# MEDICAL PRACTICE

## *Clinical Problems*

# Epidemic Listeriosis in the Newborn

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### Summary

**Within a three-month period 13 cases of listeriosis in the newborn were seen at the National Women's Hospital, Auckland. Eleven presented in the first 24 hours of life, the most common feature being respiratory difficulty in low birth weight infants. Meconium-stained liquor was noted in nine cases. The constant finding in all cases was an aspiration pneumonia which appeared to be of intrauterine origin from an infected amniotic cavity. There was also evidence of septicaemia in nine cases, and two infants survived meningitis which developed at 1 week. Maternal symptoms were mild and variable, and in only one case were they proved to be due to listerial infection. The mothers came from different suburbs of Auckland and no common source of infection was found.**


### Introduction

*Listeria monocytogenes* is a motile Gram-positive bacillus which occurs in over 50 species of mammals, birds, and fish and is an important cause of stillbirth, premature delivery, and neonatal death. Seeliger[1] distinguished nine clinical forms of the infection in man, of which listeriosis of the central nervous system and listeriosis of the newborn are the most common. About 75% of human cases occur in the neonatal period as septicaemia or meningitis.[2] Infection is usually sporadic, but an epidemic of 15 cases of the septicaemic form in the newborn was reported from the Halle region of Germany,[3] and several epidemics have been reported subsequently, including one of 189 cases in Halle in 1966.[4] The source of human infection is seldom identified.

In this paper we report 13 cases of listerial infection of the newborn seen within three months at a hospital where previously the disease had been rare.

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### Clinical Features

The clinical features of the 13 cases are summarized in Tables I and II. Though 10 mothers had a respiratory or influenza-like illness or urinary infection in the last trimester there were no specific antenatal features. The onset of labour was before 37 weeks' gestation in 12 cases. Five mothers had a temperature between 37° and 38·1°C during labour. In nine cases the liquor was stained with meconium, which was described as "old and dark."

The birth weights of the affected infants ranged from 805 to 2,980 g. Neonatal apnoea or respiratory distress was noted in the 11 cases diagnosed within 36 hours. Five infants required intubation at birth. Eight had a temperature of 37°C or more and two a temperature of 35°C or less. In four of the cases diagnosed within 36 hours there was hepatosplenomegaly, in two there was a petechial rash, and fits occurred in one. Purulent conjunctivitis was present at birth in two cases, and was noted within 24 hours in two others.

Of the two infants in whom symptoms developed later, one had had transient respiratory distress at birth and presented at 6 days with apnoea and fever, and the other presented at 7 days with fever, fits, and a tense fontanelle.

Three cases were not treated with antibiotics because of death soon after delivery (Case 7) or soon after admission in a

TABLE I—*Clinical Features of Six Cases Surviving Neonatal Listerial Infection*

| Case No. | Race | Antepartum Illness | Mother's Max. Intra-partum Temp. (C) | Date of Birth and Gestation | Condition at Delivery | Birth Weight (g) | Sex | Age at Onset of Symptoms | Presenting Features | Infant's Max. Temp. (C) | Antibiotics and Age Commenced | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Maori | Urinary infection at 30 weeks' gestation | 36° | 21/5/69 ?41 Weeks | Meconium-stained liquor. Intubated | 2,240 | F. | At birth | Fits. Hypertonicity. Frequent stools. Hepatosplenomegaly. Petechial rash | 37·7° | Ampicillin, kanamycin, cephaloridine at 36 hours | Normal development aged 14 months |
| 2 | Samoan | "Myalgia" last month of pregnancy | 36·3° | 3/6/69 ?35·6 Weeks | L.S.C.S. for fetal distress. Meconium in liquor. Intubated | 2,930 | F. | At birth | Respiratory insufficiency. Crepitations in chest | 38·8° | Ampicillin, kanamycin at 3 hours | Normal development aged 3 weeks |
| 3 | European | Cough 6 weeks antepartum. Rigor during labour | 37·8° | 26/6/69 35 Weeks | Meconium-stained liquor. Pale | 2,980 | M. | At birth | Respiratory distress. Hypotonicity. Conjunctivitis | 37·5° | Ampicillin, kanamycin at 12 hours | Normal development aged 14 months |
| 4 | Samoan | Dysuria 2 weeks before delivery | 37·8° | 18/7/69 34 Weeks | Meconium-stained liquor. Cyanosis | 2,470 | M. | At birth | Respiratory distress. Crepitations in chest. Splenomegaly. Conjunctivitis | 37·7° | Ampicillin, kanamycin at 4 hours | Normal development aged 3 months |
| 5 | Maori | Respiratory infection 12 hours antepartum. Treated ampicillin | 37° | 3/6/69 33 Weeks | Respiratory distress | 1,810 | M. | 6 days | Apnoeic attacks. Hypotonic | 37·2° | Ampicillin, kanamycin, penicillin at 6 days | Normal development aged 2 months |
| 6 | Maori | Influenza ?1 month antepartum | N.R. | 14/6/69 34 Weeks | At home. Plethoric. Twin-to-twin transfusion | 2,320 | M. | 7 days | Fever, fits. Hypertonicity. Tense fontanelle | 38·8° | Kanamycin, ampicillin at 10 days | Normal development aged 6 weeks |

