Listeria Monocytogenes Infections in Metropolitan Toronto

A Clinicopathological Study

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ABSTRACT

The clinical and laboratory findings in 21 patients with listeriosis are described and the subject is reviewed. Eleven of the infections were septicemias of newborns, eight were meningitis in infants or adults, and two other children had unusual manifestations.

Neonatal septicemia was rapidly fatal; one of 11 infants survived. The disease often seemed traceable to mild maternal infection during the third trimester usually leading to premature delivery of critically ill babies. Only awareness of the possible presence of listeriosis and early antibiotic therapy seem capable of reducing this high mortality.

Tissues from autopsies showed characteristic microscopic necrotic foci with mononuclear infiltration progressing to microabscesses containing small Gram-positive rods. Lesions were found in the one placenta examined.

Five infants with meningitis recovered, and one of three affected adults. Specific diagnosis depends on demonstrating *Listeria monocytogenes;* differentiation from other forms of acute meningitis cannot be made clinically.

One older child had septicemia and another had listerial pharyngitis. Both recovered.

SINCE the classical description of *Listeria monocytogenes* (LM) by Murray, Webb and Swann in 1926,[1] much information has been collected, but only the last 10 years have seen a renewed interest in this fascinating organism. In spite of the vast and rapidly accumulating literature, human infection is still widely regarded as a rarity.

Although the number of bacteriologically proved human cases described in the literature exceed 600,[2] many authors are convinced that the actual number of infections is considerably higher because many human cases have not been reported.[3, 4]

Possibly the first description of LM was that given by Hülphers,[5] but no verification of this observation appears possible.[2, 6] The first authentic isolation of LM from a human source was by Dumont and Cotoni in 1918. The strain was identified as LM by Paterson 20 years later (quoted by Krepler and Flamm,[7] Seeliger and Cherry[8]). Nyfeldt[9] was the first to isolate LM from a case of infectious mononucleosis. Although Burn[10] had previously described generalized infection with lesions in the liver, the most consistently fatal form of the disease was thoroughly described by Reiss, Potel and Krebs,[11, 12] who introduced the term "granulomatosis infantiseptica".

The distribution of LM is world-wide and it has been isolated from a great variety of animal species, including primates, rodents and birds and so on.[2, 6, 13] So far the organism has been found only in warm-blooded animals.[2] The wide distribution and the marked susceptibility of many species of animals are not of academic interest only, since epizoötic listeriosis may attain great economic significance involving laboratory animals[1] and herds.[14, 15]

In spite of the description by Murray, Webb and Swann,[1] LM has been repeatedly "rediscovered" and different names for it have been introduced. The grouping of strains into rodent and ruminant types[16] no longer appears tenable, because the four serotypes show no geographical boundaries or strict adherence to a particular host species.[2, 13] Furthermore, the different clinical and pathological features of LM infections in various animals are undoubtedly peculiar to the host organism and its reactivity.

The first bacteriologically proved case in Canada occurred in 1951,[17] and since that time sporadic cases have been reported.[18-23] A number of new cases were encountered recently at The Hospital for Sick Children, which prompted the authors to review all cases of *Listeria monocytogenes* infection. The series of 21 cases described in this report is comprised of all cases seen in Greater Toronto from 1951 until January 1960, including those which have been published previously.[17, 20, 23]

MATERIALS AND METHODS

Strains of LM collected from various hospitals were propagated on blood agar containing 5% defibrinated sheep's blood (Trypticase Soy Agar—Baltimore Biological Laboratories). The biochemical tests were performed with peptone water base (Proteose Peptone No. 3—Difco) containing 0.5% carbohydrate and bromcresol-purple as indicator. Antibiotic sensitivity tests were performed by a plate-disc method, using blood agar plates and 18-hour broth cultures (Penassay broth—Difco) as inocula. After flooding the plates with inoculum, the excess broth was drained and the plates were air-dried. Two concentrations of antibiotic discs (as obtainable from Baltimore Biological Laboratory) were used and the results were read at the end of

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TABLE I.—SUMMARY OF HISTORY AND CLINICAL FINDINGS

Case	Sex	Age on admission	Birth history (weeks)	Clinical signs					Maternal history	Therapy	Outcome	Remarks
				Circulatory	Respiratory	Central nervous system	Skin	Other				
1 WCH 868 1951	M	Newborn	34, premature	..	Rapid, laboured	Twitching	Rash	Discharge from nose, eyes	"Cold", cough, headache, temp. 102°F., for the last week	Penicillin	Died	Death 45 hours after delivery. Spontaneous recovery of mother
2 HSC 37556 1953	F	1 day	36, premature	Cyanosis	Periods of apnea	Generalized convulsions	Rash	Jaundice, temp. 100.2°F., "woody" muscles	Negative	Penicillin, streptomycin, sodium sulfadiazine (Solu-Diazine)	Died	Death within 48 hours after delivery
3 HSC 45855 1954	F	Few hours	35, Premature	Cyanosis	Slow and laboured	..	Rash	Flaccid	"Cold" with slight temp. for the last week	..	Died	Death within a few hours. Siblings healthy
4 HSC 70538 1956	M	3 days	34, one of twins	Dead on arrival			..	..	Negative	..	Died	On third day twitching and respiratory distress. No history available about twin
5 HSC 77705 1956	F	36 hours	37, premature	Cyanosis	Laboured, rapid, periods of apnea	Twitching	Petechial hemorrhages	Slight jaundice, temp. 100.6°F., liver—enlarged	Slight postpartum fever, purulent lochia	Chloramphenicol, streptomycin	Died	Mother has had a second child since without any evidence of disease
6 HSC 81433 1957	F	36 hours	Full-term	Cyanosis	Periods of apnea	Flaccid	Purpuric rash	Slight jaundice, liver enlarged, temp. 103.6°F.	Negative	Oxygen	Died	Died suddenly nine hours after admission
7 Mt. Si. A 73 1957	F	Stillborn	30	..	..	..	..	..	Negative	..	Stillborn	Cultures from mother's vagina and cervix negative for L M
8 HSC 5949 1958	F	1 day	32, premature	Cyanosis	Laboured	Twitching	..	Temp. 102.4°F.	Temp. 103°F. for two days. Foul-smelling amniotic fluid	Chloramphenicol	Died	Clinically—aspiration pneumonia. Death within 24 hours
9 HSC 15137 1958	F	2 days	39, premature?	P 160/min. BP 60/20	50/min. Indrawing, laboured	..	Purpuric rash	Temp. 101°F., liver and spleen palpable, eyes inflamed	Negative	Chloramphenicol, penicillin, sulfisoxazole	Died	Slow improvement over a week. Cultures negative on third day. Aspiration of feeding on ninth day
10 HSC 663 1959	M	7½ hours	Full-term	Cyanosis P 132/min.	Periods of apnea 60/min.	..	..	Temp. 100.8°F., liver palpable	Cold with cough during last two weeks	Chloramphenicol	Died	Clinically—atelectasis of lungs
11 St.M. 1146 1960	F	35 yr.	..	BP 190/110 Pre-eclampsia; four weeks after admission — Temp. 103°F.					..	Penicillin, tetracycline, chloramphenicol	Recovered	Delivery of 34-week premature girl shortly after LM from blood. Baby survived
12 HSC 56105 1955	M	6wk.	Full-term	..	Rapid	Neck stiffness, twitching	..	..	Negative	Penicillin, streptomycin, Na sulfadiazine, chloramphenicol	Recovered	Otitis media 10 days before admission. Born on a farm
13 HSC 63715 1955	M	2 wk.	Full-term	..	..	Drowsiness	..	Diarrhea, vomiting, temp. 104°F.	Negative	Penicillin, Na sulfadiazine, chloramphenicol	Recovered	No sequelae two months after discharge
14 HSC 3088 1957	M	2½ wk.	Full-term	Cyanosis	..	Convulsions	..	Diarrhea, temp. 101°F.	Negative	Penicillin, Chloramphenicol, Na sulfadiazine, erythromycin	Recovered	Slow recovery in two to three wks. Living on farm. No sequelae in three months
15 HSC 4528 1957	F	4 mo.	Full-term	..	..	Drowsy, convulsions	..	Temp. 101°F.	Negative	Penicillin, chloramphenicol, Na sulfadiazine	Recovered	Living on farm

