Part 1.

Hazard Identification

1.1 HISTORICAL

Early reports suggest that *Listeria monocytogenes* may have been isolated from tissue sections of patients in Germany in 1891, from rabbit liver from Sweden in 1911, and from spinal fluid of meningitis patients in 1917 and again in 1920 (Reed, 1958; McCarthy, 1990). However, it was not until 1926 that the microorganism was fully described, when Murray, Webb and Swann (1926) isolated a small, Gram-positive rod bacterium that had caused an epizootic outbreak in 1924 among rabbits and guinea pigs. They named the organism *Bacterium monocytogenes*. This was a year after listeriosis in sheep was recognized in Germany as a disease syndrome, though the causative agent had not been isolated. At approximately the same time, Pirie (1927) isolated and described the same organism from gerbils in South Africa. He named the bacterium *Listerella hepatolytica*, and subsequently recommended in 1940 that the name be changed to *Listeria monocytogenes* (Reed, 1958; McCarthy, 1990). The first report of human listeriosis was in 1929, and the first perinatal case was reported in 1936 (Gray and Killinger, 1966). The microorganism has been reported to cause disease in a wide range of wild and domestic animals, and has been isolated from numerous species of mammals, birds, amphibians, fish, crustaceans, insects and reptiles (Hird and Genigeorgis, 1990; McCarthy, 1990; Ryser and Marth, 1991).

It is now widely recognized that human listeriosis is largely attributable to foodborne transmission of the microorganism. However, the first case of foodborne listeriosis was not reported until 1953, when the stillbirths of twins was linked to consumption by the mother of raw milk from a cow with listerial mastitis (Potel, 1953). It was not until several large, common-source outbreaks of listeriosis occurred in North America and Europe during the 1980s that the significance of foods as the primary route of transmission for human exposure to *L. monocytogenes* was recognized (Broome, Gellin and Schwartz, 1990; Bille, 1990). While the modes of transmission for *L. monocytogenes* can include vertical (mother to child), zoonotic (contact with animal to man), and nosocomial (hospital acquired), it is generally considered that most cases of human listeriosis involve foodborne transmission.

1.2 CHARACTERISTICS OF *LISTERIA MONOCYTOGENES*

L. monocytogenes is a Gram-positive, facultatively anaerobic, non-sporeforming rod, which expresses a typical tumbling motility at 20–25°C, but not at 35°C. The organism is psychrotrophic and grows over a temperature range of 0° to 45°C, with an optimum around 37°C. *L. monocytogenes* can grow at pH levels between 4.4 and 9.4, and at water activities ≥0.92 with sodium chloride (NaCl) as the solute (Miller, 1992). The effects of temperature, pH, water activity, oxygen availability and antimicrobials on the growth of *L. monocytogenes* have been studied extensively in both model systems and foods, and there are a number of mathematical models available for describing the interaction of these factors with the growth rate (Buchanan and Phillips, 2000).

L. monocytogenes is widely distributed in the environment and has been isolated from a variety of sources, including soil, vegetation, silage, faecal material, sewage and water. The bacterium is resistant to various environmental conditions, such as high salinity or acidity, which allows it to survive longer under adverse conditions than most other non-sporeforming bacteria of importance in foodborne disease (McCarthy, 1990; Ryser and Marth, 1991). *L. monocytogenes* occurs widely in food processing environments (Ryser and Marth, 1991, 1999), and can survive for long periods in foods, in processing plants, in households, or in the environment, particularly at refrigeration or frozen storage temperatures. The ability of *L. monocytogenes* to survive in foods and model systems has been studied extensively, and mathematical models are available that describe the effect of various environmental parameters on the microorganism's survival (Buchanan and Golden, 1994, 1995, 1998; Buchanan, Golden and Whiting, 1993; Buchanan et al., 1994; Buchanan, Golden and Phillips, 1997).