N.R. = Not recorded.
L.S.C.S. = Lower segment caesarean section.

TABLE II—*Clinical Features and Necropsy Findings of Seven Fatal Cases of Listerial Infection*

| Case No. | Race | Antepartum Illness | Mother's Max. Intra-partum Temp. (C) | Date of Birth and Gestation | Condition at Delivery | Birth Weight (g) | Sex | Age at Onset of Symptoms | Presenting Features | Infant's Max. Temp. (C) | Antibiotics and Age Commenced | Age at Death | Placenta | Necropsy Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | European | Respiratory infection treated tetracycline 1 month ante-partum | N.R. | 6/7/69 26 Weeks | Respiration not established | 805 | M. | At birth | Apnoea. Pinpoint white "vesicular" rash | N.R. | — | 1 hour | Chorio-amnionitis. Infected "infarct" | Pneumonia. Cutaneous microabscesses |
| 8 | Maori | Fever 1 day antepartum | 36·8° | 3/8/69 36 Weeks | Secondary apnoea at 10 minutes | 1,910 | F. | At birth | Respiratory insufficiency. Cyanosis | 32·8° | — | 3½ hours | Chorioam-nionitis | Pneumonia. Abscesses liver, spleen. Portal fibrosis, biliary atresia. Oesophageal ulceration |
| 9 | European | Ampicillin given 4 hours ante-partum for amnionitis | 38° | 3/8/69 34 Weeks | Meconium-stained liquor | 1,745 | M. | At birth | Neonatal apnoea | 35° | Ampicillin, kanamycin at birth | 4 hours | Chorio-amnionitis. Decidual abscesses | Pneumonia. Abscesses liver, adrenals. Oesophageal ulceration. Intestinal ulceration |
| 10 | European | Antibiotics 18 days antepartum for respiratory infection | 37° | 30/6/69 32 Weeks | Meconium-stained liquor. Intubated | 1,870 | M. | At birth | Respiratory distress. Hepatospleno-megaly | 36·8° | Ampicillin, kanamycin at 3 hours | 9 hours | Chorio-amnionitis | Pneumonia. Abscesses adrenals. Intestinal ulceration. Meningitis |
| 11 | Maori | "Urinary infection" 12 hours antepartum | 38° | 24/6/69 36 Weeks | Meconium-stained liquor | 2,630 | M. | At birth | Hypotonicity. Respiratory insufficiency | N.R. | — | 11 hours | Not examined | Pneumonia (biopsy only) |
| 12 | Niue Islander | Nil | 37·5° | 23/6/69 33 Weeks | Meconium-stained liquor. Intubated | 1,670 | F. | At birth | Respiratory distress. Petechial rash. Conjunctivitis | 37° | Ampicillin, kanamycin at 16 hours | 35 hours | Not examined | Pneumonia. Abscesses adrenals, liver, lymph nodes. Intestinal ulceration. Meningitis |
| 13 | European | Nil | 36·6° | 18/7/69 31 Weeks | Meconium-stained liquor. Intubated | 2,140 | M. | At birth | Apnoea. Hepato-splenomegaly. Conjunctivitis | 38·2° | Ampicillin, kanamycin at ?21 hours | 36 hours | Not examined | Pneumonia. Abscesses adrenals. Meningitis |

