ACM/667

INFORMATION PAPER

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD (ACMSF)

RECENT TRENDS IN LISTERIOSIS IN THE UK

Background

1. This paper summarises the rising trend in reported cases of human listerosis in the UK focussing particularly on increases seen in the Yorkshire and Humberside and Northeast regions of England. Molecular typing, particularly AFLP, has been helpful in unraveling what appears to be a complex epidemiological picture.

2. The paper also summarises two outbreaks of foodborne listeriosis in 2003.One outbreak occurred predominantly in the Yorkshire and Humberside region in the first half of 2003 and was linked to butter from a local dairy. A small outbreak in Wales in June was linked to sandwiches.

Action required

The committee's views are sought on a number of issues arising from the paper.

Secretariat

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RECENT TRENDS IN LISTERIOSIS IN THE UK

Introduction

1. Listeriosis is a rare bacterial infection in humans caused by *Listeria monocytogenes.* Between 1990 and 2000 there were between 114 and 136 laboratory confirmed cases in the UK per year. Around 16% of cases in England and Wales between 1990 and 2003 were pregnancy-associated, the remainder being associated with other vulnerable groups particularly the elderly and immunocompromised. Most cases of listeriosis are sporadic and outbreaks in the UK are rare. The disease can result in abortion and stillbirth in pregnant women and has a high mortality rate in the elderly and immunocompromised. *Listeria* can also infect animals, with cattle and sheep being most affected.

2. Contaminated food is considered to be the main source of *Listeria* infections in humans. A number of different foods have been implicated in outbreaks in various parts of the world, including dairy products (e.g. milk, soft cheeses), processed meats (e.g. pate, rillettes, deli meats), seafood (e.g. mussels, smoked fish) and vegetable/cereal products (coleslaw, corn-meal) (Ryser 1999). In the UK in 1987-89 there was a large outbreak of listeriosis linked primarily to the consumption of pâté particularly by pregnant women. Action to address this problem and the concerns raised about the finding of the organism in certain soft mould-ripened cheeses and cooked chill foods led to a raft of government and industry advice to consumers, much of which remains in place today.

3. Outbreaks present as either localised or geographically dispersed depending on the distribution of a contaminated food vehicle. Recognition of outbreaks is hampered by the prolonged incubation period for the disease and periods ranging from 1 to 90 days are cited, although in pregnancy-associated cases the time between exposure and onset of illness is likely to be shorter. Recent developments in molecular typing/fingerprinting such as Amplified Fragment Linked Polymorphisms (AFLP) and Pulsed Field Gel Electrophoresis (PFGE) should enable better detection of clusters of cases and outbreaks where previously these may have gone undetected (Graves *et al.,* 1999; Guerra *et al*., 2002; Sauders *et al.,* 2003).

4. This paper reports on the recent trends in listeriosis in the UK and provides details on outbreaks in 2003 linked to butter and sandwiches. A number of issues are raised by these findings and the Food Standards Agency is seeking the committee's views to inform further work in this area.

Increase in reports of listeriosis in humans in England and Wales

5. Listeriosis is a rare disease in the UK. During the 1990s the annual number of reported cases ranged from 90 to 128 per year in England and Wales, 6 to 17 per year in Scotland and 1 to 6 per year in Northern Ireland.