TABLE I.—SUMMARY OF HISTORY AND CLINICAL FINDINGS (*Continued*)

Case	Sex	Age on admission	Birth history (weeks)	Clinical signs					Maternal history	Therapy	Outcome	Remarks
				Circulatory	Respiratory	Central nervous system	Skin	Other				
16 HSC 5153 1958	F	3 wk.	Full-term	Cyanosis	..	Convulsions, irritable	..	Infected umbilicus, temp. 102°F.	Negative	Penicillin, chloramphenicol	Recovered	Upper respiratory infection three days before admission
17 TGH 12345 1954	M	63 yr.	..	Pulse 80/min.	25/min.	Neck stiffness	..	Rigor, nausea, anorexia, temp. 103°F.	..	Penicillin, streptomycin, chloramphenicol, erythromycin	Recovered	Slow recovery. Persisting headaches. Garment worker, but no contact with furs
18 St.M. 7562 1955	M	65 yr.	..	Pulse rapid, strong. BP 150/88	Rapid, shallow. Early pneumonia	Cheyne-Stokes breathing, positive Kernig	..	Temp. 103°F.	..	Penicillin, Na sulfadiazine	Died	Chronic alcoholic, living in filthy conditions with a dog
19 TEGH 111 1956	M	49 yr.	..	BP 140/100	Dyspnea, poor air entry	Decreased reflexes, generalized convulsion	..	Temp. 105°F. liver enlarged	..	Na sulfadiazine, penicillin, tetracycline, hydrocortisone	Died	Chronic alcoholic
20 HSC 7534 1957	M	9½ yr.	Full-term	Cyanosis	..	Drowsy, semi-comatose, positive Kernig	..	Temp. 102°F.	Negative	Chloramphenicol	Recovered	Sister had "flu" two weeks prior to onset. Temp. normal in 24 hours. Clinically encephalitis
21 HSC 1139 1957	F	15 mo.	Full-term	..	Cough, coryza, inflamed throat	Repeated convulsions. Temp. 105°F.	..	Enlarged infected tonsils, slight otitis	Negative	Penicillin, chloramphenicol, phenobarbital	Recovered	Acute tonsillitis and pharyngitis

24 hours and 48 hours. The results of sensitivity tests are reported as follows:

Sensitive: presence of zones of inhibition around both discs.

Not fully sensitive: absence of zone around low concentration disc.

Resistant: absence of zones around both discs.

Although several media were tried in order to determine sulfonamide sensitivities by the disc method, consistent and reproducible results could not be obtained.

Serological typing of the strains was performed by Dr. R. F. Girard, McGill University, Montreal; Dr. H. P. R. Seeliger, University of Bonn, Germany; Dr. J. Donker-Voet, Institute for Veterinary Bacteriology, University of Utrecht, Holland; and Dr. M. L. Gray, Montana State College, Bozeman, U.S.A.

CLINICAL FINDINGS

A summary of the history and clinical findings in the 21 cases is presented in Table I. From the diversity of symptoms and signs two groups emerge, the clinical pictures of which seem more dependent on the age of the patient and the possible mode of infection than on any other factor.

Cases 1-11 are grouped together as listeriosis of newborns and of pregnancy, while Cases 12-19 comprise listeriosis of the central nervous system. Cases 20 and 21 illustrate other clinical manifestations of the disease.

When the entire group is examined, the sex incidence was equal. In listeriosis of the newborn, females predominated 2:1; in the older group with meningitis the ratio was reversed.

1. *Listeriosis of Newborn (Granulomatosis Infantiseptica)*

This group of 11 cases (52%) comprises the most consistently fatal form of the disease, with a mortality rate of 91%. It appears that only the earliest recognition of the disease and the most vigorous antibiotic therapy may give the patient a chance for survival (Case 11). Although the patients were not critically ill at birth, all fatal cases had an extremely rapid downhill course, and none survived more than 72 hours.

The reports in the literature concerning premature delivery of the affected babies are fully confirmed: in this series, eight were premature babies, one was a stillbirth and only two were full-term deliveries.

