Aspects of the epidemiology of human *Listeria monocytogenes* infections in Britain 1967–1984; the use of serotyping and phage typing

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Summary. Strains of *Listeria monocytogenes* from 475 cases of human listeriosis collected during 1967–1984, belonged to one of three serogroups (1/2, 3 or 4). They were phage typed with a set of 28 phages to investigate three aspects of the epidemiology of listeriosis. (i) Three patients each had two episodes of listeriosis, 3 months to 2 years apart, with strains of the same serogroup and indistinguishable by phage typing. (ii) Ten episodes of possible cross-infection between pairs of neonates in the same hospital occurred; the first baby was ill at or within 1 day of birth, and the second baby became ill 8–12 days after contact with the first. In each pair the *L. monocytogenes* strains were of the same serogroup and indistinguishable by phage typing. (iii) In three clusters of cases there may have been a common source of infection. *L. monocytogenes* strains from 10 of 11 cases of listeriosis in the Carlisle area in Jul.–Dec. 1981 were of the same serogroup; nine strains were non-phage-typable. The second cluster involved four adults treated at one hospital and the third a pair of neonates who were ill shortly after birth. In each cluster, strains were of the same serogroup, and were indistinguishable by phage typing. These last two clusters occurred during a short period when an unusually high proportion of strains from all cases of human listeriosis in Britain were indistinguishable by phage typing from the cluster strains, suggesting the possibility of common source infection.

Introduction

Listeria monocytogenes is a gram-positive bacillus first described in England causing a disease characterised by a mononuclear leukocytosis in laboratory animals (Murray *et al.*, 1926). In 1929, Nyfeldt, in Denmark, isolated the same organism from infectious mononucleosis-like infections in man (Gray and Killinger, 1966). Burn (1936), in the USA, established *L. monocytogenes* to be a cause of infection in man during the perinatal period, and also described meningitis as a form of listeriosis in adults. However Dumont and Cotoni (Cotoni, 1942) had isolated a “diphtheroid” organism from the cerebro-spinal fluid of a soldier in France in 1919 that was held in the culture collection of the Pasteur Institute (Paris) for >20 years before it was identified as *L. monocytogenes*.

It is now clear that *L. monocytogenes* causes a wide range of disease in man; this includes meningo-encephalitis, septicaemia, pneumonia,

endocarditis, localised abscesses, cutaneous lesions, conjunctivitis, urethritis, an infectious mononucleosis-like syndrome (Gray and Killinger, 1966), hepatitis (Yu *et al.*, 1982; Hardie and Roberts, 1984) and arthritis (Newman *et al.*, 1979).

In the perinatal period, listeriosis is most commonly an intra-uterine infection but can also present after the first week of life, frequently as meningitis. A pregnant woman who develops listeriosis may have a low grade septicaemia that appears clinically as an influenza-like illness in the later stages of the pregnancy. Trans-placental infection of the fetus may result in premature delivery of a stillborn or acutely ill infant with disseminated abscesses in the viscera (granulomatosis infantiseptica) and in the placenta. In less severe infections abscesses may be present in the lungs, digestive tract, skin and eyes but not in the placenta (Seeliger, 1961; Gray and Killinger, 1966).

In adults, meningo-encephalitis and bacteraemia are the commonest clinical findings (Nieman and Lorber, 1980), and although listeriosis may occur in apparently healthy individuals (Hone *et al.*,

Table I. Summary of three patients, each with two episodes of listeriosis

Patient	Age	Sex	Other medical condition	Clinical type of listeriosis	Date of onset of illness	<i>L. monocytogenes</i>	
						Serogroup	phage type*
A	8	M	Acute lymphoid leukaemia	Bacteraemia	Jun. 1984	1/2	3, 6
				Bacteraemia	Sep. 1984	1/2	3, 6
B	38	F	Hodgkin's disease	Bacteraemia	Sep. 1976	4	11
				Pneumonia and meningitis	Nov. 1977	4	11
C	NK	F	Renal transplant	Bacteraemia	1968	4	NT
				Bacteraemia	1970	4	11

NK = not known.

NT = not phage-typable.

* Phages that gave strong (+ +) lytic reactions with strains. (For designation of phages see McLauchlin *et al.* (1986).)