N.R. = Not recorded.

moribund state (Cases 8 and 11). Of the 10 infants given antibiotics (ampicillin 200-400 mg/kg/day and kanamycin 15 mg/kg/day) respiratory insufficiency progressed to death in four despite supportive therapy. The six who survived the first 36 hours made a full recovery after an initial period of respiratory difficulty treated with parenteral antibiotics for from 10 to 20 days. All survivors were apparently developing normally when last seen at ages varying from 3 weeks to 14 months.

## Laboratory Investigations

*L. monocytogenes* type 4B was isolated (see Appendix for methods) in all cases but from varying sites (Table III). Rapid diagnosis was often possible by the direct identification of Gram-positive bacilli in meconium or in swabs of the external auditory canal, conjunctiva, nose, or throat, and, in Case 9, in amniotic fluid. Swabs taken from the external auditory canal within a few hours of birth gave the greatest number of positive results. The two cases presenting after a week were diagnosed by microscopy and culture of cerebrospinal fluid and from blood cultures.

TABLE III—*Summary of Bacteriological Results*

| Site | No. Examined | No. of Positive Cases | |
|---|---|---|---|
| | | Gram-positive Bacilli on Direct Examination | Isolation of *L. monocytogenes* |
| C.S.F. | 10 | 1 | 4 |
| Blood | 8 | — | 7 |
| Placenta | 3 | 1 | 2 |
| Liquor | 2 | 1 | 1 |
| Auditory canal | 8 | 6 | 8 |
| Nose | 7 | 1 | 5 |
| Throat | 8 | — | 6 |
| Conjunctiva | 7 | 3 | 5 |
| Umbilical cord | 7 | 1 | 4 |
| Rectum | 8 | 3 | 5 |

All strains isolated were sensitive to penicillin and ampicillin at minimal concentrations of 0·62 μg/ml. One strain was sensitive to kanamycin at a minimal concentration of 2·5 μg/ml, and the remainder at a minimal concentration of 1·25 μg/ml. All were sensitive to cephaloridine at a concentration of 1·25 μg/ml or less.

Cerebrospinal fluid examined at varying intervals after the onset of symptoms in 10 cases showed a pleocytosis ranging from 40 W.B.C./mm³ in Case 8 (death at 3½ hours) to 6,800 W.B.C./mm³ in Case 5 at 7 days. From 10 to 100% of cells were polymorphonuclear leucocytes. Protein varied from 61 to 494 mg/100 ml, and sugar from 10 to 169 mg/100 ml. *L. monocytogenes* was isolated from the C.S.F. in four cases. The blood count varied from 11,000 to 35,000 W.B.C./mm³, with up to 16% myelocytes. Monocytes ranged from 6 to 18%. Acid base and blood gas estimations on capillary blood showed a moderate to severe acidosis in all infants with respiratory difficulties.

## Radiology

Satisfactory chest radiographs were obtained in 11 cases within 1½ to 12 hours after birth. The appearances ranged from slight

peribronchial infiltration (Fig. 1) to widespread coarse mottling (Fig. 2). All were interpreted as non-specific aspiration phenomena.