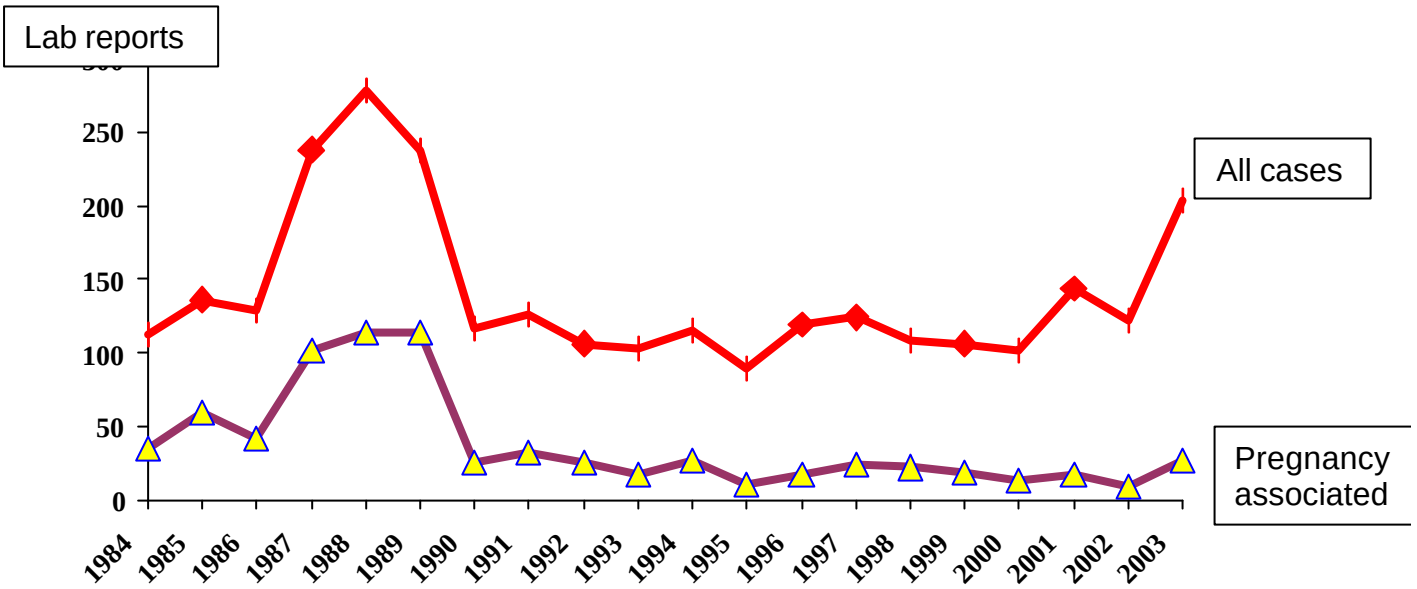

Figure 1. Number of cases of listeriosis in England and Wales 1983-2003. Data provided by HPA-CDSC and FSML. Data for 2003 is up to 14 November 2003. The data for 2002 and 2003 are provisional.

6. During the first ten months of 2003 there was a marked increase in the number of listeriosis cases reported in England and Wales but no evidence of a noticeable increase in cases elsewhere in the UK. Up to 14 November the Health Protection Agency's (HPA) Communicable Disease Surveillance Centre (CDSC) and Food Safety Microbiology Laboratory (FSML) were aware of 204 cases in England and Wales in 2003 compared to 144 cases in 2001 and 122 in 2002 (Figure 1). In Scotland and Northern Ireland there have been 8 and 3 cases respectively in 2003 up to 14 November The figure for England and Wales represents the first significant increase in cases of listeriosis since 1990. The peak of listeriosis cases in 1987-89 is considered to have been associated with consumption of contaminated pâté (McLauchlin *et al.,* 1991).

7. An HPA report earlier this year highlighted the rise in listeriosis cases in England and Wales between January and May and attributed most of the rise to increases in the Yorkshire and Humberside and Northeast regions (Anon 2003). This trend has continued and although some other regions have shown a slightly elevated incidence rate compared to 2002, the rates in Yorkshire and Humberside and Northeast regions remain higher than elsewhere (Figure 2).

