



Feidhmeannacht na Seirbhíse Sláinte  
Health Service Executive



INSTITUTE OF OBSTETRICIANS  
& GYNAECOLOGISTS  
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

## **CLINICAL PRACTICE GUIDELINE**

### **LISTERIOSIS IN PREGNANCY**

Institute of Obstetricians and Gynaecologists,  
Royal College of Physicians of Ireland  
and the  
Clinical Strategy and Programmes Division,  
Health Service Executive

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## 1. Revision History

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1.0	April 2015	Dr. Rupak K Sarkar	Version 1.0 Draft for review

## 2. Key Recommendations

1. Listeriosis is mainly a foodborne infection. Pregnant women should avoid eating food with a high risk of contamination with *Listeria*. This information may be incorporated into formal antenatal education. Special attention should be paid towards food handling, preparation and storage.
2. Pregnant women who are exposed to, or who develop symptoms of Listeriosis should be assessed to determine if maternal and fetal investigations are required.
3. No testing, including blood and stool cultures, or treatment is indicated for an asymptomatic pregnant woman who reports consumption of a product that was recalled or implicated during an outbreak of listeria contamination. An asymptomatic patient should be instructed to return if she develops symptoms of Listeriosis within two months of eating the recalled or implicated product. There is no reason to alter or begin fetal surveillance in asymptomatic women with known or presumptive exposure to *Listeria*.
4. There are no data to guide the management of an exposed, afebrile pregnant woman with mild symptoms that do not strongly suggest Listeriosis. Such a woman can be managed expectantly, alternatively, such a woman could be tested with blood culture for *Listeria*, but if such a course is elected, specific instruction should be given to the microbiology laboratory and treatment only commenced if blood cultures yield *Listeria*. A baseline fetal assessment may be performed and only continued if cultures or symptoms dictate so.
5. If suspicion for Listerial infection is high, blood cultures should be considered in any pregnant woman presenting with fever, especially if accompanied by flu like or gastro intestinal symptoms. After obtaining cultures, care providers should consider starting treatment. Initiating a program of fetal surveillance seems prudent for women in whom Listeriosis is diagnosed or strongly suspected because of exposure and fever with or without other symptoms, although studies and data do not exist to point to one best plan for such testing.

### 3. Purpose and Scope

The purpose of this guideline is to outline investigations and management of pregnant women exposed to / experiencing symptoms of Listeriosis.

This guideline summarises the relevant evidence and provides practice recommendations related to the investigation and management of cases of Listeriosis in pregnancy. Consultation with the multidisciplinary team including obstetrician, feto maternal specialist, microbiologist and neonatologist is recommended.

These guidelines are intended for healthcare professionals, particularly those in training, who are working in HSE-funded obstetric and gynaecological services. These guidelines are designed to guide clinical judgement but not replace it. In individual cases a health care professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interest of the woman and her baby.

### 4. Background and Introduction

#### 4.1 Definition

*L.monocytogenes* is a small facultatively anaerobic, gram-positive flagellated, linear motile rod, which is non spore forming (Buchner et al., 1968; Nieman et al., 1980). The current name *Listeria monocytogenes* was agreed upon in 1940 in honour of the father of antiseptics Lord Joseph Lister (Gellin et al., 1989).

Listeriosis is mainly a food borne infection, and sporadic cases as well as epidemics have been linked to contaminated food (Linnan et al., 1988; Schlech et al., 1983; Southwick et al., 1996). Human listeriosis typically occurs sporadically but occasional nosocomial clusters have been reported. (Filice et al., 1978; Larsson et al., 1978; Simmons et al., 1986). In the USA, routine screening and surveillance performed by the FDA (Food and Drug Administration) and USDA (United States Dept of Agriculture) often leads to recall of food products due to concern over listerial contamination (Janakiraman, 2008).

Outbreaks of listeriosis are more common in the summer. *Listeria* is a resilient organism and can survive temperatures ranging from 4°C to 37°C. *Listeria* maintains its motility best at room temperature, where it can multiply rapidly in a short space of time. As a result it replicates well in soil, dust, water, silage and animal feeds (Al-Ghazali et al., 1986; Fenlon et al., 1986; Kampelmacher et al., 1980; Watkins et al., 1981; Welshimer et al., 1971).