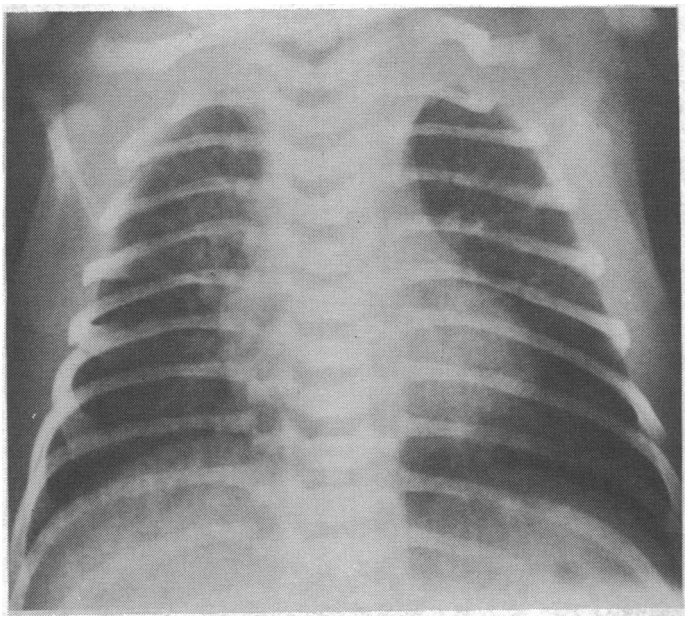

FIG. 1—Chest radiograph at 11½ hours of age showing slight peribronchial infiltration mainly in the right upper lobe.

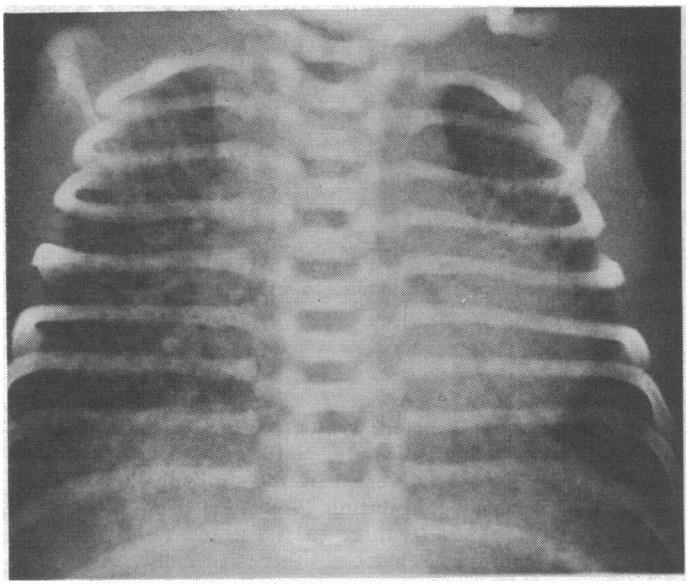

FIG. 2—Case 4. Chest radiograph at 6 hours of age showing extensive and disseminated coarse mottling with some prominent air-filled bronchi. The first radiograph taken at 2½ hours of age gave similar appearances.

## Representative Case Histories

### CASE 4—PNEUMONIA WITH SURVIVAL

Boy born after spontaneous premature labour at 34 weeks' gestation. Membranes ruptured 30 minutes before normal delivery; liquor heavily stained with meconium. Baby pale and limp, but responded to intranasal oxygen with intermittent positive pressure: weight 2,470 g. On admission his dusky colour showed an immediate improvement when he was placed in an incubator with oxygen. The skin was meconium-stained. There were signs of moderate respiratory distress, and an *x*-ray film taken at 2½ hours showed extensive and disseminated coarse mottling, with some prominent air-filled bronchi (Fig. 2). Gram-positive bacilli were seen on direct examination of smears from the placenta and external auditory canal. Swabs from throat, nose, external auditory canal, rectum, and placenta grew *L. monocytogenes*: blood and C.S.F. were sterile on culture.

A 14-day course of parenteral ampicillin and kanamycin was started, together with intravenous fluids. On the second day abdominal distension and an enlarged spleen were noted. A chest *x*-ray film at 24 hours showed some clearing, which was complete at 3 days. The C.S.F. at 10 days contained 75 W.B.C./mm³ (10% neutrophils, 90% lymphocytes), 135 R.B.C./mm³, protein 162 mg/100 ml, and sugar 30 mg/100 ml: culture was sterile. He made satisfactory progress and was discharged after 24 days weighing 2,780 g. At 2 months he weighed 4,480 g and appeared normal.