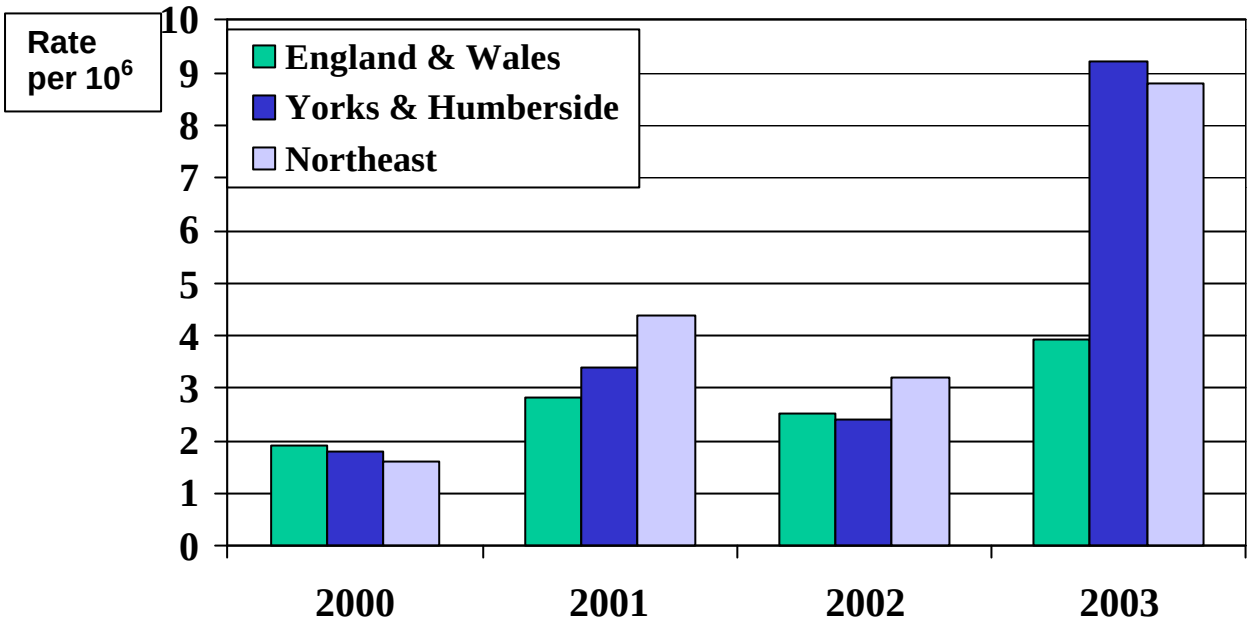

Figure 2. Incidence of listeriosis (rate per million population) in Yorkshire and Humberside and the Northeast compared to England and Wales as a whole 2000-2003. Data provided by HPA-CDSC and FSML. Data for 2003 is up to 14 November.

8. The increase in the number of reported listeriosis cases in England and Wales during the first ten months of 2003 is unusual. There is no clear indication that the increase is due to enhanced ascertainment, reporting or surveillance. The increase also appears to have occurred earlier in the year than expected since human listeriosis in England and Wales has tended to peak in late summer or autumn.

9. Unexpected increases in reported listeriosis cases have previously been seen in the USA and France and involved multiple *L.monocytogenes* types (Louria *et al*., 1990; Rocourt *et al.,* 1989; Schwartz *et al.*, 1989; Schwartz & Broome 1990). Whilst there appears to be no clear explanation for this, changes in susceptibility associated with external factors, have been postulated as a possible factor.

10. Individual cases of human listeriosis within foodborne outbreaks can be very widely geographically and temporally separated. This is because of both the long incubation periods shown by some of the patients between exposure to onset of illness (up to three months and possibly longer), the low attack rates, the national and international distribution of food and also the persistence of the organism in colonising sites within food manufacturing environments for extended periods.

11. Clinical and food isolates of *L.monocytogenes* examined by the HPA's Food Safety Microbiology Laboratory are now subtyped by serotyping, phage typing, AFLP and PFGE. During 2003, the combined subtyping methods were applied to all cultures except for PFGE, which was applied to selected cultures. The combined approach has been helpful in identifying clusters of cases in 2003, which share a particular AFLP profile, serotype, and phage type combination. Isolates from previous years are also being examined. For example, during 2003 there were 11 possible clusters of 5-17 cases per cluster which comprised 53% (102/192) of the cases with typing date in England and Wales.

12. Microbiological subtyping can prove useful in confirming the vehicle of infection in foodborne outbreaks. In two investigations this year common strains of *L. monocytogenes* were isolated from epidemiologically linked cases as well as from contaminated foods and environmental samples taken from food producers. Sandwiches were implicated in both outbreaks and in one of these the source of infection was traced to butter from a single production plant. However, it is important to recognise that although this approach has been helpful in defining cases involved in particular foodborne outbreaks, other clusters remain to be explained despite the screening of food isolates from routine testing and surveys.

13. Further work is needed to evaluate the combined typing approach for routine use and to build up information on subtypes present in foodstuffs. It is hoped that when combined with epidemiological data and food testing it will help explain current and future patterns and trends in listeriosis in the UK.