*Listeria* grow at refrigerator temperatures and can therefore contaminate refrigerated food and raw meat. Although it can survive for many months in soil, pasteurization and most disinfecting agents eliminate the organism. The incubation period for listeria has not been well established. However, according to case reports, the incubation period is from 24 hours to 70 days with a median of 21 days. (www.health.ny.gov)

## 4.2 Prevalence

In Europe the rates vary between 0.1 and 11.3 per million population and approximately 20% involve neonatal infection. In Ireland in 2007, 21 cases of Listeriosis were reported, 9 of which were pregnancy-related / neonatal cases- an estimated rate of 14 notifications per 100,000 live births (HSPC 2007). In 2000 the prevalence in the USA was estimated to be four per million population (CDC., 2008). Though no seasonal pattern exists, illness in humans tend to present in late summer and early autumn. When the disease occurs in children, up to 54 % have no apparent immunocompromising condition (Ciesielski et al., 1988; Tim et al., 1984). Asymptomatic carriage of Listeria in the gastrointestinal tract is not unusual (up to 5% of the population) (Walvekar et al., 2005)

The three at risk groups for developing clinical infection are pregnant women, fetus and neonates and the elderly and the immunocompromised (those with a history of splenectomy, Human Immunodeficiency virus (HIV) infection, steroid use, diabetes or those on immunosuppressive medication).

The presentation of Listeriosis during pregnancy includes mild flu like symptoms, backache, vomiting/diarrhoea, muscle pains and sore throat. Some women may be asymptomatic. Infection with listeria does **not** confer any immunity.

## 5. Methodology

Medline, EMBASE , PubMed and Cochrane database of Systematic reviews were searched using terms relating to Listeria monocytogenes, listeriosis, pregnancy, Newborn, neonate, Transmission, Food Borne infection, management. Searches were limited to humans and restricted to the titles of English language articles published between 1980 to date. Relevant meta-analyses, systematic reviews, intervention and observational studies were reviewed. Guidelines / recommendations reviewed included American College of Obstetricians and Gynaecologists, Society of Obstetricians and Gynaecologists of Canada, NICE (National Institute for Health and Care Excellence) UK and Health Protection Surveillance Centre (HPSC), Ireland.

The principal guideline developers were Dr Rupak K Sarkar and Dr Mairead Kennelly (Coombe Women and Infants University Hospital, Dublin).

The guideline was reviewed by Dr Darina O Flanagan (Health Protection Surveillance Centre, Ireland), Dr Nirmala Kondaveeti (Sligo). Dr Vicky O Dwyer (SpR,).

## 6. Clinical Guidelines on Listeriosis Infection in Pregnancy

The incidence of Listeriosis associated with pregnancy is approximately 18 times higher than in the general population and 16-27 % of all infections with *Listeria* occur in pregnant women, (Jackson et al., 2010; Janakiraman., 2008; Voetsch et al., 1990).

Using repeated sampling, *Listeria* can be detected in the feces of nearly 70% of healthy *asymptomatic non pregnant* individuals and 44% of *asymptomatic pregnant women* (Kampelmacher et al., 1972). Pregnancy does not appear to affect the fecal, cervico-vaginal or oropharyngeal carriage rate of *Listeria*, but such carriage has been reported as a possible predisposing factor for perinatal listeriosis (Lamont et al., 1986)

Data from the United States suggest the incidence of pregnancy associated Listeriosis is markedly higher among Hispanic women 8.9 per 100,000 compared to non Hispanic women 2.3 per 100,000. Nearly all pregnancy-associated cases of Listeriosis occur in otherwise healthy women with no additional predisposing factors. (Mylonakis et al., 2002)

Although Listeriosis has been mainly diagnosed in the third trimester, the incidence at earlier gestations may be under reported because of the relative infrequency of culturing products of conception in cases of early fetal loss (Lamont et al., 2011).

### 6.1 Clinical Presentation

The presentation of Listeriosis during pregnancy includes mild flu-like symptoms. In a series of 191 cases of Listeriosis in pregnancy, 32% of women had symptoms of a flu-like illness, 65% had a fever, and other symptoms included backache (21.5%) (which may be mistaken for a urinary tract infection), headache (10.5%), vomiting/diarrhoea (7%), muscle pains (4%) and sore throat (4%). Approximately 29% of the women were asymptomatic (Mylonakis et al., 2002)

### 6.2 Fetal effects of *Listeria* infection

Fetal and neonatal infections can be severe, resulting in fetal loss, preterm labour, neonatal sepsis, meningitis and death with a case fatality rate of 20-30% (Schwarze et al., 1989). Fetal transmission from maternal Listeriosis is not invariable (Hume et al., 1976) and discordant infection in utero has been observed in a set of twins (Smith et al., 1983). Once the placenta is infected it becomes a reservoir for re-infection and placental macro abscesses may be histologically evident.