### CASE 12—PNEUMONIA AND GENERALIZED INFECTION

Girl born after spontaneous premature labour at 33 weeks' gestation. Liquor heavily stained with meconium. Baby (weight 1,670 g) required intubation and intermittent positive-pressure oxygen. Chest *x*-ray picture at 1½ hours: medium coarse mottling throughout both lungs (Fig. 3). At 17 hours the condition deteriorated suddenly and a widespread, red, macular and petechial rash

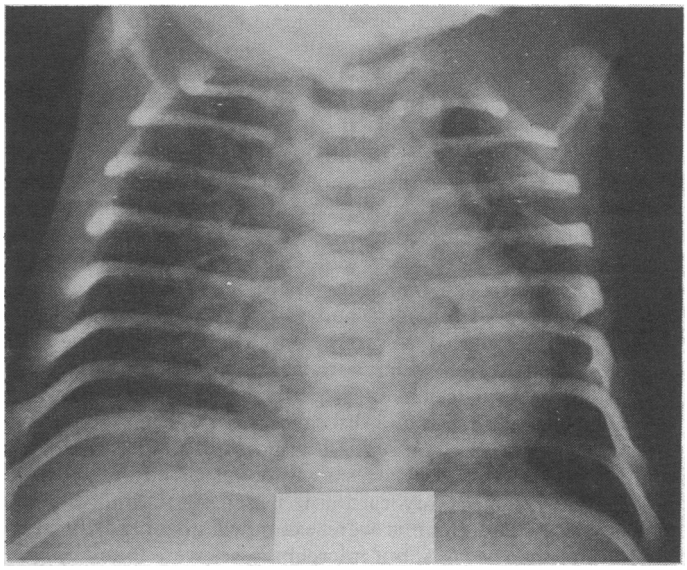

FIG. 3—Case 12. Chest radiograph at 1½ hours showing medium coarse mottling throughout both lungs and some peribronchial infiltration.

developed. *X*-ray film showed increase in abnormal shadowing, probably owing to enlargement of pulmonary vessels. C.S.F. yellow, hazy, with 640 R.B.C./mm³, 370 W.B.C./mm³, protein 494 mg/100 ml, and sugar 10 mg/100 ml. Gram-positive bacilli were seen in smears from C.S.F., meconium, and conjunctiva. Cultures from C.S.F., throat, external auditory canal, conjunctiva, and meconium grew *L. monocytogenes*.

Treatment was with intravenous fluids, corticosteroids, ampicillin, kanamycin, and digitalis, but the baby died at 35 hours.

### CASE 6—MENINGITIS AND SEPTICAEMIA

Boy weighing 2,320 g, twin 1 of twins born at home after spontaneous premature labour at 34 weeks' gestation. The haemoglobin was 24 g/100 ml; by comparison, twin 2, also a male (weight 1,430 g) had a haemoglobin of 12 g/100 ml, suggesting the possibility of a fetofetal transfusion.

On admission to hospital at the age of 4 hours twin 1 was cold and plethoric, appeared to be premature, but was otherwise in fair condition. A chest *x*-ray picture was consistent with a moderately severe degree of the aspiration syndrome. A total of 40 ml of blood was removed via the umbilical cord and replaced with 40 ml of plasma. On the seventh day the temperature rose, and on the 10th day there was slight cyanosis and increased tone: the baby became irritable and the fontanelle tense. C.S.F. contained 2,800 R.B.C./mm³, 2,300 W.B.C./mm³ (20% neutrophils and 80% lymphocytes), protein 450 mg/100 ml, and sugar 32 mg/100 ml. No organisms were seen in the stained deposit, but *L. monocytogenes* was cultured from both C.S.F. and blood. He made good progress on intramuscular ampicillin for 20 days and kanamycin for 10 days, and was discharged at 6 weeks. He did not attend follow-up clinic.

Twin 2, being much smaller, made slower progress but showed no signs of infection at any stage. However, he had a four-day prophylactic course of ampicillin and kanamycin against sepsis arising from a catheter in the umbilical vein.