Outbreak of listeriosis linked to butter

14. The increase in listeriosis in the Yorkshire and Humberside and Northeast regions was referred to in the preceding section. Within this increase one cluster was defined by the same unusual AFLP profile, serogroup and phage type combination – (AFLP type V, serotype 4b, phage type A). To date 17 laboratory-confirmed cases of this type have been reported in 2003, 11 of which were pregnancy-associated. All cases had specimen dates between 31 January and 8 July 2003, and all but 3 of the cases were from the Yorkshire and Humberside region. Most of the cases occurred in May and June.

15. An unusual feature is the way in which the investigation developed. In most outbreaks that are not obviously due to a point source, cases are identified on the basis of microbiological typing data and epidemiological studies undertaken to try to identify vehicle(s) of infection. Microbiological investigations of suspect foods and/or premises would follow if practicable, for example, in continuing source outbreaks or where suspect batches of food are available for testing. In this outbreak, information on the probable food vehicle came to light as a result of routine testing arrangements, quite independently of the outbreak investigation and hence the microbiology and epidemiology ran in parallel and at different rates.

16. The outbreak was first detected in May when there were indications of localised clustering of cases in the Huddersfield area. At the same time, it was noted that there had been a problem with low level, intermittent *L.monocytogenes*

contamination of butter produced at a dairy also in the Huddersfield area. This had been identified as a result of routine sampling by the Local Authority in April and further testing had confirmed the presence of *L. monocytogenes* at a count of 180 cfu/g in one batch of butter. In other batches the organism was only detectable or present at low levels (<20 cfu/g). Following further positive samples of butter (albeit at levels <20 cfu/g) and investigations of hygiene at the dairy, a positive release system for butter production was introduced in the middle of May coupled with revised cleaning procedures. No *L.monocytogenes was* detected in subsequent butter production although it was detected in a drain at the factory in June and July.

17. Initially the amount of information about molecular typing of human and butter isolates was limited because the discriminatory power of the AFLP technique for *L.monocytogenes* was not well established and few food isolates had been screened. In mid June the results of a case-control study provided no conclusive evidence of an association with a single food item although the number of cases for inclusion in the study was small. However, the hypothesis that contamination of a locally produced butter or cream, perhaps as an ingredient used in garlic butter in Italian restaurants, remained plausible. There was also an association with chicken Korma, possibly related to the use of cream and yoghurt in this type of dish. Descriptive evidence gathered from interviews with cases who had listeriosis subsequently pointed more strongly to an association between the pregnancy-associated cases and consumption of sandwiches. However, it was not until the end of June that a clear picture began to emerge that provided a microbiological link between contaminated butter and the cases of illness. This was further complicated by the fact that the butter was distributed more widely than the cases of illness. However, there was descriptive evidence to suggest that cases could have been exposed through the use of the 2kg catering packs of butter in local sandwich outlets rather than consuming contaminated product in the home.

18. Steps were taken by the dairy to recall 2kg packs produced prior to the middle of May when the positive release system was put in place and at the request of the Food Standards Agency this was subsequently extended to cover any 2kg product. A Food Hazard Warning was issued by the FSA on 15 July. There have been no further cases of the *L.monocytogenes* strain (AFLP type V, serotype 4b, phage type A) since 8 July and the outbreak in Yorkshire and Humberside was declared over on 17th November.

19. There are two outbreaks in the literature linked to butter. An outbreak of listeriosis in Finland in 1998-9 due to *L.monocytogenes* serotype 3a has some features in common with the present outbreak (Lyytiksinen *et al*., 2000; Maijala *et al*. 2001). Although contaminated product was widely distributed to retail, catering and hospitals the 25 cases all occurred in a single long-stay hospital suggesting that local factors (prolonged daily consumption of a single brand, handling practices) may have influenced whether people became ill. A cluster of 11 pregnancy-associated cases of listeriosis due to *L.monocytogenes* serotype 1/2a occurred in Los Angeles County, USA in 1987. A case control study identified butter as a possible food vehicle although the organism was not isolated from butter (Mascola *et al*., 1988).