Symptoms and signs relating to the cardiovascular and respiratory systems predominated. Most of the infants showed cyanosis, a rapid respiratory rate and poor air-entry at birth. Rapidly deepening cyanosis accompanied by respiratory distress, characterized by poor air-entry, laboured, shallow breathing, dyspnea and periods of apnea indicated the severity of the process. Twitching of muscles and generalized convulsions were frequently present, and skin and tissue turgor was poor. The temperature was usually elevated but subnormal values were not uncommon. Jaundice appeared to be infrequent, but clinically recognizable hepatomegaly was present in almost 50% of the cases. Skin rashes, stressed so much by German authors, were present in half of the cases, but were described as purpuric, hemorrhagic in appearance rather than maculopapular. Vomiting, diarrhea and

TABLE II.—SUMMARY OF LABORATORY AND NECROPSY FINDINGS

	Laboratory findings			*Necropsy findings*		
Case	*Hematology*	*Cerebrospinal fluid (CSF)*	*Source of positive cultures*	*Location of the lesions*	*Other findings*	*Remarks*
1 WCH 868	Hb. 85%	....	Baby —Eyes Nose Mother—Vagina	No permission		Clinically, baby died of septicemia.
2 HSC 37556	Hb. 11.9 g.% W.B.C. 4000 Capillary fragility test positive Coombs' test negative	Cells 180, 80% neutrophils xanthochromic	Baby —Blood CSF Lung Mother—Vagina	Bone marrow, stomach, small and large bowel, urinary bladder, kidneys, liver, spleen, adrenals, thymus, lungs	Early hyaline membrane disease of lungs. Marked purulent meningitis	Lesions in various stages of development. Extensive involvement of large bowel.
3 HSC 45855	Coombs' test negative	....	Baby —Lung Blood Mother—Vagina	Trachea, lungs, thymus, brain, adrenal, spleen, bone marrow, stomach	Hyaline membrane disease of lungs	Lesions in various stages of development
4 HSC 70538	....	....	Necropsy—Blood Lung	Esophagus, stomach, lungs, liver, adrenal, brain	Small tear in tentorium cerebelli	Purulent meningitis
5 HSC 77705	....	....	Baby —Lung Nose Blood Brain Mother—Vagina	Bone marrow, lungs, liver, adrenal, pancreas, kidney, brain	..	Many foci involving portal vein. Purulent meningitis
6 HSC 81433	Hb. 18.5 g.%	....	Baby —Blood Lung Brain	Duodenum, lungs, liver, spleen, adrenal, brain	Subarachnoid hemorrhage	Purulent meningitis
7 Mt. Si. A 73	....	....	....	Lungs, liver, spleen, brain, adrenals	Generalized anasarca	No cultures obtained. Morphologically lesions due to LM. Gram-positive rods in sections
8 HSC 5949	....	....	Baby —Nose Throat, Lungs, Vagina, Blood, Liver Mother— Amniotic fluid	Stomach, pancreas, liver, adrenals, kidney, lungs, brain	Hyaline membrane disease of lungs. Aspiration of amniotic fluid. Small subarachnoid hemorrhage	Foci deep in brain
9 HSC 15137	W.B.C. 7600	Cells 650—all mononuclear	Blood Eyes CSF Stool	No permission		Died from aspiration of feeding
10 HSC 663	....	Cells 5— mononuclear	Lungs at necropsy Mother—Vagina	Lungs, adrenal, liver	Subarachnoid hemorrhage. Torn falx cerebri	Principal lesions in lung
11 ST.M. 1146	Hb. 13.5 g.%	....	Mother—blood	Lesions in placenta	Multiple infarcts in placenta	Admitted with pre-eclampsia
12 HSC 56105	W.B.C. 20,000 60% neutrophils 40% lymphocytes	Cells 600—all mononuclear. Chlorides 119 mg.% Protein 480 mg.% Sugar 84 mg.%	CSF Blood	..	..	CSF culture—negative in 48 hr. First CSF showed mononuclear cells; subsequent specimen neutrophils.
13 HSC 63715	W.B.C. 38,000 88% neutrophils 12% lymphocytes	Cells 700— 90% mononuclear Protein 660 mg.% Xanthochromia	CSF	..	..	CSF culture—negative in 24 hr. and 2 wk. later—W.B.C. 20,000 with 50% lymphocytes
14 HSC 3088	Hb. 17.2 g.% W.B.C. 8900 56% neutrophils 39% lymphocytes	Cells 34,500—all neutrophils	CSF	..	..	CSF pleocytosis almost disappeared within 14 days. Culture negative in 24 hr.
15 HSC 4528	Hb. 9.7 g.% W.B.C. 31,000 55% neutrophils 39% lymphocytes 6% monocytes	Cells 4300— 90% neutrophils	CSF	..	..	CSF culture—negative in 48 hr. Temp. normal in 6 days
16 HSC 5153	Hb. 22 g. % W.B.C. 26,300 shift to left	Only very few neutrophils	CSF	..	..	Infected umbilicus, but LM not found. Temp. normal on third day.
17 TGH 12345	Hb. 63% W.B.C. 5000 80% neutrophils 20% lymphocytes Sed. rate 130 mm./1 hr.	Cells 350 - 750 85% neutrophils later mononuclear. Chlorides 670 mg.% Protein 89 mg.% Sugar 0	CSF Blood	..	..	Agglutination 1:128 3 wk. after onset
18 ST.M. 7562	NPN 22—122 mg.% Serum chloride 53 mEq./l.	Cells 186 90% mononuclear Protein 182 mg.% Sugar 27 mg.%	CSF	No lesions found other than subacute meningitis	Portal cirrhosis. Acute sulpha nephrosis. Blood clot in third ventricle of brain	Death not due to LM
19 TEGH 111	Hb. 11.9 g.% W.B.C. 5400 92% neutrophils 8% lymphocytes	Cells 2000, over 90% neutrophils Sugar 40 mg.% Chlorides 480 mg.%	CSF	Chronic meningitis but no focal lesions	Acute bronchopneumonia. Fatty liver	Gradual decrease of cells in CSF. Death due to bronchopneumonia
20 HSC 7534	Hb. 14.3 g.% W.B.C. 6900 Shift to left	Negative	Blood Stool	..	..	Rapid recovery
21 HSC 1139	Hb. 12 g.% W.B.C. 13,000 Calcium 6.2 mEq./l. Phosphorus 4.95 mEq./l.	....	Nasopharyngeal secretions	..	..	Rapid recovery

purulent discharge from the nose, eyes and vagina were infrequent.