## Pathological Findings

The major necropsy findings are summarized in Table II. The external appearance was unusual only in Case 7, in which there were many pin-point white vesicles on an erythematous background on the skin of the trunk. One of these proved histologically to be a microabscess situated subdermally and intradermally. Careful search was made for the multiple, minute, yellow or yellow-white visceral lesions typical of listeriosis. Such lesions, all less than 3 mm in diameter, were seen macroscopically in the fetal adrenal cortex in four cases, but in only two of these were there similar foci in the liver, and none were seen in other organs. Organ enlargement was inconstant, and organ weights were always less than two standard deviations from the mean expected for body weight. The lungs in all cases were poorly aerated. In two cases there was macroscopic evidence of meningitis.

Histologically the adrenal and hepatic lesions were sharply demarcated spherical abscesses in which there was necrosis of parenchymal cells and connective tissue and a heavy infiltration by neutrophils. The necrotic areas contained numerous Gram-positive bacilli. There were some histiocytes and other cells which may have been immature granulocytes similar to those observed in the peripheral blood in several cases. No microabscesses were found in a search of multiple blocks of the liver in Cases 10 and 11, in which adrenal abscesses were numerous. In Case 8 the liver lesions were periportal and appeared to be resolving. Portal fibrosis and disorganization of the extrahepatic bile ducts were also present—the possibility that listeriosis could be a cause of biliary atresia will be discussed in a separate report. The kidneys, myocardium, pancreas, thyroid, spleen, bone marrow, and thymus were examined histologically in at least five of the six cases, but microabscesses were found only in the bone marrow in one case and the spleen in another. Suppurative foci were also seen in the tracheobronchial and mesenteric lymph nodes in Case 12. There were neutrophils and many Gram-positive bacilli in the subarachnoid spaces in three cases, but no intracerebral lesions were found.

Numerous Gram-positive bacilli were seen in the small and large intestines in all five cases in which the bowel was examined microscopically. In three of these there was focal ulceration of the large intestine and Gram-positive bacilli were invading deeply into the submucosa. Focal oesophageal ulceration was found in two cases.

Collections of neutrophils and macrophages without accompanying fibrinous exudation were seen in the alveoli and alveolar ducts of the lungs in all seven cases (Fig. 4). The distribution was essentially focal, but the infiltration was present to some extent in all lobes examined, and there were large or confluent areas in the lungs in three cases. No abscesses and no meconium or other aspirated material were found in the lungs. Gram-positive bacilli were seen in lung sections from all seven cases, and *L. monocytogenes* was cultured in the five cases in which this was attempted.

The placenta was examined in four cases. Microscopically there were neutrophilic infiltrations of the chorionic plate (Fig. 5A), the related amnion, the connective tissue of the umbilical cord, and the walls of fetal vessels in the cord and chorionic plate. Clumps of Gram-positive bacilli were found adhering to the amniotic surfaces in each case (Fig. 5B). Small foci of villous necrosis and intervillous fibrin deposition were observed near the maternal surface of the placenta in Case 7. Gram-positive bacilli were numerous in one of these necrotic foci, but were not found in others. Multiple microabscesses containing Gram-positive bacilli were found on the maternal aspect of the decidua basalis of the placenta in Case 9.

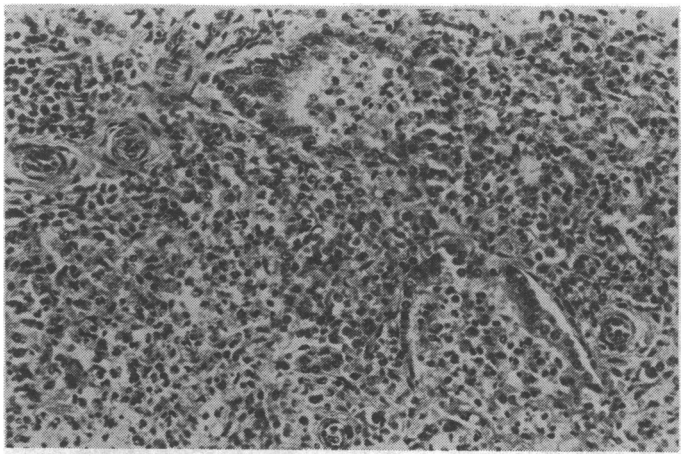

FIG. 4—Case 10. Photomicrograph of lung showing aspiration pneumonia. Degenerate neutrophils and macrophages fill bronchioles and alveolar ducts. (H. and E. × 210.)

