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Association between raw milk and human *Salmonella dublin* infection

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Summary and conclusions

Between 1971 and 1975 the mean annual incidence of human *Salmonella dublin* infection in California increased more than five-fold. Investigation of the increase showed an association with exposure to raw milk in 44 out of 113 cases. Of these 44 patients, 35 had used certified raw milk from a single dairy. Faecal swabs confirmed *S dublin* infection in the dairy herd and the milk, and so a pasteurisation order was issued. *S dublin* appears to be an unusually invasive and life-threatening salmonella serotype: 65% of isolations were obtained from non-faecal specimens (mainly blood cultures), 89 patients (80%) were admitted to hospital and 22 patients died. Almost three-quarters of the patients were aged 20 or over, and half had serious underlying diseases, particularly leukaemias and lymphomas. Five patients presented with infected vascular lesions that included aneurysms with abscesses and infections of previous arterial graft sites.

The public's increasing desire for a "health food" such as raw milk should be tempered with an appreciation of its attendant risk to health.

Introduction

Salmonellosis is one of the most prevalent zoonotic diseases. More than 20 000 cases in man are reported annually in the USA,¹ but the true incidence is probably about 100 times greater.² Four clinical types of salmonella infection occur—namely, gastroenteritis, enteric fever, focal abscess, and an asymptomatic carrier state.³ These are not mutually exclusive, and one person with the infection may rarely exhibit all four patterns in succession. Over 1700 salmonella serotypes have

been identified.¹ Each is potentially capable of producing any of the four clinical patterns, but gastroenteritis is the most common. Some serotypes cause more invasive disease—for example, patients infected with *Salmonella paratyphi* and *S typhi* commonly present with enteric fever, while patients with *S cholerae-suis* commonly present with focal abscesses such as osteomyelitis as well as enteric fever.^{3 4}

The pattern of infection characteristic of *S dublin* in man has not been identified, partly because this serotype, which is host-adapted to cattle, has rarely been reported. Between 1963 and 1970 an average of only four cases of *S dublin* per year were identified in California. When a sudden increase occurred in 1971 we undertook an investigation to identify possible sources of infection and to define the epidemiology of *S dublin* infection. We here report the epidemiological features of patients infected with *S dublin*, the invasiveness of this serotype, and the association of this disease with the use of raw milk during 1971-5.

Materials and methods

Under California State regulations all laboratories that isolate *Salmonella* spp are required to submit the isolates to the State Department of Health Services for serotype identification. These specimens are examined at the Microbial Diseases Laboratory according to standard methods.⁵ The salmonella surveillance programme, based on these laboratory reports and conducted by the infectious disease section, signalled the increased incidence of *S dublin* infection in 1971.

Questionnaire survey—In 1971 we developed a comprehensive questionnaire to obtain clinical and epidemiological information from all patients in California known to be infected with *S dublin*. The questions covered any history of contact with people, pets, or other animals ill with diarrhoea or salmonellosis; customary diet before the onset of the illness—for example, type of eggs (cracked, powdered, raw, etc), milk (powdered, raw, etc), other milk products, and many other foods previously implicated in salmonella infection; use of pharmaceutical preparations derived from animal sources (thyroid, pancreatic hormones, etc); previous admissions to hospital or outpatient investigation, especially of the gastrointestinal tract (where we were concerned about the use of carmine dye to study bowel transit time,⁶ sigmoidoscopy,⁷ or gastrointestinal endoscopy⁸); and travel before onset and participation in any sports entailing contact with water. The questionnaires were administered mainly during home visits and less commonly by telephone. If a patient died before he had been contacted the part of the questionnaire relating to diet was completed with the help of a family member, neighbour, or close friend.

Study of implicated dairy—A large proportion of patients reported using certified raw milk from one dairy (dairy X). Thus a study was conducted to identify and remove any salmonella-infected cattle from the two herds totalling 3100 milking cows owned by this dairy. In November 1971 we requested that the county milk commission

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(under whose supervision the dairy produces and distributes certified raw milk) obtain faecal cultures from each cow. Samples of 10-20 g were collected from about 600 animals per week until all cows had been cultured twice. Refrigerated specimens were delivered to the Agricultural Veterinary Laboratory, Fresno, California, where standard procedures to isolate salmonellae were used.⁵ Bacteriological cultures of certified raw milk from this dairy were begun by the Los Angeles County Department of Health Services Laboratory in 1974. All isolations were confirmed by the State's Microbial Diseases Laboratory.

