoresis revealed that the strains from the humans and the cattle had identical plasmid complements (Fig. 1). Each of them carried two rather large plasmids having masses of approximately 88 and 60 megadaltons and a smaller, 4.0-megadalton molecule

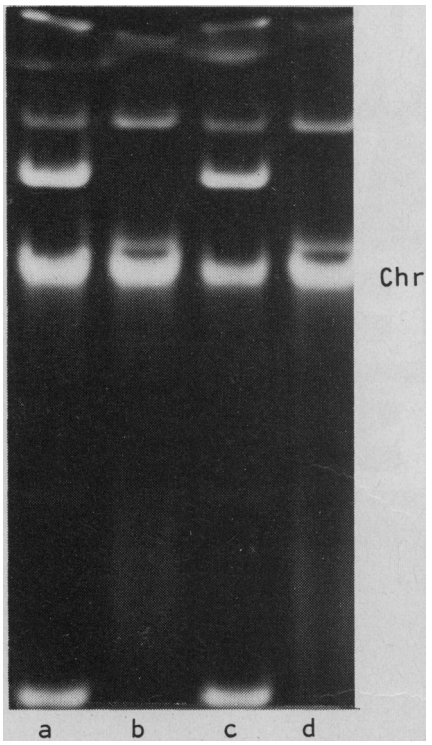

FIG. 1—Electrophoretic analysis of plasmid contents of multiply resistant *Salmonella typhimurium* and their conjugal derivatives. Lanes a and c: *S. typhimurium* resistant to ampicillin, chloramphenicol, kanamycin, streptomycin, sulfadiazine and tetracycline isolated from human and bovine sources respectively. Lanes b and d: ACKSSu-resistant strains derived by mating *S. typhimurium* from lanes a and c with appropriate *Escherichia coli* recipient. Four isolates from each source gave identical patterns. Agarose gels were run for 2.5 h at 80 V. Chr = nonplasmid chromosomal deoxyribonucleic acid.

(lanes a and c). Similar characterization of the strains constructed in the conjugation studies (lanes b and d) established that the 88-megadalton plasmid carried the genes coding for ACKSSu resistance.

Thus, the genetic and molecular studies provided unequivocal evidence that the *S. typhimurium* isolates from the humans and the cattle were identical. A review of the patients' records revealed the probable link between the two outbreaks: the mother of the index patient lived on the farm where the outbreak had occurred and was in the habit of consuming raw milk obtained from this herd. She had delivered her child in the hospital during the bovine outbreak. Although asymptomatic she was shedding *S. typhimurium* several days after the delivery. Because the child became ill within 24 hours of birth it most likely had acquired the infection from its mother. Other children in the nursery fell ill 3 to 4 days later, presumably through cross-contamination. Subsequent enquiries revealed that raw milk from this farm had been sold to at least nine other people living in the area. Testing revealed that two of these plus the farmer, the father of the index patient, carried *S. typhimurium*. No milk samples were tested.

Pasteurization of milk to destroy disease agents was recommended years ago and has been widely implemented. Yet consumption of raw milk is still common in Canada.[6] Part of the difficulty lies in the implementation of uniform and stringent pasteurization standards in the 10 provinces.[7]

Other *Salmonella* species, among them *S. anatum*,[8] *S. muenster*[9] and *S. dublin*,[10] have been implicated in the acquisition of human disease through the consumption of unpasteurized dairy products. In this particular outbreak not only did a strain of S. *typhimurium* pass via raw milk from cattle to human beings, but so did resistance to six antibiotics. Further, this resistance could be transferred to other enteric organisms by conjugation. Previously such an event contributed to the failure of antibiotic therapy in a very young child.[11] Fortunately no deaths occurred during the outbreak reviewed here.

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