Although frequently present in raw foods of both plant and animal origin, it is also present in cooked foods due to post-processing contamination if the cooked food is handled post-cooking. *L. monocytogenes* has been often isolated from food processing environments, particularly those that are cool and wet. *L. monocytogenes* has been isolated in foods such as raw and pasteurized fluid milk, cheeses (particularly soft-ripened varieties), ice cream, raw vegetables, fermented raw meat and cooked sausages, raw and cooked poultry, raw meats, and raw and smoked seafood (Buchanan et al., 1989; Farber and Peterkin, 1991; FDA/FSIS, 2001; Ryser and Marth, 1991, 1999). Even when *L. monocytogenes* is initially present at a low level in a contaminated food, its ability to grow during refrigerated storage means that its levels are likely to increase during storage of those foods that can support the growth of the microorganism. A survey of a wide variety of foods from the refrigerators of listeriosis patients in the United States of America found *L. monocytogenes* in at least one food specimen in 64% of the patient's refrigerators. Food in 33% of the refrigerators had the same strain as the patient strain (Pinner et al., 1992). However, because the frequency at which people are exposed to *L. monocytogenes* is much higher than the incidence of listeriosis, there has been a public health debate about the significance of ingesting low levels of the pathogen, particularly for the portion of the population who are not immunologically compromised (Farber, Ross and Harwig, 1996; ICMSF, 1994).

1.3 OVERVIEW OF LISTERIOSIS

Listeriosis is a relatively rare disease. The reported yearly incidence of human listeriosis ranges from 0.1 to 11.3 cases per million persons (references cited in Notermans et al*.,* 1998), with for example 0.3 to 7.5 cases per million people in Europe (EC, 2003), and 3 cases per million people in Australia. The data from the U.S. Centers for Disease Control and Prevention (CDC) active food surveillance programme, FoodNet, for the years from 1996 to 1998 indicate that there were about 5 reported cases of listeriosis per 1 000 000 population annually. Using the CDC 1996–97 surveillance data (CDC, 1998) and extrapolating to the 1997 total United States of America population, Mead et al. (1999) estimated that there were 2493 cases, including 499 deaths, due to foodborne listeriosis Although listeriosis is a relatively rare foodborne illness (Table 1.1), its severe nature makes it likely that individuals will seek medical care. In the United States of America, where listeriosis is a "reportable" disease, CDC estimates that it recognizes and identifies approximately half of all listeriosis cases, as compared to the 3% identification rate for most other foodborne pathogens (Mead et al., 1999).

Table 1.1. Estimated incidence of foodborne disease from epidemiological surveillance.

Pathogen	Cases per 1 000 000 population
Vibrio	3
Listeria	5
Yersinia	10
E. coli O157:H7	28
Shigella	85
Salmonella	124
Campylobacter	217
All bacterial pathogens	472

SOURCE: FoodNet data for 1997 (CDC, 1998).

One of the difficulties in characterizing the hazard associated with foodborne listeriosis is that there are no clear definitions for infection or cases in humans. In general, most cases that are reported to medical authorities are severe infections requiring medial intervention. Thus, for the purposes of the current hazard characterization, an infection in humans will be based on the colonization of the host, i.e. attachment and growth, which can include individuals that are asymptomatic, displaying febrile gastroenteritis, or suffering from severe symptoms or death. The terms "severe infection" or "invasive listeriosis" will be used to describe those infected individuals with life-threatening, systemic infections, such as perinatal listeriosis, meningitis or septicaemia, and where *L. monocytogenes* is present in normally sterile body tissues.

Invasive *L. monocytogenes* infections can be life threatening, with fatality rates of 20 to 30% being common among hospitalized patients. In 2000, the CDC (2000) reported that, of all the foodborne pathogens tracked by CDC, *L. monocytogenes* had the second-highest case fatality rate (21%) and the highest hospitalization rate (90.5%).