It is obvious that no characteristic clinical picture emerged. The severity of the condition and the extremely rapid course of the disease in a premature baby hardly permitted time for thorough laboratory investigation. Thus the specific nature of the infectious process was frequently missed.

The clinical picture of a critically ill, often moribund infant contrasts sharply with the manifestation of the disease in the mother. Since there is enough evidence from the present series to suggest that the mother is the source of the infection of the newborn, it is considered that the two groups, although clinically very different, should be treated as an entity.

LM was isolated from 70% of the mothers, and 60% of those mothers had clinical symptoms and signs.

Most frequently, a slight elevation of temperature was present for a short period of time, accompanied by cough, "head cold" and mild generalized malaise. This ill-defined "flu"-like illness was usually of short duration, and the temperature subsided after delivery. In most cases this symptom complex appeared just before delivery. Only one of the mothers had an elevated temperature during the postpartum period. Although many of the mothers received antibiotic therapy, the impression was gained that the delivery of the infected infant was the decisive factor in influencing the course of the disease.

The infection of mothers seemed to be self-limiting and no permanent ill-effects could be noted. Although a paucity of symptoms characterizes this syndrome, the clinical picture may vary and more severe forms can be encountered (Case 11).

Table II presents the summary of the available laboratory findings. It is apparent that the rapid lethal outcome precluded any extensive investigations of this group, and no generalizations can be made in this regard.

Two case reports are described in detail to illustrate the clinical features in a newborn as well as a somewhat unusual case of infection of the mother.

CASE REPORTS

CASE 8.—A 23-year-old Italian primigravida was admitted because of onset of pains at 32 weeks of gestation. The mother developed a temperature of 103° F. rectally 48 hours prior to delivery, without any apparent cause. The membranes were ruptured and an uncomplicated low forceps delivery followed 10 hours later. The amniotic fluid was foul-smelling and meconium stained. The baby showed some cyanosis, and once the respirations were started they were shallow. Cyanosis and respiratory distress of the baby increased rapidly during the next 24 hours, accompanied by an elevation of temperature to 102.4° F. rectally. The baby was admitted to The Hospital for Sick Children where her condition rapidly deteriorated, followed by death within 24 hours of admission. A chest radiograph taken before death was reported as compatible with an aspiration pneumonia. The temperature of the mother returned to normal within 24 hours after delivery and she received only one injection of 400,000 units of penicillin and 0.5 g. of streptomycin.

CASE 11.—A 35-year-old Italian woman (para II, gravida III) was admitted to hospital because of a moderately severe toxemia of pregnancy. While in hospital she developed chills and fever (25 days after admission), and blood cultures were positive for LM. The clinical response was good within four days of chloramphenicol and penicillin therapy. Seven days after the onset of the febrile illness, a premature baby girl was delivered in good clinical condition. The baby was placed on chloramphenicol therapy and she remained healthy throughout. The postpartum period was uneventful, and the mother and child were discharged two weeks after delivery. The mother was readmitted 24 hours later with a high temperature and generalized convulsions. She became afebrile within two days on penicillin and chloramphenicol, but developed nystagmus and ataxia while on diphenylhydantoin sodium (Dilantin) and phenobarbitone therapy. With the discontinuation of the last two drugs the cerebellar signs disappeared, and the patient was discharged 24 days after the second admission. No positive cultures for LM were obtained during the second admission.

There is no satisfactory explanation for the second episode, and the possibility of a relapse of a listerial infection cannot be ruled out. It was felt that the differential diagnosis lay between epilepsy, relapse of the infection or a postpartum toxemia with convulsions. However, no definite diagnosis was possible.

II. *Listeriosis of Central Nervous System (CNS)*

The clinical picture differs little from other types of bacterial meningitis and offers no clue as to the identity of the causative agent. The five cases in infants will be discussed separately from the three adult cases.

All of the affected babies were the product of full-term normal pregnancies; their ages varied from two weeks to four months. In three cases the parents were investigated for the presence of LM, but positive cultures were not obtained. No fatalities and no sequelae occurred among the infants.

The initial symptoms appear to be unrelated to the central nervous system, and are not characteristic. The disease may begin as an acute upper respiratory infection accompanied by some degree of cyanosis; this is followed after a few days by the development of irritability in the child, and sometimes a convulsive episode occurs just before admission to hospital. In two cases the children developed diarrhea, cyanosis, vomiting and, later on, drowsiness and convulsions. Usually the symptomatology had existed for several days; only in one case had the symptoms been present for as short a period as 12 hours, and in this case they were suggestive of involvement of the central nervous system. Localizing neurological signs were usually absent, and only in one case was there flaccid paralysis on one side. The fontanelles may be under tension, but in two patients they were quite nor-

mal. The temperature ranged from 101° to 104°F. rectally.

In one patient (Case 12), otitis media preceded the meningitis by several days.

The laboratory data were more complete, and positive cultures were obtained in every instance. In one patient LM was isolated from the blood as well as from cerebrospinal fluid.

The cerebrospinal fluid (CSF) showed pleocytosis, the number of cells varying from 600 to 34,500 per c.mm. In two patients the cell response was entirely mononuclear, and in one of these there were many large vacuolated cells mixed with small mononuclears. In both, the cell count was below 1000 per c.mm. The other changes were similar to those seen in other types of purulent meningitis. The cerebrospinal fluid protein was elevated and ranged from 89 to 660 mg.%; sugar 27 to 84 mg.%, and chlorides 480 to 660 mg. %. Minimal xanthochromia was present in two patients. The peripheral blood showed leukocytosis with a shift to the left, the values varying from 20,000 to 38,000 per c.mm. In one patient only, the value was 8900 with a differential count of 56% neutrophils and 34% lymphocytes. However, the same case showed the highest content of cells in the cerebrospinal fluid (34,500 per c.mm.) with 100% neutrophils. There were no marked changes in hemoglobin values.

On vigorous combined antibiotic therapy, cultures became negative within 72 hours. The infants were usually afebrile by the third day, but on two occasions fever persisted until the sixth day.

The following case report will serve as an illustration.