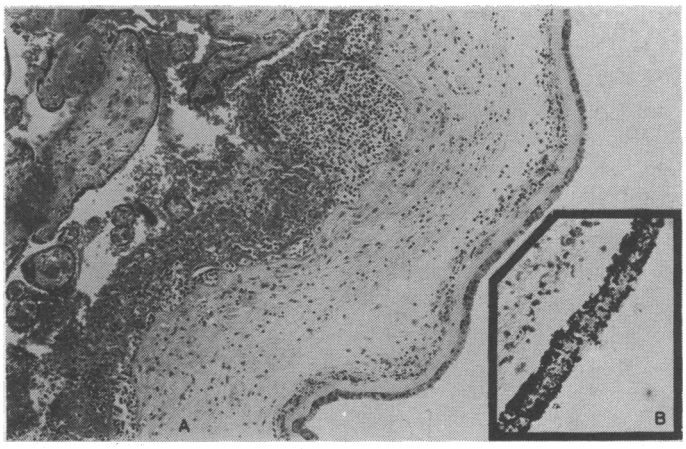


FIG. 5—Case 10. A, Photomicrograph of placenta showing chorion and amnion infiltrated by neutrophils. (H. and E. × 85.) B, The dark colour of the amniotic epithelium is due to masses of invading bacteria. (Gram. × 255.)

## Epidemiology

In the 10-year period before 1969 only three cases of neonatal listeriosis were diagnosed at the National Women's Hospital, where up to 5,000 infants were delivered annually. The mothers of the 13 infants affected during 1969 came from 12 different suburbs of Auckland. In three cases the mother or husband worked at an abattoir; in five cases there was daily contact with domestic animals; and in two cases there was contact with birds. Two mothers ate raw meat or fish during their pregnancy. Six infants, of whom four had symptoms at birth, were born at other hospitals or at home (Case 6). Eight of the 13 patients were Maori or Polynesian, who constitute 10% of Auckland's population of about 500,000.

From August 1969 to February 1970 meconium from all infants admitted to the premature or special care unit was examined by direct Gram staining of a smear and by culture. A vaginal swab for immediate culture in conjunction with a throat swab and three others for storing for examination at intervals over three months were taken from mothers seen at the 28th week of pregnancy. No carriers were found in over 1,000 infants and 200 pregnant women. During the epidemic any patient with unexplained intrapartum fever had a diagnostic amniocentesis.

Dr. Margery Carter,[5] at Ruakura Animal Research Station (about 80 miles (130 km) from Auckland), stated that she was unaware of an increased incidence of listeriosis in animals in 1969.

## Discussion

Disease in animals caused by *L. monocytogenes* was first reported in New Zealand in 1931,[6 7] but human infection has been uncommon and sporadic.[8] In Auckland in particular a low incidence of neonatal listeriosis has been confirmed by the necropsy studies at the National Women's Hospital during the past 10 years. Therefore it was hoped that some factor could easily be identified to account for the remarkable rise in incidence during this epidemic.

The major alternatives were (1) some common source of infection for all cases, or (2) a coincidental incidence of inapparent infections in the community. The latter possibility cannot be excluded, but was unsupported by the surveys of pregnant women and neonates when the epidemic was subsiding: nor does it seem a likely explanation for an epidemic which was both widely distributed and of brief duration. A common source of infection seemed more likely, but none was identified. Our search for animal products as a possible source of infection[3 4] was inconclusive. Bojsen-Møller and Jessen[9] found *L. monocytogenes* in the faeces of some slaughter-house workers, and the parents of three infants in the present series worked in a slaughter-house. Alternatively, this association might be related to a higher incidence in lower socioeconomic groups.[10] Socioeconomic rather than racial predisposition might also account for the disproportionate number of cases among Maoris and Polynesians.