Listeriosis during pregnancy carries a poorer prognosis for fetuses who are affected at earlier gestations, as opposed to later gestations and commonly results in spontaneous abortion or stillbirth (Johnson et al., 1955; Reiss et al., 1951)

Preterm birth is common and the highest mortality rate is predictably among infants born at the earliest gestations. Two studies have been reported, one with 222 pregnant women comprising 11 culture confirmed cases and 211 cases reported in the literature (Mylonakis et al., 2002) and the other study with 722 pregnant women who were either culture positive or had clinical suspicion of Listeriosis (McLauchlin et al., 1990). Spontaneous abortion occurred in 10-20% cases, approximately 50% delivered preterm, intrauterine death occurred in 11 % (McLauchlin et al., 1990), 34% had fetal distress and 75% developed meconium staining of the amniotic fluid particularly at early gestation.

### 6.3 Neonatal Listeriosis

While maternal illness due to Listeriosis may be mild, neonatal illness is often severe and may be fatal. Neonatal Listeriosis may occur by vertical transmission of *L. monocytogenes* from mother to fetus, either by inhalation of infected amniotic fluid, transplacentally from maternal circulation (Becroft et al., 1971) or by ascending colonization from the vagina.

Neonatal Listeriosis (NL) occurs in approximately 8.6/100,000 of live births and is one of the most common causes of neonatal meningitis. The clinical manifestations of NL are similar to GBS and there is a high mortality rate 20-60% (Albritton et al., 1984; Linnan et al., 1988; McLauchlin et al., 1990., Mylonakis et al., 2002; Schwarze et al., 1989). One study reported that 68% of newborns whose mothers were diagnosed with Listeriosis as a result of positive cultures from placenta, maternal blood or cervix developed neonatal infection: of those 68.2 % made a complete recovery, 12.7% developed long term neurological sequelae, and the infant mortality rate was 24.5% (Mylonakis et al., 2002) The disease has two forms - early and late suggesting different modes of transmission -vertical and nosocomial (Tessier et al., 1986).

#### Early Onset

Symptoms of early-onset Listeriosis occur at a mean of 36 hours after birth (Relier et al., 1979). In 50-74% of cases, the mother is likely to have had a flu-like illness with symptoms of fever, headache and myalgia (Halliday et al., 1979; Linnan et al., 1988), and isolation of *L. monocytogenes* from maternal blood or genital tract is common (44-89%) [Linnan et al., 1988; McLauchlin et al., 1990]. Neonates with early-onset infection are more frequently born preterm and associated with chorioamnionitis.

The fetus presents with clinical features like septicaemia (81-88%), respiratory distress or pneumonia (38%), meningitis (24%) and occasionally disseminated inflammatory granulomata (Granulomatosis infantisepticum) [Barber et al., 1965; Buchner et al., 1968; Hood 1961; Johnston et al 1955; Rappaport et al., 1960; Ray et al., 1964], from which pure culture of *L. monocytogenes* can be obtained (Reiss et al., 1951). Granulomatosis Infantisepticum was reported for

the first time in 1893 (at which time, the disease was named pseudo tuberculosis), and is a pathognomonic feature of Listeriosis (Kelly et al., 1972).

### **Late Onset**

In contrast, late-onset neonatal listeriosis (commonly due to serotype 4b) (Albritton et al., 1976), tends to occur between five days and two or more weeks postpartum, typically in term neonates (Albritton et al., 1984; McLauchlin et al., 1990). Also typical of these cases is that the neonate is born to asymptomatic mothers with failure to isolate *L. monocytogenes* from maternal cultures (Linnan et al 1988). The clinical features may be non-specific, but septicaemia (17-95%) and meningitis (67-93%) are common (Posfay-Barbe et al., 2004; Skidmore et al., 1981). Neonatal Listeriosis is one of the few congenital infections in which antibiotic therapy can improve outcome (Cruikshank et al., 1989; Fleming et al., 1985; Mylonakis et al., 2002; Zervoudakis et al., 1977).

## **6.4 Diagnosis**

Diagnosis of Listerial infection can only be made by culturing the organism from a sterile site such as blood, amniotic fluid or cerebrospinal fluid (CSF) (Southwick et al., 1996). The organism grows well from blood or CSF, without the need for enrichment or selective media, and postpartum histological evidence of micro abscesses in the placenta can be found (Driscoll et al., 1962).

*Listeria* grows well in broth, blood agar and most routine culture media. Selective enrichment and subculture may be necessary to avoid false negatives from overgrowth of gram negative organisms from contaminated sites like the vagina and rectum (Manganiello et al., 1991; Kampelmacher et al., 1972; Lamont et al., 1986). Invasive Listeriosis, defined as isolation of listeria from a normally sterile site (typically blood or cerebrospinal fluid) is uncommon.