CASE REPORT

CASE 12 was a six-week-old male infant admitted to The Hospital for Sick Children because of refusal of feeding, irritability and vomiting. Ten days before admission, the infant had developed an acute otitis media with a temperature of 104°F., which had improved only slightly on chloramphenicol and penicillin therapy. Three days after the onset of otitis media, spiking temperatures to 101°F. occurred daily, accompanied by head retraction, slight nuchal rigidity, irritability and muscle twitching. There were no localizing neurological signs and the CSF showed 600 mononuclear cells, many of which were large and vacuolated. Laboratory tests showed a CSF chloride level of 119 mEq./l.; sugar 84 mg. %; protein 480 mg. %; and LM was isolated from both CFS and blood. The CFS was sterile after 48 hours and the cell count slowly decreased over the next 10 days. The white blood count was 20,000 per c.mm., with 60% neutrophils and 40% lymphocytes. The patient was afebrile on the third day of therapy with streptomycin, penicillin, and sodium sulfadiazine (Solu-Diazine) for the first three days, followed by chloramphenicol for the next nine days. LM was not isolated from the nasopharyngeal secretions of the parents or of one sibling, or from the vaginal cultures of the mother.

All three cases of meningitis in adults occurred in males, and it is noteworthy that two were chronic alcoholics living in filthy, inadequate conditions. Once again the onset of infection was insidious and resembled a "pyrexia of unknown origin" rather than a meningitis. Furthermore, the clinical picture was complicated by a history of acute alcoholism on two occasions. The most clear-cut history was obtained in Case 17 where the onset was characterized by high temperatures, rigors, anorexia, nausea and marked prostration for seven days, but without neurological signs. Only at the end of the first week did the patient develop neck stiffness. LM was repeatedly cultured from the CSF and from the blood.

The other two patients had less clear-cut histories. One was found unconscious on the floor after prolonged alcohol intake; the other complained of weakness, loss of sensation, inability to walk and dyspnea.

The laboratory data revealed evidence of acute bacterial meningitis with changes similar to those seen in young infants. The only patient of these three to survive had a prolonged hospital course (eight weeks) and had persisting headaches thereafter for three to four months. The two deaths were difficult to attribute directly to meningitis, and both patients probably died of complications related to alcoholism. However, both showed subacute to chronic meningitis, though typical focal lesions could not be seen in any of the organs. In one of the patients there was some hydrocephalus and a small amount of blood in the third ventricle, but all cultures were negative at necropsy.

III. *Other Clinical Syndromes*

The clinical features of the remaining two cases are best presented as short case histories.

CASE 20 was a 9½-year-old boy who had been struck on the head by a playmate 24 hours before admission. There was no loss of consciousness. However, during the night the boy vomited twice and by morning was drowsy and had a high fever. In the afternoon of the same day he was found after he had fallen out of bed; he had clenched teeth, was drooling from the mouth and had cyanosis of the lips. In spite of sedatives the boy remained tense; he curled up and lapsed into a semicomatose state until admission. In hospital he was irritable and hard to manage, and had a positive Kernig's sign with some neck stiffness and an injected throat. The remainder of the physical examination was negative. The cerebrospinal fluid was clear and contained no cells; there was no increase in globulin (Pandy) and a normal pressure. The laboratory tests showed a hemoglobin of 14.3 g. %; leukocyte count 6900 per c.mm. with a differential of 54% neutrophils, 30% band forms, 1% metamyelocytes, 9% lymphocytes, and 6% monocytes. The provisional diagnosis was encephalitis of unknown origin. However, a blood culture and a stool culture grew LM. The boy received chloramphenicol, 500 mg. four times daily, and was afebrile within 24 hours. With the subsiding temperature, his sensorium cleared and he felt well 48 hours after the initiation of antibiotic therapy.

In view of his rapid recovery and the positive cultures for LM, the final diagnosis was septicemia.

CASE 21.—A 15-month-old girl was first seen in the Emergency Department of The Hospital for Sick Children after a convulsive episode at home. She had had a temperature of 104°-105° F. with coryza and cough for several days. Although the child had been seen by a physician and had received tetracycline, no improvement occurred. The girl was given penicillin and phenobarbitone and released. However, she returned four hours later, having had further convulsions at home, and was admitted with a temperature of 105° F., slightly injected ear drums, markedly inflamed throat and enlarged tonsils. The rest of the physical examination was negative. Nasopharyngeal secretions grew LM. The other laboratory findings were: blood sugar 116 mg. %; serum calcium 6.2 mEq./l.; serum phosphorus 4.95 mEq./l.; hemoglobin 12 g. %; leukocyte count 13,000 per c.mm.; radiographs of chest and long bones for lead were negative. Repeated attempts to secure cerebrospinal fluid were unsuccessful. On aqueous penicillin, 600,000 units daily, the temperature returned to normal within 36 hours, with marked general improvement.

It would be difficult to classify the two cases, but Case 20 could be best described as a septicemia in an older child, and Case 21 could represent an acute tonsillitis and pharyngitis due to LM.

PATHOLOGY AND PATHOGENESIS

The study of the lesions of human listeriosis is based on autopsy material from newborn babies only. It is likely that the same tissue reaction would be provoked in adult cases.

In the newborn, the basic macroscopic lesion is a small miliary nodule which is usually greyish-white to greyish-yellow in colour. The size varies from that of a pinpoint to 2-3 mm. in diameter. In the present series these have been noted only in the liver. No mucous membrane lesions were seen, although these have been stressed by European authors.[7, 24]

Microscopically the earliest lesion appears to be damage to the parenchymal cells, which undergo degenerative change. This is followed by infiltration of mononuclear cells, which increase in numbers as the lesion progresses (Fig. 1). These mononuclear cells show some peculiarities which appear rather characteristic of human listeriosis. The cytoplasm of the cells stains only faintly, and the cells have indistinct borders. The nuclei have a faintly basophilic central area, whereas the chromatin appears to accumulate underneath the nuclear membrane, giving a rather densely staining rim of varying thickness. The nuclei show bizarre forms and tend to be very uneven, so that one has to focus the microscope up and down to appreciate fully their odd shape (Fig. 2). Many apt descriptions could be given: pear-shaped, hook forms, handle-shaped, club-shaped, and so on. These cells are best seen in early lesions, and no difference could be noted between various organs. With beginning necrosis of the cells of the parenchymal organs, the reticulin framework may collapse, and only after necrosis has occurred are polymorphonuclear leukocytes seen in the lesions (Fig. 3). In advanced foci the necrotic centre is filled with cellular debris, remnants of pyknotic nuclei and purulent exudate; nothing remains of the original structure, but the advancing peripheral edge contains well-preserved