The clinical findings in most cases presenting were nonspecific; therefore early diagnosis depended largely on the increased awareness of the disease as the epidemic developed, particularly in low birth weight infants with meconium-stained liquor. The diagnosis could often be confirmed rapidly by finding Gram-positive bacilli in direct smears from various sites. Our experience suggested that swabs from the external auditory canal might give better results than meconium.[11]

The susceptibility of the organisms to ampicillin reported by Nelson, Shelton, and Parks [12] was confirmed. Ampicillin is to be preferred to tetracycline because of the known side effects of tetracycline. Both infants who presented with meningitis later in the neonatal period survived, which is in keeping with the better prognosis in this type of case.[2] Mortality rates of over 90% were recorded in earlier studies of neonatal listeriosis,[1] and the overall mortality rate of 54% in our series presumably can be attributed to earlier diagnosis. Alison and Sarrut,[13] who routinely examined all newborn infants for listerial infection, reported an even lower mortality.

The first descriptions of the pathological changes in fatal perinatal listerial infection stressed the occurrence of multiple granulomatous lesions in the viscera, and referred to the disease as "granulomatosis infantiseptica." Most of our fatal cases had evidence of systemic infection but not all had focal visceral lesions, which were never numerous or widely disseminated, and histologically they were abscesses rather than granulomata. But five of the infants died within 12 hours, and there had therefore been little chance for the lesions to develop further.

Three of our cases showed the coarse mottling in the lung fields, which has been attributed to multiple granulomatoma.[14] Nevertheless, at necropsy one child had pneumonia without abscess or granuloma formation, and the same appearance has been seen in other infants with no evidence of listerial infection.

The constant histological finding in all cases was a pneumonia which appeared to be of intrauterine origin from an infected amniotic cavity. This interpretation was consistent with the early clinical and radiological findings and was supported by the presence of a severe chorioamnionitis in all four placentas examined. The alimentary canal was heavily infected in all cases, and random sections of macroscopically normal oesophagus or intestine showed focal ulceration in four infants, suggesting that this was a frequent source of systemic infection.

These findings support the concept of infection of the amniotic cavity preceding infection in the infant, rather than infection of the amniotic cavity occurring secondarily and inconstantly to an infection in the fetus transmitted from the mother via the placenta.[1 15] Sarrut and Alison,[16] in a prospective study of 21 placentas from affected infants, concluded that there was evidence for the "classical" haematogenous route of infection in only five cases. In 16 cases the infection was believed to be via the amniotic cavity, and the authors suggested that local endometrial infection might be the underlying source.

The pathogenicity of *L. monocytogenes* seems to remain relatively low, even during pregnancy. Presumably the amniotic cavity provides an unusually favourable site for the organism to multiply. Delivery, by eliminating this reservoir of infection, greatly modifies the course of the disease,[17] and this would explain the surprising frequency of asymptomatic neonatal infections with associated amnionitis reported in some studies.[13 18] Our Case 8, in which the liver abscesses had been resolving in utero, demonstrated that the fetus may also show active resistance to the heavy infection from the amniotic cavity. The relative importance of maternal and fetal immune reactions and the factors favouring infection within the amniotic cavity are among the many points requiring clarification in this puzzling disease.

## Appendix

### ISOLATION OF L. MONOCYTOGENES—BACTERIOLOGICAL METHODS

Swabs were cultured on to nutrient blood agar and incubated at 37°C for 18 to 24 hours in an atmosphere of 5% carbon dioxide. If growth did not occur cultures were incubated for a further 24 hours. Swabs that were likely to give a mixed flora—for example, vaginal swabs—were cultured on to trypticase-soy agar (BBL), incubated at 37°C for 48 hours, then viewed with a lens by using obliquely transmitted illumination, according to the method of Henry.[19] *L. monocytogenes* gives a distinctive blue-green colour, enabling rapid separation and identification from other organisms. Isolates suspected of being *L. monocytogenes* were identified by using fermentation and biochemical reactions.[20] All isolates confirmed by this method were forwarded to a reference laboratory for serological typing.

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