Vaginal or stool cultures are not helpful in the diagnosis because some women are carriers but do not have the clinical disease. Faecal carriage of *Listeria* occurs in to 1% to 15% of the population: the incidence of women carrying *Listeria* in the vagina is lower. Gram stain is only useful in about 33% of cases, both because *Listeria* is an intracellular organism and can be entirely missed and because the organism can resemble pneumococci (diplococci), diptheroids (*Corynebacteria*), or hemophilus species. Informing the microbiologist of suspicion of listerial infection can improve the specificity of Gram Stains.

Because Listeriosis in pregnancy is serious and difficult to diagnose, blood cultures should be considered in any pregnant patient presenting with fever, especially if accompanied by flu like or gastro intestinal symptoms. After obtaining cultures, providers should consider starting treatment if suspicion for Listerial infection is high.

## 6.5 Management

The following recommendations provide guidance for the management of pregnant women with presumptive exposure to *Listeria* in three clinical scenarios in: (ACOG 2014)

Women who are

1. Asymptomatic
2. Mildly symptomatic but afebrile
3. Febrile with or without other symptoms consistent with listeria

### **Asymptomatic**

No testing, including blood and stool cultures, or treatment is indicated for an asymptomatic pregnant woman who reports consumption of a product that was recalled or implicated during an outbreak of listeria contamination.

An asymptomatic patient should be instructed to return if she develops symptoms of Listeriosis within 2 months of eating the recalled or implicated product. There is no reason to alter or begin fetal surveillance in asymptomatic women with known or presumptive exposure to *Listeria*.

### **Mildly Symptomatic but Afebrile**

There are no data to guide the management of an exposed, afebrile pregnant woman with mild symptoms that do not strongly suggest Listeriosis. A pregnant woman who ate a product that was recalled because of listeria contamination and who is afebrile but has signs and symptoms consistent with a minor gastrointestinal or flu-like illness (such as mild myalgia, mild nausea, vomiting, or diarrhoea) can be managed expectantly (ie, the same as for an exposed, asymptomatic pregnant woman). This is a reasonable approach that limits low-yield testing. Alternatively, such a patient could be tested with blood culture for listeria, but if such a course is elected, specific instruction should be given to the microbiology laboratory.

If such diagnostic testing is performed, some experts would withhold antibiotic therapy unless the culture yielded *Listeria*. Others would initiate antibiotic therapy, although no effectiveness data exist to help clinicians and patients evaluate the risks and benefits of such a treatment choice. If testing is undertaken and the blood culture yields *Listeria*, standard antimicrobial treatment for Listeriosis, typically including intravenous ampicillin, would be indicated (see following section). Assessments of fetal well-being should be addressed on an individualized basis with consideration given to the degree of concern for infection and the patient's clinical status.

### **Febrile With or Without Other Symptoms Consistent With Listeriosis**

An exposed pregnant woman with a fever higher than 38.1°C (100.6°F) and signs and symptoms consistent with Listeriosis for whom no other cause of illness is known should be simultaneously tested and treated for presumptive Listeriosis. Diagnosis is made primarily by blood culture. Placental cultures should be obtained in the event of delivery. If blood cultures are negative after

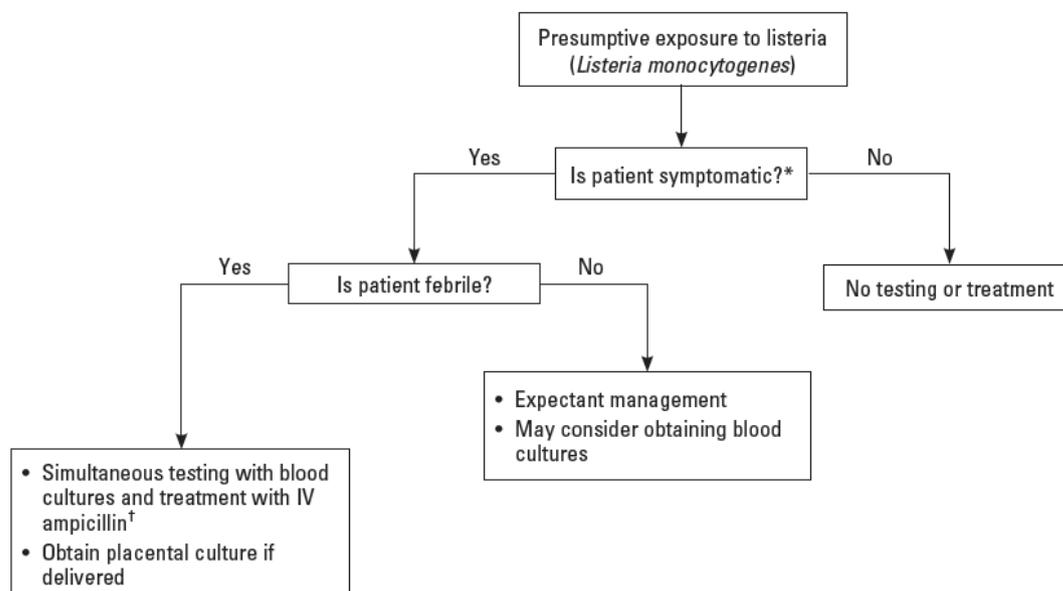
the recommended antibiotic regimen has begun, the decision about whether or not to continue antibiotics should be made using clinical judgment combined with consultation(s) with an infectious disease specialist, a maternal–fetal medicine specialist, or both.