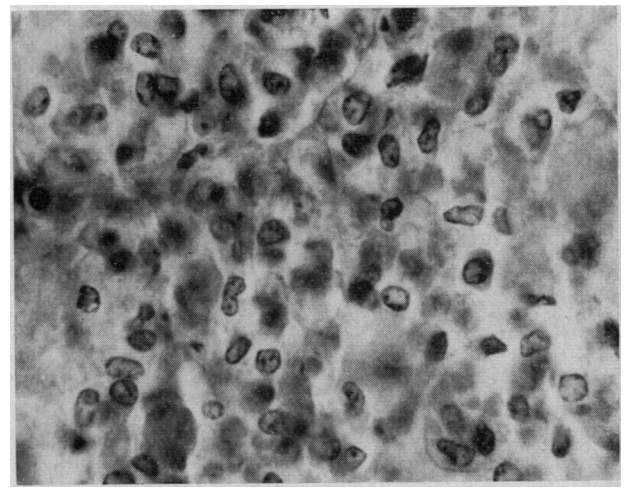

Fig. 1.—Early lesion in adrenal gland. Note the mononuclear cell infiltrate. (Hematoxylin-eosin, × 336.)

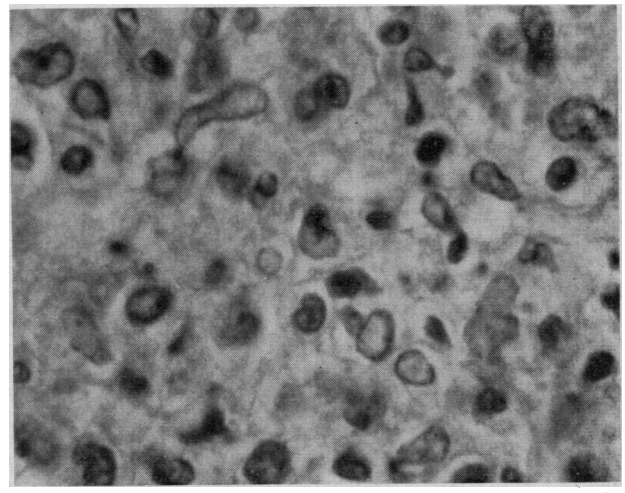

Fig. 2.—Bizarre nuclear forms of mononuclear cells in early lesion in liver. (Hematoxylin-eosin, × 640.)

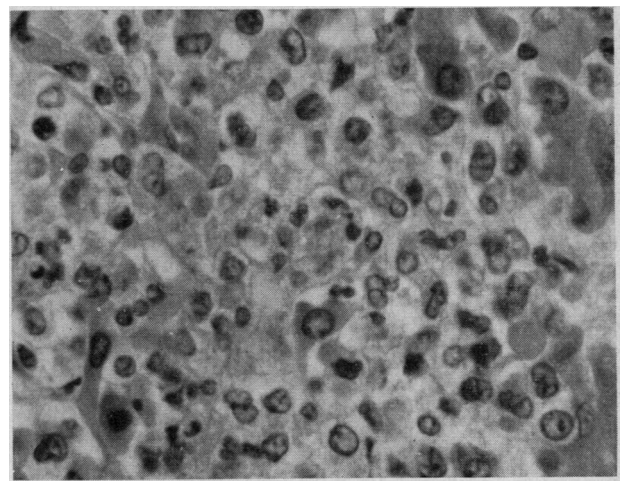

Fig. 3.—Early but more advanced lesion in liver. Note the beginning of polymorphonuclear leukocytic infiltration. (Hematoxylin-eosin, × 336.)

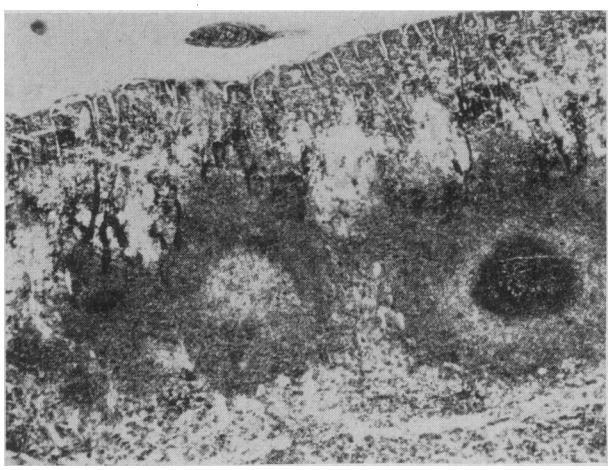

Fig. 4.—Advanced lesions in adrenal with massive central necrosis. Note the various stages of development of the foci. (Hematoxylin-eosin, × 26.)

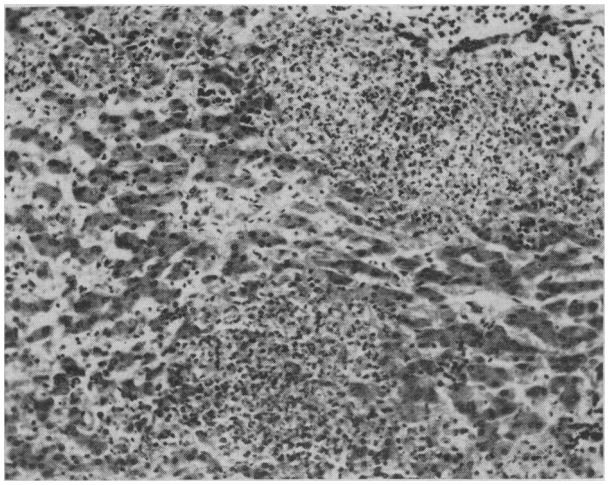

Fig. 5.—Moderately advanced lesions in liver. There is no definite localization of the foci. (Hematoxylin-eosin, × 120.)