Results

During the five-year study period 113 cases of human *S dublin* infection were reported (figure), 20-27 cases being identified annually. No particular seasonal pattern was apparent. Altogether, 59 patients (52%) were male and 54 (48%) female. The age distribution was

Numbers of patients (n = 113) in California from whom *S dublin* isolated during 1971-5 according to history of exposure to raw milk.

unusual for salmonella infection, being skewed toward older age groups: 81 patients (72%) were aged 20 years or over and 50 (45%) 50 years or over (table I). The distribution of cases by race reflected California's racial composition; that by county of residence showed the greatest concentration in southern California, especially Los Angeles County, which contained 45% of cases but only 35% of the State's population.

TABLE I—Number and percentage of people with *S dublin* infections by age, California, 1971-5*

Age (years)	Total No	%	Cumulative %
<1	8	7	7
1-4	15	13	20
5-9	5	4	24
10-19	3	3	27
20-29	15	13	40
30-39	7	6	46
40-49	9	8	54
50-59	10	9	63
60-69	14	12	75
≥70	26	23	98
Unknown	1	1	99
Total	113	100	

*Obtained from California Department of Health Services, morbidity and laboratory records.

S dublin infections tend to be systemic: nearly two-thirds of the isolates were from non-faecal sources, principally blood (table II). Fever was reported more often (in 86%) than diarrhoea (66%). Bloody diarrhoea was reported in 15%. The illness was often severe, with 89 patients (80%) requiring admission to hospital and 22 (21%) dying. Nearly half of our series had serious underlying diseases at the time of infection; immunosuppressed states and haematopoietic disorders, particularly leukaemia and lymphoma, were the most common (table III). At least eight patients were taking corticosteroids for various conditions.

TABLE II—Number of isolates of *S dublin* according to source *

	No of isolates
Blood	58
Faeces	45
Urine	10
Aneurysm or arterial graft	5
Bone marrow	2
Ascitic fluid	2
Synovial fluid	2
Tracheal aspirate	1
Throat	1
Skin	1
Cerebrospinal fluid	1
Not stated	2
Total	130†

*Obtained from California Department of Health Services, laboratory records.
†Ten of the 113 patients had multiple sources of positive isolates.

TABLE III—Details of 62 chronic disorders* and 19 deaths in patients with *S dublin* infection

	No of disorders	No of deaths
Haematopoietic disorders: 8 leukaemia (4 taking immunosuppressants, 1 receiving frequent transfusions); 3 hypoplastic anaemia (2 receiving corticosteroids and 3 blood transfusions); 3 lymphoma; 2 sickle-cell anaemia; 2 Hodgkin's disease; 1 hypogammaglobulinaemia; 1 cryoglobulinaemia	20	4
Gastrointestinal disorders: 1 ulcerative colitis; 1 cirrhosis (with alcoholism, erysipelas, gastric ulcer, polycythaemia, arrhythmia); 1 SPO repair of hernia and ruptured oesophagus; 1 bleeding ulcer (alcoholism, cirrhosis, and diabetes); 1 chronic hepatitis (taking corticosteroids)	5	2
CNS disorders: 2 cerebrovascular accident; 1 brain-stem infarction with subarachnoid haemorrhage	3	3
Malignancies (non-haematopoietic): 1 carcinoma of bladder; 1 carcinoma of breast (taking corticosteroids and antibiotics); 1 cystic teratoma of ovary; 1 carcinoma of colon	4†	2
Vascular diseases: 1 SPO aortoiliac graft repair; 1 SPO repair of ruptured aortic aneurysm with transfusion of 9 units of blood; 3 mycotic aneurysms	5	1
Genitourinary disorders: 2 pyelonephritis; 1 prostatic disease (unspecified); 1 testicular disease (unspecified)	4	
Metabolic and endocrine disorders: 5 diabetes mellitus (1 with pyelonephritis and hypertension, 1 with leukaemia, 1 with mycotic aneurysm, 1 with lymphoma); 2 receiving thyroid, 2 SPO renal transplant recipients, taking corticosteroids and azathioprine; 1 alcoholism; 1 myasthenia gravis; 1 hyperparathyroid	12	1
Connective-tissue disorders: 3 systemic lupus erythematosus (1 receiving corticosteroids, 1 with alcoholism); 1 rheumatoid arthritis (receiving corticosteroids)	4	2
Traumatic disorders: 2 fractured skulls with cerebral trauma; 1 orthopaedic repair	3†	3
Psychiatric disorders: 1 paranoid schizophrenia	1	1
Allergic disorders: 1 food allergy	1	

*Represents 54 patients, of whom 19 died.
†Outcome not known in one case.
SPO = Status postoperatively.