L. monocytogenes causes invasive listeriosis by penetrating the lining of the gastrointestinal tract and establishing infections in normally sterile sites within the body. Once *L. monocytogenes* penetrates the intestinal tissue it is taken up by cells of the immune system, the phagocytes. However, inside the phagocyte it is capable of escaping from the phagosome and subsequently growing. Phagocytes appear to be the means by which the bacterium can be transported to various parts of the body (Shelef, 1989; Farber and Peterkin, 1991).

The likelihood that *L. monocytogenes* will invade the intestinal tissue depends upon a number of factors, including the number of organisms consumed, host susceptibility, and virulence of the specific isolate (Gellin and Broome, 1989). Incubation periods can be long, e.g. typically 2-3 weeks, and up to three months (Gellin and Broome, 1989). *L. monocytogenes* can produce a wide range of symptoms. In non-pregnant adults, disease syndromes most commonly linked to *L. monocytogenes* include bacteraemia, meningitis and encephalitis (Rocourt and Cossart, 1997). In pregnant women, *L. monocytogenes* often causes an influenza-like bacteraemic illness, which leads to amnionitis and infection of the fetus and results in abortion, stillbirth or premature birth. Listeriosis occurs most often either very early in life or after 60 years of age. Figure 1.1 shows listeriosis incidence by age, using 1997 FoodNet data. The incidence of listeriosis in males and females is approximately equal.

As more information became available linking listeriosis with food consumption, food control agencies and private industry developed programmes to reduce the incidence of foodborne listeriosis. Industry initiated HACCP programmes and increased sanitation efforts to eliminate contamination. Food control agencies expanded programmes to prevent contaminated foods from entering commerce. There were also consumer education campaigns that focused on food safety. In the United States of America, a reduction in listeriosis from 7.9 per million in 1989 to 4.4 per million in 1993 was observed (Tappero et al., 1995). Rates of listeriosis simultaneously declined in the United Kingdom after the British government issued health warnings regarding *L. monocytogenes* (Fyfe et al., 1991; McLauchlin et al., 1991). Similar declines have been reported as a result of public health initiatives in other parts of Europe and in Australia (Jacquet et al., 1999). For example, it is reported that preventative measures implemented by the French food industry played a substantial role in the 68% reduction observed in France between 1987 and 1997 (Goulet et al., 2001a). However, since that time, the incidence of listeriosis has remained relatively constant (CDC, 2000). The reported yearly incidence of human listeriosis in Europe ranges from 0.1 to 11.3 cases per 10^6 persons (references cited in Notermans et al., 1998). A more recent study within the European Union indicates a slight decrease, with the reported yearly incidence of listeriosis for 2000-2001 ranging from 0.3 to 7.8 cases per million persons (de Valk et al., 2003). However, the accuracy of these values is dependent on the vigour with which individual countries conduct national surveillance programmes for listeriosis.