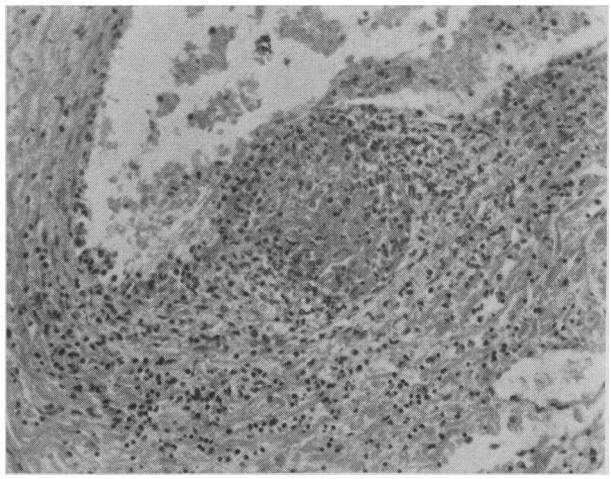

Fig. 6.—Involvement of portal vein as a manifestation of severe septicemia. (Hematoxylin-eosin, × 84.)

polymorphonuclear leukocytes, mononuclear cells and parenchymal cells undergoing necrosis. One finds numerous foci side by side in various stages of development, but despite the proximity of these lesions, the foci do not tend to coalesce (Fig. 4). In several instances the impression was gained that the foci showed an advancing periphery leaving

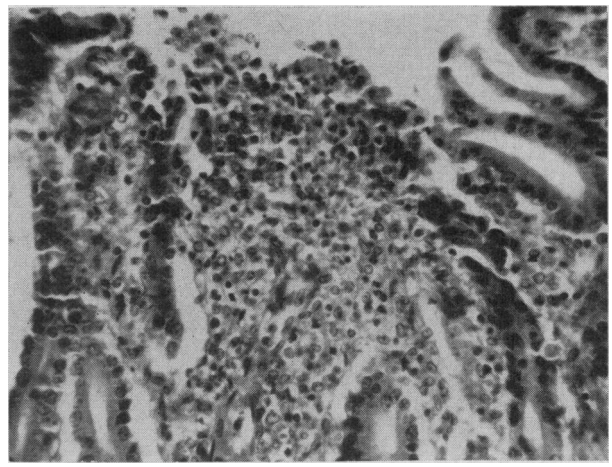

Fig. 7.—Early lesion in pyloric end of stomach. Beginning central necrosis and ulceration. (Hematoxylin-eosin, × 187.)

the centre relatively acellular, but exhibiting a coagulation type of necrosis with no polymorphonuclear leukocytic infiltration. It is not apparent why some of the foci tend to enlarge in this particular fashion and not form small microabscesses, since both types may be seen side by side in the same organ. It is only natural that the polymorphonuclear response may vary and at times may be minimal, depending on the age of the patient—i.e. prematurity of the newborn. There was no definite pattern of localization of the lesions in parenchymatous organs (Fig. 5), and only in the kidney were the foci seen in the cortex and not in the medulla. In some instances well-defined lesions were found in the branches of the portal vein (Fig. 6), and although it is tempting to accept this as proof of a possible route of infection in terms of specific venous drainage area (e.g. umbilical vein → portal vein → liver; alimentary tract → portal vein → liver), it is felt that finding of foci in blood vessel walls is only indicative of the severity of the infection, since similar involvement of arteries was seen in the pancreas and the urinary bladder.

The gastrointestinal tract was involved in varying degrees, ranging from a few isolated mucosal foci to rather extensive involvement with ulceration and sloughing of the mucosa. Microscopic lesions were observed in all parts, including the esophagus and stomach. The earlier lesions were seen in the superficial areas of the mucosa, and once again mononuclear cells predominated (Fig. 7) until necrosis had occurred. With larger foci there was ulceration of the mucosa, but even in cases of extensive involvement one could appreciate the focal nature of the disease (Fig. 8). The earliest foci were more frequently seen in the pyloric end of stomach than in the small and large intestine. However, this may not be a true distribution, since the specimens of tissue taken from the intestines may not have been representative. The most extensive involvement was found in the large bowel (Fig. 8), resulting in ulceration of the mucosa and involvement of the serosa. In no case was there any

Fig. 8.—Marked involvement of large bowel with extensive ulceration. Note the demarcation of individual lesions. (Hematoxylin-eosin, × 75.)

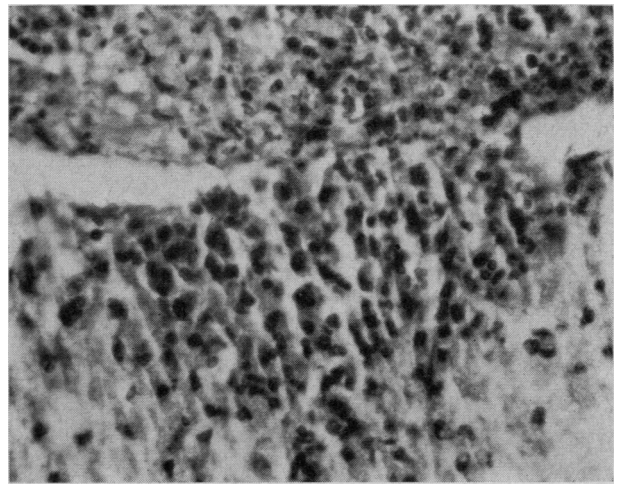

Fig. 10.—Heavy purulent exudate and a focal lesion extending into underlying cortex. This is typical of listeriosis. (Hematoxylin-eosin, × 180.)

evidence of peritonitis. On several occasions polymorphonuclear leukocytes were seen in the lumen of the intestine, and Gram-stained sections showed the presence of Gram-positive rods in the meconium.

The central nervous system was involved in every case. Interestingly, the diagnosis of meningitis was made on gross examination in only half of the cases. The earliest lesions were noted near capillaries and consisted of accumulations of mononuclear cells (Fig. 9) similar to those seen in other organs. In well-marked cases the inflammatory exudate was present commonly around the base of the brain, and in one case it was described as greenish and gelatinous in appearance. Microscopically the exudate consisted of polymorphonuclear leukocytes, mononuclear cells and cellular debris. Mononuclear cells were seen frequently, and on two occasions they predominated in the exudate. The superficial areas of the cortex showed edema, and in many instances focal lesions were seen extending from the meninges into the cortex (Fig. 10). This focal extension into the superficial cortex appears to be typical of listeriosis, since a similar histological picture appears to be lacking in other types of bacterial meningitis. In addition to the superficial foci, deep-seated lesions were noted, and frequently the ventricular system showed loss of ependymal lining with superficial focal involvement of the underlying brain (Fig. 11). No real glial reaction was noted in relation to these lesions. Occasionally small petechial hemorrhages were noted in the brain, and frequently small amounts of blood were seen in the subarachnoid space and in the ventricles. In only one instance could this be explained by a small tear in the tentorium cerebelli. It is believed that there is a widespread damage to capillaries as evidenced by the hemorrhages in the central nervous system as well as by the purpuric skin rash. The choroid plexus was markedly congested and at times showed foci similar to those seen in other parts of the brain.