1972; Howard *et al.*, 1981), most patients are elderly or have predisposing factors such as malignant disease or immunodeficiency (Pollock *et al.*, 1984). Because *L. monocytogenes* is an opportunist pathogen, whenever a "new" disease or treatment is described which predisposes an individual to infection, reports of listeriosis soon follow, e.g., in the acquired immune deficiency syndrome (Wetli *et al.*, 1983; Real *et al.*, 1984; Read *et al.*, 1985) and in continuous ambulatory peritoneal dialysis (Myers *et al.*, 1983). Seeliger (1972), on the basis of accidental laboratory infections, described *L. monocytogenes* as a "relatively mild pathogen for the healthy adult". The extent to which subclinical infection occur is speculative.

The epidemiology of listeriosis in man remains obscure. In this paper we present evidence about certain aspects of that epidemiology with particular reference to possible means of transmission.

Materials and methods

A phage-typing study was performed with 807 cultures of *L. monocytogenes* isolated from 479 cases of human listeriosis in the UK during 1967–1984 and collected at The Central Public Health Laboratory, Colindale. Strains were confirmed as *L. monocytogenes* by the criteria of Seeliger and Höhne (1979) and Rocourt *et al.* (1983), and serotyped by the method of Seeliger and Höhne (1979) as serogroup 1/2 (O Factor I), serogroup 3 (O Factor IV), or serogroup 4 (O Factor V/VI).

Subcultures were sent to Tours under code in batches of about 50 strains over a period of 3 years for phage typing as described by Audurier *et al.* (1977 and 1979). Results were returned to Colindale for decoding and analysis. Strains were defined as distinguishable if there were >1 major phage-reaction differences for serogroup-1/2 strains, or >2 major differences for serogroup-4 (McLauchlin *et al.*, 1986).

Results

Recurrent episodes of disease

Strains of *L. monocytogenes* were received from three patients in each of whom two episodes of listeriosis had occurred. The periods between the pairs of episodes were 3 months to 2 years. The results of phage typing and serotyping are shown in table I, which also includes a brief clinical history of each patient. All had predisposing conditions and patient B died from the second episode of listeriosis. The two strains of each pair of isolates were of the same serogroup and were indistinguishable by phage typing. (Because of the limits of reproducibility of the system, the single phage-reaction difference between the strains from patient C does not indicate that the strains were distinguishable).

Hospital cross-infection amongst neonates

During the period 1967–1984, strains of *L. monocytogenes* were received from 10 pairs of neonates in whom hospital cross-infection was suspected because the infections occurred in the same hospitals within short periods of time. Four of these incidents have been described (Campbell *et al.*, 1981; Isaacs and Liberman, 1981; Sinha *et al.*, 1983; Shrestha TL, Sunderland District General Hospital, personal communication).

Information was not available about two incidents, but in the other eight there was a common pattern: the first baby (baby 1) had congenital listeriosis clinically evident at or within 1 day of birth, and the second baby (baby 2) became ill (usually 8–12 days *post partum*) after direct or indirect contact

Table II. Clinical summary of 10 pairs of neonates involved in episodes of hospital cross-infection by *L. monocytogenes*

Clinical features	Baby 1 (ill at birth)	Baby 2 (apparently healthy at birth)
Onset of symptoms (post partum)	8 within 1 day	1 on day 3 1 on day 4 6 on days 8–12
	2 NK	2 NK
Symptoms	5 respiratory distress 3 septicaemia 2 meningitis	8 meningitis 1 respiratory distress 1 pyrexia, fits and jaundice
Duration of pregnancy	1 30 weeks 1 31 weeks 1 33 weeks 1 34 weeks 1 38 weeks 2 term (40 weeks) 3 NK	1 35 weeks 1 36 weeks 1 37 weeks 1 38 weeks 1 39 weeks 2 term (40 weeks) 3 NK
Caesarian section	3	2
Fatal outcome	2 (2 NK)	0 (2 NK)
Illness in mother during pregnancy	5 pyrexial 'flu '-like' illness	1 mild cold 1 laryngitis
<i>L. monocytogenes</i> isolated from HVS of mother	4	0

NK = not known; HVS = high vaginal swab.

with baby 1. A summary of clinical information about these incidents is shown in table II. Cross-infection was deduced by finding that strains isolated from the pairs of babies were always of the same serogroup (two pairs yielded strains of serogroup 1/2, and the other eight pairs of strains were of serogroup 4), and that each pair was indistinguishable by phage typing (table III) except in one episode from which one of the strains was not available for examination. Cross-infection was also suggested in four of the pairs of cases by the detection of anti-*Listeria* antibodies in the serum of the mother of baby 1 but not in the serum from the mother of baby 2 (McLauchlin and Taylor, unpublished results).