The antimicrobial regimen of choice for treatment of Listeriosis is high-dose intravenous ampicillin (at least 6 g/day) for non-allergic patients for at least 14 days (Janakiraman., 2008). Frequently, Gentamicin is added to the treatment regimen because it has demonstrated synergism with ampicillin (Temple et al., 2000). Women who are allergic to penicillin, ampicillin, or both present a clinical conundrum; trimethoprim with sulfamethoxazole is the generally recommended alternative to ampicillin (Janakiraman., 2008).

The CDC in USA and the Health Protection Surveillance Centre, Ireland, considers Listeriosis a nationally notifiable disease, and once diagnosis is confirmed, health care providers should contact public health departments to comply with local requirements for reporting.

Although blood cultures are the standard for diagnosis in cases of fever and symptoms consistent with Listeriosis, if an amniocentesis has been performed, it usually reveals meconium staining and gram-positive rods (Mazor et al., 1992). This information may help guide management when the diagnosis is uncertain (Craig et al., 1996).

Initiating a program of fetal surveillance seems prudent for women in whom Listeriosis is diagnosed or strongly suspected because of exposure and fever with or without other symptoms, although studies and data do not exist to point to one best plan for such testing.



**Fig. 1.** Management of pregnant women with presumptive exposure to listeria.

Abbreviation: IV, intravenous.

\*Symptoms include flu-like symptoms, such as myalgia, abdominal or back pain, nausea, vomiting, or diarrhea.

†Trimethoprim with sulfamethoxazole should be used if patient is allergic to penicillin.

## 7. Prevention

Pregnant women should avoid eating food with a high risk of contamination with *Listeria*:

- Hot dogs, lunch meats, cold cuts (when served chilled or at room temperature; heat to internal temperature of 74°C [165°F] or steaming hot)
- Refrigerated pâté and meat spreads
- Refrigerated smoked seafood
- Raw (unpasteurized) milk
- Unpasteurized soft cheeses such as feta, queso blanco, queso fresco, Brie, queso panela, Camembert, and blue-veined cheeses

As with other food borne illnesses, there are several measures that will help to reduce the risk of infection of a pregnant woman with *Listeria monocytogenes*: (HPSC 2008)

- Keep foods for as short a time as possible and follow storage instructions including 'use by' and 'eat by' dates
- Cook food thoroughly, especially meat, ensuring that it is cooked through to the middle
- Keep uncooked meats separate from vegetables and from cooked and ready-to-eat foods
- Wash salads, fruit and raw vegetables thoroughly under running tap water before eating, even if it will be peeled or cut.
- Wash hands, knives, and cutting boards after contact with uncooked food.
- Make sure that the refrigerator is working correctly.
- When heating food in a microwave, follow heating and standing times recommended by the manufacturer.
- Throw away left-over reheated food. Cooked food which is not eaten immediately should be cooled as rapidly as possible and then stored in the refrigerator.
- If contact with ewes at lambing time is unavoidable for pregnant women, the elderly, or people with weakened immune systems, washing of hands after handling animals should reduce any possibility of infection.

Data from Centers for Disease Control and Prevention. *Listeria* (listeriosis). Prevention. Available at: <http://www.cdc.gov/listeria/prevention.html>.

Patient information leaflet regarding *Listeria* and pregnancy is available to download at [www.safefood.eu](http://www.safefood.eu)

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## 9. Implementation Strategy

- Distribution of guideline to all members of the Institute and to all maternity units.
- Distribution to the Director of the Acute Hospitals for dissemination through line management in all acute hospitals.
- Implementation through HSE Obstetrics and Gynaecology programme local implementation boards.
- Distribution to other interested parties and professional bodies.

## 10. Qualifying Statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advising women of their choices and ensure informed consent is obtained.
- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.