S dublin was recovered from vascular lesions, especially aneurysms with abscesses and infected arterial graft sites, in five men aged 57-72. Case histories of two of these patients were as follows. The patient in case 1 had an episode of febrile gastroenteritis one week before surgery for a ruptured aortic aneurysm. *S dublin* was isolated from blood and faeces. Seven months after surgery he was readmitted with *S dublin* infection at the site of the aortic graft (knitted Dacron), when his faeces were similarly positive. The patient in case 2 had an iliofemoral bypass graft (knitted Dacron) in 1968. In 1971 a false aneurysm appeared at the right groin where the graft anastomosed with the common femoral artery. At surgery an abscess was found, which on culture yielded *S dublin*, as did a blood culture. The false aneurysm was repaired, the abscess drained, and the local site irrigated long after closure. He received parenteral chloramphenicol for two weeks, then oral ampicillin for two weeks. He developed another false aneurysm at the same site in 1972, and *S dublin* was again isolated from the lesion. He recovered after similar treatment and later returned to work. Interestingly, he had used a particular brand of certified raw milk. This "health food" was purchased primarily for

his wife, who had multiple sclerosis, for whatever benefit it might confer.

An association with the same brand of certified raw milk was noted in many of the patients. No other food item was commonly reported. Only a few patients reported contact with people, pets, or other animals ill with diarrhoea, and few used pharmaceuticals derived from animal sources. An impressive temporal association with this brand of certified raw milk was noted in an 81-year-old woman, who was admitted to a community hospital in 1974 with a myocardial infarction. Two weeks later she suffered a cerebrovascular accident. As she was eating poorly, her daughter brought to the hospital the particular brand of certified raw milk. She drank the milk on 7 February, developed diarrhoea and fever on 8 February, had a blood culture taken on 9 February, and died on 10 February. The blood culture grew *S dublin* post mortem.

Of the 113 patients, 44 (39%) had used raw milk and 35 (31%) used certified raw milk from dairy X. Laboratory study of the dairy herd yielded 51 isolates of *Salmonella* spp from 31 cows, 29 of the isolates being *S dublin*. The infected cattle were removed from the herd, and the county milk commission instituted a requirement that each cow admitted to the herd have one faecal culture negative for salmonellae. Of 98 one-quart (1.14 l) containers of certified raw milk cultured, one was positive for *S dublin*. A temporary pasteurisation order was issued, and three serial faecal cultures were ordered from the particular herd producing the contaminated milk specimen. No faecal shedders of *S dublin* were identified, but 17 cows were shedding salmonellae of other serotypes and were culled from the herd. After April 1974 the association of *S dublin* infection with that particular brand of raw milk diminished (see figure).

Discussion

Infection with *S dublin* differs considerably from salmonellosis due to other serotypes. Although 54% of all patients with salmonella infection reported in the US are aged under 10 years and 65% are under 20,¹ only 27% of our patients were under 20 and nearly half were aged 50 or over. Our patients also had pre-existing, serious debilitating conditions. The symptoms in our cases were also unusual, fever being reported more often (86%) than diarrhoea (66%). *S dublin* appears to be an especially invasive serotype, with 65% of the isolates being from non-faecal sources, principally blood, urine, and deep tissue sites. By contrast, only 15% of salmonella isolations (all serotypes) were made from non-faecal sources in California during the same five-year period. National figures show that even *S typhi* had a lower proportion of isolations from non-faecal sources (38%) during those years than did *S dublin* (65%).⁹ Eighty-nine of our patients (80%) required admission to hospital and 22 (21%) died, owing particularly to the seriousness of their underlying diseases. We regard the *S dublin* infection as an associative feature in their death but not necessarily the underlying cause. Our overall case-fatality ratio of 21% contrasts appreciably with that for all cases of salmonella infection (0.5%) reported in the national data.¹ For patients aged over 50 with *S dublin* infection the case-fatality ratio was 43%.