Possible modes of transmission were suggested in nine of the episodes (no information was available about one). In one episode "contact" between the two neonates was specified. In seven others the neonates were either delivered and nursed in the same room, or attended by the same obstetric staff

Table III. Serogroups and phage types of strains involved in cross-infection between neonates

	Serogroup	Phage type
Episode 1		
Baby 1	4	10, 12, 14
Baby 2	4	not tested
Episode 2		
Baby 1	4	11, (12)
Baby 2	4	11
Episode 3		
Baby 1	1/2	1, 3
Baby 2	1/2	1, 3
Episode 4		
Baby 1	4	(8), 10, 13, 24, 27
Baby 2	4	(8), (10), 13, ((24)), 27
Episode 5		
Baby 1	4	(8), 10, 12, 14
Baby 2	4	(8), 10, 12, 14
Episode 6		
Baby 1	1/2	(2), 4
Baby 2	1/2	(2), 4
Episode 7		
Baby 1	4	20, 27
Baby 2	4	20, 27
Episode 8		
Baby 1	4	8, 9, 11, 13, 15
Baby 2	4	8, 9, 11, 13, 15
Episode 9		
Baby 1	4	8, 10, 12, 14, 27
Baby 2	4	8, 10, 12, 14, 27
Episode 10		
Baby 1	4	8, 9, 11, ((12)), 13, 15, 19
Baby 2	4	8, 9, 11, 13, 15, 19

() phages that gave moderate lytic reactions;

(()) phages that gave weak lytic reactions.

or delivered with the same obstetric equipment. In the final case there was contact between baby 2 and the mother of baby 1 when both mothers and baby 2 were nursed in adjacent beds in an open ward (Isaacs and Liberman, 1981).

Common source infection in hospital or community

(a) *Common source of listeriosis in East Cumbria.* During the period Jul.–Dec. 1981, 11 cases of listeriosis in Carlisle and the surrounding area were diagnosed by bacterial isolation (S. Hall, CDSC Colindale, personal communication). Four were perinatal infections and all four infants were either still-born or died within 24 h of birth. The other seven patients were adults, one of whom died. All the adults had signs of meningitis and only one had a severe underlying disease (Hodgkin's lymphoma). Ten of the strains were available for typing—all were serogroup 1/2, and nine were non-phage-typable.

Fig. 1. Monthly occurrence of cases of listeriosis caused by serogroup 4 in Britain 1976-1979; ▨ strains indistinguishable by phage typing from strains isolated in Liverpool outbreak (Green and Macaulay, 1978); □ strains of other phage types.

(b) *Common source or cross-infection episodes in hospitals and clusters of cases in the community.* It was noted that many cases of listeriosis that occurred over relatively short periods were caused by strains indistinguishable by phage typing. In the following two clusters of cases, >55% of the *L. monocytogenes* serogroup-4 strains isolated in Britain during a 6-month period were indistinguishable by phage typing.

CLUSTER 1. We (Taylor *et al.*, 1981) previously described phage typing of strains from four cases of listeriosis caused by serogroup-4 strains in the same Liverpool hospital during a 2-month period (Feb.-Apr. 1978) in which there could have been case-to-case transmission or a common source for the outbreak (Green and Macaulay, 1978). We then reported that the strain isolated from one of the four cases was probably different in origin from the other three, but on completion of phage-typing reproducibility studies (McLauchlin *et al.*, 1986) this strain was indistinguishable from the isolates from the other three cases. Furthermore, retesting this strain yielded an almost identical phage-lysis pattern to that of the strains isolated from the other three cases. During the period (Dec. 1977-Jul. 1978) 24 out of 34 (70%) of the serogroup-4 strains sent from cases of listeriosis in Britain were indistinguishable by phage typing from the Liverpool isolates described above. The proportion of listeriosis cases due to these "Liverpool type" serogroup-4 strains in the period 1976-1979 is shown in fig. 1, and the distribution by Regional Health Authority of this "type" during the period Dec. 1977-Jul. 1978 is shown in fig. 2.