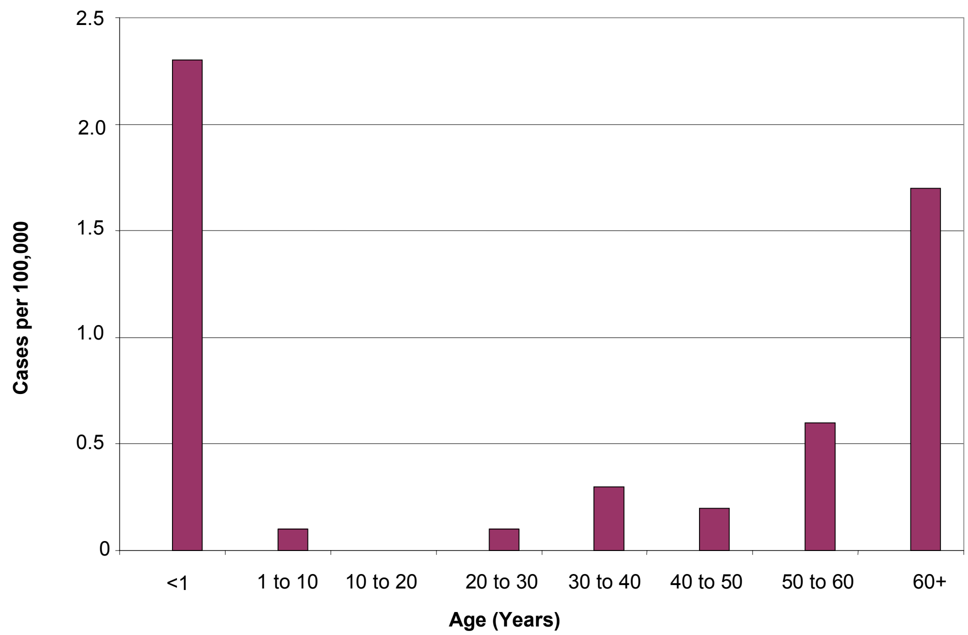

Figure 1.1. Estimated rate of listeriosis by age.
SOURCE: FoodNet 1997 data (CDC, 1998).

1.4 STATEMENT OF PROBLEM AND SCOPE OF RISK ASSESSMENT

Foodborne listeriosis represents a relatively rare but clinically serious disease that largely affects specific higher-risk segments of the population. The microorganism is widely dispersed in the environment and foods and it appears to be ingested in low numbers by consumers on a routine basis. Despite the fact that a wide variety of foods may be contaminated with *L. monocytogenes*, outbreaks and sporadic cases of listeriosis appear to be predominately associated with ready-to-eat (RTE) products. A number of risk assessments and related evaluations of foodborne listeriosis have been conducted by investigators and national governments. The current risk assessment was undertaken to determine, in part, how previously developed risk assessments done at a national level could be adapted or expanded to address concerns related to *L. monocytogenes* in RTE foods at an international level. This included an international team conducting a risk assessment to answer questions posed by an international organization. Data from different countries were used. This does not imply that the risk assessment reflects the global food supply or that the specific results are universally applicable, as different countries will have differences in contamination levels, processing and consumption patterns that are not addressed in this risk assessment. In addition, after initiation of the risk assessment, the risk assessment developers were asked by the Codex Committee on Food Hygiene (CCFH), through FAO/WHO, to consider three specific points related to RTE foods in general, namely:

- Estimate the risk of serious illness from *L. monocytogenes* in food when the number of organisms ranges from absence in 25 grams to 1000 colony forming units (CFU) per gram or millilitre, or does not exceed specified levels at the point of consumption.
- Estimate the risk of serious illness for consumers in different susceptible population groups (elderly, infants, pregnant women and immunocompromised patients) relative to the general population.
- Estimate the risk of serious illness from *L. monocytogenes* in foods that support its growth and foods that do not support its growth at specific storage and shelf-life conditions.

Considering the resources available and the time constraints placed on the risk assessment developers, it was impossible to consider all RTE foods that could be contaminated with *L. monocytogenes*. Accordingly, it was decided to limit the risk assessment to a small number of RTE foods selected to represent various classes of product characteristics. These foods were selected to provide realistic examples of how microbiological risk assessment techniques could be used to evaluate food safety questions at an international level. This educational component is a stated goal of the FAO/WHO microbiological risk assessment programme under the auspices of which the current risk assessment was developed. It was also decided to limit the scope of the risk assessment to foods at retail and their subsequent public health impact at time of consumption. This was done for two reasons. The first is that such a scope was sufficient to address the charge provided by the requestors of the risk assessment within the time frames and resources made available to the developers. Second, most of the exposure data for *L. monocytogenes* that are currently available are frequencies and extents of contamination at the retail level. More detailed examination of factors contributing to the levels found at retail as a result of manufacturing parameters would have either restricted evaluation to a much smaller range of foods, or required that substantially greater resources and data be made available. Accordingly, the assessment does not evaluate the risks associated with different means of manufacturing the products selected. However, the risk assessment does consider several post-retail factors that could influence the consumers' risk of acquiring foodborne listeriosis, such as the temperature and duration of refrigerated storage.