Predominant among the underlying diseases in our cases were haematopoietic disorders (especially leukaemias and lymphomas) and immunosuppressed states. The underlying systemic conditions that predispose to salmonella infection have been reviewed elsewhere,^{10,11} but conditions also exist that predispose to localised salmonella infection (after transient systemic bacteraemia)—for example, osteomyelitis has been reported as an infrequent complication (apart from that occurring in sickle-cell anaemia) and occurs usually at an area of previous trauma such as a fracture site.^{3,10} Infection with *S dublin* at sites of aneurysms or previous graft repairs, as noted in five of our cases, probably also relates to reduced local resistance in areas of vascular disease.⁴ Zak *et al* similarly noted that elderly men with atherosclerotic aneurysms predominated in their series of 12 patients who ruptured diseased large arteries in the course of enterobacterial (mostly salmonella) infection.¹²

Analysis identified the use of raw milk as the only common association, which was not unexpected. *S dublin* is almost as

host-adapted to cattle as *S typhi* is to man and *S gallinarum* to poultry.^{13,14} *S dublin* is not common in the USA but is the most prevalent salmonella serotype infecting cattle throughout the world.¹⁵ Data from the US Department of Agriculture for 1967-71 indicate that 97% (147/151) of all non-human isolations of *S dublin* were made from cattle and that 90% were from Utah and California.¹⁶ Past outbreaks of *S dublin* infection in man have generally been associated with use of raw milk.¹⁷ Bovine faecal contamination is probably the most important factor in milk contamination,¹⁷ although *S dublin* has been isolated from the udders of cattle with chronic mastitis.¹⁸ This suggests that milk may be contaminated without exposure to faeces or other exogenous sources of contamination.

Of the 44 patients who used raw milk, 35 (80%) reported using one particular brand, yet that dairy produced less than 0.5% of all fresh milk sold in California. Our findings are consistent with the hypothesis of intermittent low-grade contamination of milk, in which the cases most readily recognised were those in which the patients became severely ill because of advanced age or serious, pre-existing conditions. Sources of infection were not identified in 69 (61%) of our cases. Possible but unproved sources included ingesting raw or rare beef and beef products such as hamburger, veal, and liver; person-to-person transmission by faecal-oral spread from infected, possibly asymptomatic people; food-borne disease by food handlers infected with *S dublin*; and ingesting raw milk and milk products not recognised as such, particularly when served away from home and as one ingredient among many.

A case-control study of a subset of our cases was conducted by Dr Keith Marton and others of the Los Angeles County Acute Communicable Disease Control Division. In 1973-4 they investigated all human group D (the group to which *S dublin* belongs) salmonella infections in Los Angeles County before results of definitive serotyping were available. Of 36 consecutive group D salmonella isolates studied, 16 were eventually serotyped *S dublin* and 20 were due to other serotypes. When diets were compared in the two groups of patients only one item could be implicated—namely, certified raw milk produced by dairy X. That brand was consumed in 10 of the 16 households (63%) in which *S dublin* infection occurred but in none of the 20 households infected by the other group D serotypes ($P < 0.01$, χ^2 test). Dairy X had been implicated in outbreaks of *S dublin* infection in California in 1958¹⁹ (47 cases) and 1964²⁰ (two cases). Pasteurisation orders were also issued in those years. California patients accounted for 114 (68%) of the 167 human cases of *S dublin* infection identified nationwide between 1971 and 1975, although California represents only 10% of the nation's population. Dairy X did not distribute raw milk outside the State during that period. Most cases were in southern California and corresponded to the dairy's location and largest distribution.

Salmonellosis is one of many diseases that have been contracted from raw milk. The best safeguard is pasteurisation, since this not only kills milk-borne pathogens that are infective at low doses but also protects consumers from the multiplication of pathogens (infective at only high doses) that would occur if contaminated milk were not continuously refrigerated. The inherent danger of salmonella infection in certain raw foods (for example, poultry) is recognised,²¹ but adequate cooking and avoidance of cross-contamination after cooking can prevent infection. Contamination of food items not intended to be further treated by the consumer, whether these be chocolate candy,²² powdered milk,²³ ice cream,²⁴ or dietary supplements,²⁵ however, is not tolerated. When such contamination is identified measures are taken (recall and embargo) to protect the public's health. Contaminated milk might be especially hazardous since it can probably infect with fewer salmonellae than other foods: its high fat content protects against gastric acid, and, since it is fluid, milk can pass out of the stomach rapidly.

We conclude that infection with *S dublin* may be serious and that raw milk is an important source of the infection. In view of the large public demand for raw milk that exists in California,

it is unlikely that its sale will be prohibited. The public, however, should be informed of its potential danger, particularly when fed to infants, old people, and those with already compromised health.