CLUSTER 2. A pair of cases of perinatal listeriosis occurred that was similar to those already described except that cross-infection was not thought

to have taken place. The two cases occurred within 48 h in Oct. 1983 in the same hospital in the North West Thames Regional Health Authority, and *L. monocytogenes* serogroup 4 was isolated from both neonates. Each was ill within 24 h of birth. *L. monocytogenes* of the same serogroup was also isolated from both mothers (table IV). The four strains were indistinguishable by phage typing. Common source infection was further supported by the presence of anti-*Listeria* antibodies in sera from both mothers (McLauchlin and Taylor, unpublished observation). However, during the period Aug.-Dec. 1983 when this pair of cases occurred, strains from 23 (56%) out of the 41 cases of listeriosis due to serogroup-4 strains received at Colindale from UK hospitals were indistinguishable by phage typing from the strains isolated from this pair of cases. The proportion of cases due to these serogroup-4 strains in the preceding 3 years is shown in fig. 3, and their distribution by Regional Health Authority during Aug.-Dec. 1983 is shown in fig. 4.

Discussion

Recurrent episodes

There appear to be at least four possible explanations for the epidemiology of listeriosis when patients are affected by recurrent episodes of the disease—(i) chance re-infection by different strains; (ii) re-infection by different strains because of a genetic predisposition to the disease; (iii) re-infection from the same or similar environmental source; or (iv) incomplete eradication of the original infection, persistence of the strain and subsequent recrudescence of infection. Listeriosis may

Fig. 2. Distribution of cases of listeriosis caused by serogroup-4 strains by Regional Health Authority, Dec. 1977–Jul. 1978. A. Strains indistinguishable by phage typing from strains isolated in the Liverpool outbreak (Green and Macaulay, 1978). B. Strains of other phage types.

Table IV. Common source outbreak of perinatal listeriosis

	Case 1	Case 2
Date of birth and onset of symptoms	28/10/83	30/10/83
<i>L. monocytogenes</i> serogroup-4 isolated from:		
baby	Gastric aspirate and eye	Gastric aspirate, ear and rectal swab
mother	Blood culture	HVS
Phage type*	8, 9, 11, 13, 15, 28	8, 9, 11, 13, 15, 28

HVS = high vaginal swab.

* Strong (++) lytic reactions only.

be much commoner and have a wider spectrum of severity than is generally realised so that subclinical forms are largely undiagnosed and unreported. All three patients with two episodes were immunosuppressed and, as well as being investigated more intensively, they may have suffered more severe illness than previously healthy individuals. However, because the incidence of listeriosis even in patients with serious underlying disease is low, it seems

unlikely that recurrent episodes caused by indistinguishable strains could be due to chance alone.

Genetic factors appear to be important in the pathogenesis of infection with mycobacteria in man (Van Eden *et al.*, 1983). Like *L. monocytogenes*, these are intracellular pathogens and similar pathogenic and host defence mechanisms may be involved. Genetically inbred lines of mice show differences in susceptibility to listeria infection and in inflammatory responses (Skamene, 1983), but whether there are analogous effects in man is not known. Three reports (Becroft *et al.*, 1971; Lennon *et al.*, 1984; Canfield *et al.*, 1985) describe outbreaks in New Zealand and the USA in which higher than expected proportions of particular ethnic groups were infected. However these authors did not discuss the possibility of genetic predisposition but suggested that diet and socioeconomic factors may have been important. The finding that in each of our patients the first and second isolates were of the same serogroup and were indistinguishable by phage typing provides strong evidence that these recurrent episodes were not caused by different strains and therefore the first and second explanations would seem unlikely.

Re-infection from the same or a similar source

Fig. 3. Monthly occurrence of cases of listeriosis caused by serogroup-4 strains in Britain 1980–1983; ▨ strains indistinguishable by phage typing from strains isolated in cases described in table IV; □ strains of other phage types.