20. Butter is a water in oil emulsion and unlike many other ready-to eat foods would not appear to be a good growth medium for *L.monocytogenes*. Salt is added

during manufacture and concentrates in the water phase ideally at concentrations at or close to the limit for growth of the organism at chill temperatures. However, although some studies have shown no or poor growth of the organism in butter or butter-margarine blends and other spreads (Maijala *et al*., 2001; Holliday & Beuchat 2003) in others growth of approx. 2-3 logs was observed during storage for 6-7 weeks at 4-6^{o}C or 13^{o}C (Olsen *et al*.,1988). Lanciotti *et al*. (1992) reported growth in commercially prepared light butter (approx. 6% salt in aqueous phase) stored at 4^{o}C and 20^{o}C. The shelf-life of the butter in the 2003 outbreak was reported to be 6-7 weeks. The incident has raised a number of questions concerning the growth and survival of *L.monocytogenes* in relation to the formulation and structure of butter and the Agency will be giving due consideration as to whether further research is needed in this area.

21. In the present outbreak, butter supplied in 2kg tubs from the dairy is considered to have been the most likely source of infection although, given the complexity of the outbreak, other sources cannot be entirely ruled out. The evidence for butter being the source of the outbreak strain is based on the same rare type of *L.monocytogenes* (V-4b-A) being isolated on more than one occasion from butter at the dairy, from a drain at the dairy and from cases of listeriosis in the outbreak. Additional work using another molecular typing method (PFGE) has provided further evidence in support of the identical nature of the isolates from the different sources. *Listeria w*as not isolated from other dairy products produced by the dairy during the outbreak.

22. The Local Authority test results at the time of the outbreak were technically a failure for the *L.monocytogenes* standard under the Dairy Products (Hygiene) Regulations 1995. However, given the low levels reported, the nature of the product and the absence of further positive tests, this would not normally be considered an immediate danger to human health. The guidance to Environmental Health Officers on Code Of Practice 18 for enforcement of the regulations indicates that, where operators encounter problems in meeting standards, then immediate attention to hygiene, coupled with further testing would be an appropriate course of action which is what happened in this case. However, it may well be that those who became ill were exposed to food containing much higher levels of *L.monocytogenes*, possibly because the contamination peak occurred in an earlier batch than those tested, or because of the way in which the product was handled and used subsequently.

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Outbreak linked to sandwiches

23. At the end of May an outbreak of listeriosis occurred in Wales involving 2 outpatients who were reported to have consumed pre-packed ham salad and tuna salad sandwiches at a hospital. Follow-up testing of a wide range of sandwiches at the hospital and investigations at the factory revealed evidence of *Listeria* contamination although the majority of food results were within the PHLS guidelines for ready-to-eat foods. Isolates from the 2 cases were indistinguishable by AFLP, serogroup and phage type. Isolates from the sandwiches were of the same type, which had not been seen in other food and environmental isolates from England and Wales at that time.

24. A similar incident occurred during April and May 1999 involving 4 cases of listeriosis in the Tyne and Wear area (Anon 1999; Graham *et al*., 2002). The clusters comprised people who had underlying illness and who were either already in hospital or were outpatients. Isolates from 2 of the cases could be linked by typing to a strain of *L.monocytogenes* isolated from a cheese and salad sandwich. The caterer producing the sandwich supplied shops within the 2 hospitals where the 4 cases occurred.

Action required

The committee's views are sought on the following points:

1. What further action could be taken to identify the source of the rising trend in cases of listeriosis including surveillance, molecular typing and epidemiological investigation.

2. Whether, in the light of recent trends, the advice targeted to different vulnerable groups needs to be a) re-emphaised b) updated and c) evaluated.

In relation to future incidents:

3. Whether in future, when *Listeria monocytogenes* is found in a ready-to-eat product and there are associated cases of illness, that product should be (a) withdrawn and (b) recalled.

4. Whether, in the absence of illness, ready-to-eat products where *Listeria monocytogenes* is not normally expected (including butter), should be (a) withdrawn, (b) recalled if any *Listeria monocytogenes* is detected, notwithstanding the existing consensus that products containing levels below 100 cfu/g can be safely consumed. This consensus currently forms the basis for proposed microbiological criteria in the EU.

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