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ONE HUNDRED YEARS AGO Dr Packard of Philadelphia has lately reviewed the mode of infliction of the death-penalty as at present carried out in the United States, as well as in this country. He objects to the process of death by hanging on grounds which appear to us to be very inadequate. In his opinion, it often adds to the difficulty of procuring convictions, even upon very positive evidences of guilt. It also "adds much to the force of the sympathy which is apt to be developed for criminals under sentence, and increases the frequency of pardons, by which the salutary effect of the law is seriously lessened. Under this head may be mentioned the facilitating of the abuse of the pardoning power for political or private reasons, since this would be less likely to occur if it did not fall in with public sentiment." We cannot agree in these views; the objections advanced by Dr Packard are really directed against the punishment of death in any shape, and not against executions by hanging. Executions as they are at present conducted in this country—namely, by allowing to the body a fall of at least six feet—are, we believe, attended with instantaneous death; and there is no reason to suppose that there can be any amount of suffering sufficient to create or justify public sympathy. The experiments performed by M Fleischmann on himself some years since, conclusively proved that there was no consciousness of pain; but at first merely a singing in the ears, a flash of light, then darkness and oblivion. In these experiments, there was neither the length of fall for the body nor the degree of pressure on the neck which are provided for in a public execution; and thus, in the latter, the stage for the sensations above mentioned would be considerably shortened. The privacy with which judicial sentences of death are now carried out has really taken away all reasonable objections to the English mode of execution; it contrasts favourably in this respect with the method of garotting by the Spaniards, of guillotining by the French, and decapitation by the sword as it is carried out in some of the States of Germany.

As a substitute for the execution of a criminal by hanging, Dr Packard makes the following suggestion.

"There should be fitted up in the gaol a small room, which can be made air-tight. By means of very simple arrangements, carbonic oxide can be substituted for the air of the room, and a person confined in it would then die the easiest and quietest death known to science. He would simply cease to exist. A jury should be appointed to identify the convicted person. In their presence, he should be conducted to the room, and placed in it, entering by a sliding door, of plate-glass it may be, protected by a netting of iron wire. The process of rendering the air irrespirable should then be begun, and would very soon be completed. In less than ten minutes, fresh air might be introduced by opening the sliding door and reversing the former process; and the

same jury, again identifying the body, would certify to the fact of the execution having been duly carried out." (*Bulletin of the Medico-Legal Secretary of New York*, March 1879, p. 139.)

As it would require some little time to displace the air in the small room, and replace it with a noxious proportion of carbonic oxide, it is clear that death would not be so rapid under these circumstances as in hanging. Then, again, there is reason to believe that some persons would not be so easily affected by the gas as others. Dr Packard's process is not likely to be adopted on the score of humanity. Besides, it appears to us that a jury would strongly object to be made witnesses to the execution of a man by viewing the process of gradual suffocation through a glass door, even though there may be little, if any, struggling. (*British Medical Journal*, 1879.)

ONE HUNDRED YEARS AGO We gave lately an account of the curious outbreak of hysterical religious "possession" among some of the nuns in the province of Udine. A correspondent writes that the religious mania which then raged appeared to subside for a time, but it again broke out after the ceremonies of Holy Week; and the *Capitale* gives an account of what it calls "the last act of the comedy of Verzegnis," from which it appears that the devil has again been busy in Friuli. The number of people "possessed" lately has been thirteen, the chief one a handsome girl, by name Veronica Paschini, who has been daily inspired to pour forth a torrent of words in Friulian dialect, mixed with bad Italian and dog Latin, while her father stood by, Bible in hand, to interpret the utterances of his daughter and the prophecies she put forth. These manifestations took place every evening; and a crowd of people assembled at her house to listen to the words which, while they believed they were the words of the devil, they looked on as expressing the will and the works of God. Following her example, but as minor prophets, the other girls of the place gave utterance to strange words, which were supposed to veil some prophetic revelations; and no doubt in time the whole district would have become affected by this hysterical religious mania but for the intervention of the Government. It was at first intended to remove the "possessed" to a hospital, but the people of the district rose against it, and vowed they would prevent it if it cost them their lives; so it was determined to resort to such a display of force as would render any attempt at resistance out of the question. A company of soldiers was sent down from Udine, who occupied the village; and under their protection the police removed all those who had given signs of possession, without doing harm to any one. (*British Medical Journal*, 1879.)