Fig. 4. Distribution of cases of listeriosis caused by serogroup-4 strains by Regional Health Authority, Aug.–Dec. 1983. A. Strains indistinguishable by phage typing from strains isolated in cases described in table IV. B. Strains of other phage types.

could involve direct or indirect contact with animals or animal products, and infections in veterinarians from exposure to infected animals have been reported (Owen *et al.*, 1960; Seeliger, 1961). A wide range of animals may be infected by *L. monocytogenes* or may carry and excrete it in high numbers without apparent illness (Gray and Killinger, 1966). In Britain animal listeriosis is commonest in sheep and cattle (*Veterinary Record*, 1983). Another possible source of infection could be the endogenous flora of the patient or of a household contact. Estimates of faecal carriage rates in healthy human individuals vary from 0.6 to 70% (Kampelmacher and van Noorle Jansen, 1972; Ralovich, 1984). Vaginal and pharyngeal carriage has also been reported (Gray and Killinger, 1966; Ralovich, 1984) but little is known about long term carriage. *L. monocytogenes* has been isolated from human semen (Toaff *et al.*, 1962) and the possibility of sexual transmission as an explanation of re-infection cannot be ignored. The association of listeriosis with iatrogenic immunosuppression in, for example, renal transplant patients (Isiadinso, 1975; Nieman and Lorber, 1980) further indicates that autochthonous infection occurs.

Three further possible environmental sources of *L. monocytogenes* could be soil, animal excreta (Seeliger, 1961) or food. The possibility of food borne infection is discussed below; certain foods have been implicated with the transmission of *L. monocytogenes* to man (Schlech *et al.*, 1983; Fleming *et al.*, 1985) and an individual's dietary habits may lead to re-infection.

L. monocytogenes is a facultative intracellular parasite (Mackanness, 1971) and the fourth possibility of incomplete eradication and survival in the host at sites other than the gut, respiratory tract or genital tract cannot be excluded.

Although listeriosis has been reported to cause recurrent abortion (Gray and Killinger, 1966), this is probably rare. Of the 187 cases of perinatal listeriosis from which strains were sent to DMRQC between 1967 and 1984, none of the mothers were known to have had bacteriologically confirmed listeriosis on more than one occasion. However, the occurrence of three non-perinatal cases of multiple episodes of listeriosis, of which there is only one similar report (Bodey *et al.*, 1968), suggests that re-infection, chronic infection or long term carriage of *L. monocytogenes* may occur, and that recurrent abortion due to listeriosis is possible.

Cross-infection

We have presented the largest series of cases with strong evidence of cross-infection with *L. monocytogenes* from congenitally infected newborn infants to apparently healthy neonates in hospital. These cases highlight some of the characteristics of listeriosis in neonates (Gray and Killinger, 1966; Seeliger and Finger, 1983). Early onset disease (baby 1) is characterised by septicaemia and respiratory distress, and late onset disease (baby 2) by meningitis. This difference may be related to the developmental stage of the fetus or neonate and the route of infection. Similar differences are found in other bacterial infections of the newborn, e.g., those due to Lancefield group-B streptococci (Parker, 1979). *L. monocytogenes* can be isolated from the genital tracts of mothers of babies with early onset listeriosis; the mothers may also develop a mild pyrexial illness during pregnancy or at delivery. In this series, *L. monocytogenes* was isolated from four mothers of the early onset cases; five mothers developed a pyrexial "flu-like" illness. However, the number of mothers from whom culture was attempted is not known. It is interesting that six of the ten neonates with late onset disease either were born by caesarian section or were premature, and may therefore have been especially susceptible to infection.

Several reports describe similar cases of cross-infection amongst perinates (Burn, 1936; Line and Cherry, 1952; Mencikova, 1956; Levy and Nassau, 1960; Dubois and Lefebvre, 1965; Joppich and Schulte, 1968; Becroft *et al.*, 1971; Humbert *et al.*, 1976; Larsson *et al.*, 1978; Laugier *et al.*, 1978; Dickgiesser, 1980; Kachel and Lenard, 1981; King *et al.*, 1982). In one of these, Larsson *et al.* (1978) suggested that infection was spread from one neonate to four others by common use of a rectal thermometer.

Although listeriosis in the perinate is relatively rare, hospital cross-infection in the UK is more common than is generally realised. During 1967–1984 we received strains from 187 cases of perinatal listeriosis of which 20 were associated with cross-infection (i.e., 1 in 9.4 cases). Dickgiesser (1980) reported that *L. monocytogenes* could survive well in the environment (20–30 days on dry tiled surfaces and 10 days in tap water) and suggested that clinicians should be informed of the relative numbers of cases that lead to cross-infection and the need for barrier nursing of neonates with listeriosis.

Table V. Common source outbreaks of listeriosis

Place	Time of outbreak	Number of cases			Suggested agents of serogroup transmission	Reference	
		Total	Adults	Perinates			
Prague, Czechoslovakia	Aug.-Nov. 1955	41	0	41	1/2	NK	Mencikova, 1956
Bremen, Germany	NS 1960-1961	81	NS	NS	NS	NK	Seeliger <i>et al.</i> , 1969
Bremen, Germany	NS 1963	20	NS	NS	NS	NK	Seeliger <i>et al.</i> , 1969
Halle, Germany	Apr.-Dec. 1966	279	0	279	1/2	NK	Ortel, 1968
Auckland, New Zealand	Apr.-Sep. 1969	20	6	14	NS	NK	Flight, 1971
Greenville, USA	Mar.-Oct. 1975	6	0	6	4b	NK	Filice <i>et al.</i> , 1978
Anjou, France	Jan.-Jun. 1976	162	36	126	4b	NK	Carbonnelle <i>et al.</i> , 1979
Perth, Australia	Jan.-Mar. 1978	4	0	4	NS	NK	Le Souef and Walters, 1981
Perth, Australia	Jan.-Mar. 1979	6	0	6	NS	NK	Le Souef and Walters, 1981
Auckland, New Zealand	Jan.-Jun. 1980	21	3	18	1/2a	Seafood ?	Lennon <i>et al.</i> , 1984
Nova Scotia, Canada	Apr.-Sep. 1981	41	7	34	4b	Coleslaw	Schlech <i>et al.</i> , 1983
Houston, USA	May.-Jul. 1983	10	0	10	1/2b	NK	Canfield <i>et al.</i> , 1985
Massachusetts, USA	Jun.-Aug. 1983	49	42	7	4b	Milk	Fleming <i>et al.</i> , 1985
Lausanne, Switzerland	Jan. 1983-Mar. 1984	25	14	11	4b	NK	Malinverni <i>et al.</i> , 1985

NK = not known; NS = not stated.

Common source infections

(a) *East Cumbria outbreak.* Such a large number of cases in a 6-month period was not seen in the area served by the Carlisle Public Health Laboratory either before or after this cluster of strains (D. G. Davies, Carlisle Public Health Laboratory, personal communication) even though a particular interest in the organism developed. The large cluster of cases in a short time suggested a common source outbreak; the results of our serotyping and phage typing of the isolates are consistent with but do not prove this view. A mode of transmission was not established for this outbreak (S. Hall, CDSC Colindale, personal communication).

(b) *Common source or cross-infection episodes in hospitals and clusters of cases in the community.* The occurrence of listeriosis in four adults treated in a Liverpool hospital during a 2-month period (Green and Macaulay, 1978) in cluster 1 and the isolation of strains of indistinguishable phage type from each patient suggest a causal link. Either cross-infection took place as has been suggested (Green and Macaulay, 1978; Taylor *et al.*, 1981) or these patients were infected from a common source. The mode of transmission of listeriosis to the pair of neonates in cluster 2 is clearly dissimilar to that already described for the 10 pairs of neonates in whom cross-infection was suspected. Although these two neonates were born in the same hospital within a short period of time and the isolates of *L. monocytogenes* from the babies were indistinguishable by phage typing, the isolation of indistinguishable strains from both mothers, who were also seropositive, suggests an epidemiological link other

than cross-infection. They may have been infected from an unknown source (e.g., food), or cross-infection between the mothers may have occurred during pregnancy (possibly through obstetric examination). At the time when these two clusters of cases occurred a high proportion of the other cases caused by *L. monocytogenes* serogroup 4 were also indistinguishable by phage-typing from these strains, and the cases were restricted to a few Regional Health Authorities (especially in the case of cluster 1). Strains of these "epidemic" phage-types did not occur at high frequencies during preceding and following periods throughout Britain, nor in the Health Authorities where the clusters occurred in subsequent years (results not given).

These clusters may represent common source outbreaks. Several such outbreaks have been reported (table V); some affected more than 100 people, most notably those in Halle, East Germany (Ortel, 1968), and Anjou, France (Carbonnelle *et al.*, 1979). In common with clusters 1 and 2 and the East Cumbria outbreak, these occurred during a period of several months, but otherwise had few common features. They occurred throughout the year (regardless in which hemisphere they took place), affected either mainly adults or mainly perinates or similar numbers of each, and involved either serogroup 1/2 or 4.

The mode of transmission of epidemic or sporadic listeriosis is largely unknown, although one possible vehicle for *L. monocytogenes* is food. It has long been realised (Gray, 1963) that there is an apparent relationship between silage feeding and listeriosis in ruminants, but a clear relationship between food and human listeriosis has only rarely

been established and the extent to which food may be involved is unclear. Because *L. monocytogenes* grows and multiplies at +4°C, refrigerated food such as meat, eggs, poultry, vegetables and milk are implicated as potential sources of infection. Raw poultry (Kwantes and Isaac, 1975; Gitter, 1976) and red meat (Höhne *et al.*, 1975; Elischerova *et al.*, 1979) are frequently contaminated with *L. monocytogenes*, and the usual preserving agents such as sodium chloride and sodium nitrite inhibit the growth of this organism only slightly (Shahamat *et al.*, 1980). *L. monocytogenes* causes mastitis in cows (Gitter *et al.*, 1980) and large numbers of bacteria may be shed into milk. Burn (1936) suggested milk as a possible source of infection and Gray (1963) recalls that a woman who drank raw milk from a cow with mastitis subsequently gave premature birth to still-born twins infected with *L. monocytogenes* of the same serogroup as that isolated from the milk. Pasteurisation of milk may not completely eradicate *L. monocytogenes* when present in large numbers (Bearn and Girard, 1958) and in one recent outbreak (Fleming *et al.*, 1985) milk was suggested to be the vehicle of infection. In another outbreak (Schlech *et al.*, 1983), coleslaw salad was a possible source, and *L. monocytogenes* of the serotype implicated in the outbreak was grown from coleslaw from the refrigerator of one of the patients. The cabbage used in the coleslaw was from a farm where cases of ovine listeriosis had occurred. In both these clusters of cases phage-typing results were consistent with a common source food-borne outbreak (Audurier *et al.*, 1984; Fleming *et al.*, 1985).

The need for typing schemes of higher discrimination than those generally available is evident. We estimate the incidence of listeriosis in man in the UK to be at least 0.18 cases per 10⁵ of the total population per year. This figure represents the minimum incidence because it was calculated from the number of cases from which cultures were sent to DMRQC and does not include cases reported to the Communicable Disease Surveillance Centre Colindale without isolates being sent to DMRQC, or cases which were unreported to either centre.

Table VI. Incidence of human listeriosis in northern Europe and North America (adapted from Ralovich, 1984)

Country	Cases /10 ⁵ total population/year
Germany (GDR)	0.336
France	0.327
Denmark	0.227
Switzerland	0.205
Netherlands	0.169
Sweden	0.148
Germany (FRG)	0.096
USA	0.066
Canada	0.062

Estimates for the incidence of listeriosis in North America and Northern Europe (table VI) show that the incidence is considerably higher in France and the UK than in the USA and Canada. In countries with lower incidence, outbreaks will be more obvious because of the lower background of individual cases, but in countries with a higher incidence cases related by source may be much more difficult to identify without highly discriminatory typing schemes.

Listeriosis in man is sporadic in nature and of low incidence; the route of transmission is usually impossible to determine. We have highlighted some possible routes of infection and presented data which support these epidemiological relationships. Although listeriosis is a disease common to animals and man there is rarely an obvious epidemiological relationship between them, and the disease is not considered to be principally a true zoonosis. *L. monocytogenes* occurs ubiquitously in man, animals and the environment, and has many of the characteristics of a saprophyte. It has even been suggested (Maupas *et al.*, 1975) that listeriosis should be categorised as a "sapronis", i.e., a disease of "man and animals contaminated from a common origin constituted by the outer environment".

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