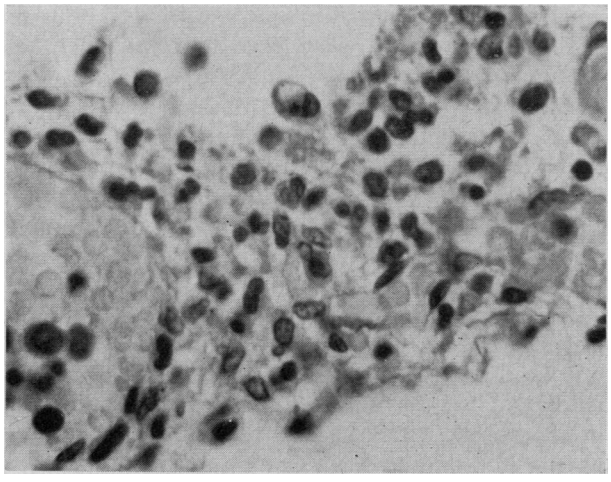

Fig. 9.—Earliest lesion in meninges. Note the absence of polymorphonuclear leukocytes and the close proximity of the lesion to capillaries. (Hematoxylin-eosin, × 240.)

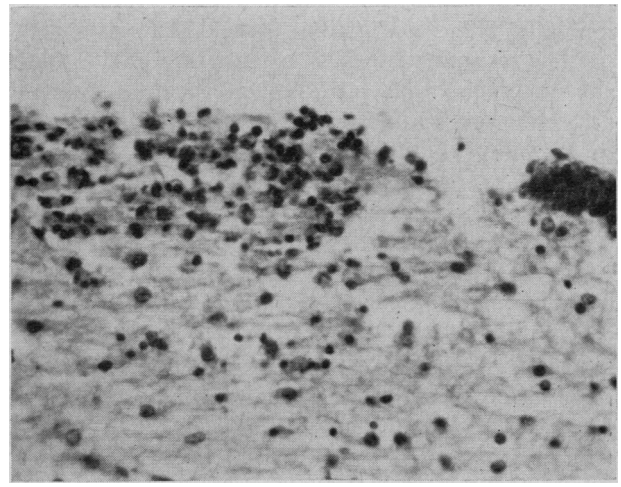

Fig. 11.—Focus in ventricle with loss of ependymal lining. (Hematoxylin-eosin, × 100.)

With severe septicemia, focal lesions were found in many organs such as the bone marrow (Fig. 12), thymus, peribronchial lymph nodes, urinary bladder, and pancreas. The lungs were often involved, and foci were seen in the trachea, the major bronchi

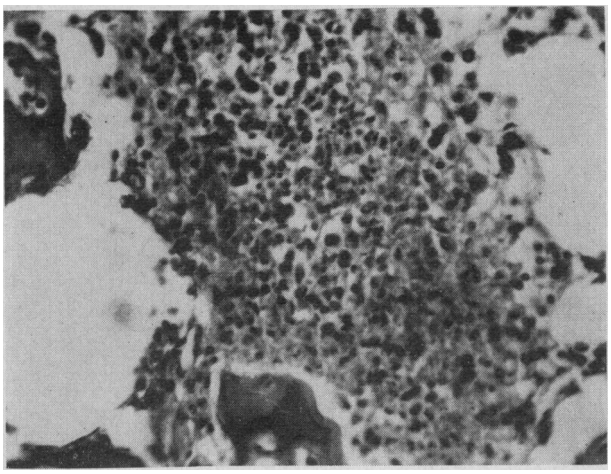

Fig. 12.—Focus in bone marrow with beginning central necrosis. (Hematoxylin-eosin, × 187.)

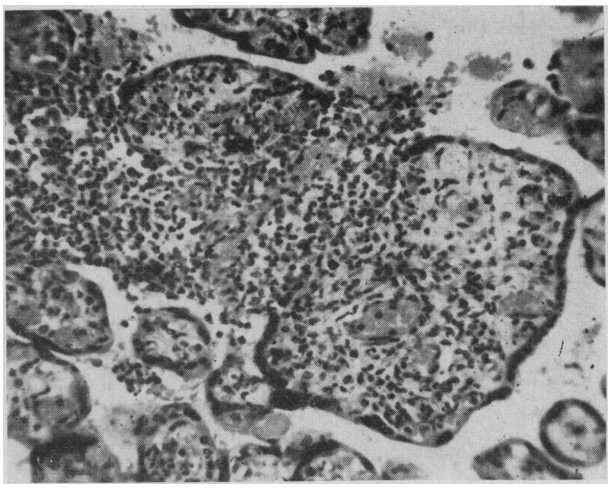

Fig. 14.—Lesions in intervillous space of placenta. Note the involvement of chorionic villi. (Hematoxylin-eosin, × 100.)

and the terminal respiratory bronchioles. The mucosa showed ulceration, and bacilli could be demonstrated with ease in the foci themselves as well as in the lumen. With marked involvement there was a varying amount of exudate distending the alveolar ducts. In most instances the exudate was quite purulent, but in several instances there was a relative paucity of polymorphonuclear leukocytes (Fig. 13). An interesting observation was noted in Case 10 which showed a massive involvement of the lungs but only occasional early small foci in the liver and adrenal glands. This type of involvement suggests a possible mode of infection of the fetus, as discussed below.

Unfortunately only one placenta could be examined. This came from Case 11 in which the mother responded well to treatment and the infant survived. The placenta showed focal lesions and scattered small infarcts. The foci were mainly seen in the intervillous spaces with involvement and destruction of the chorionic villi (Fig. 14). Although the infant was perfectly well clinically, it was interesting to find such well-developed foci in the placenta seven days after the onset of the disease in the mother and without any evidence of repair. The demonstration of Gram-positive rods in these foci was equally interesting.

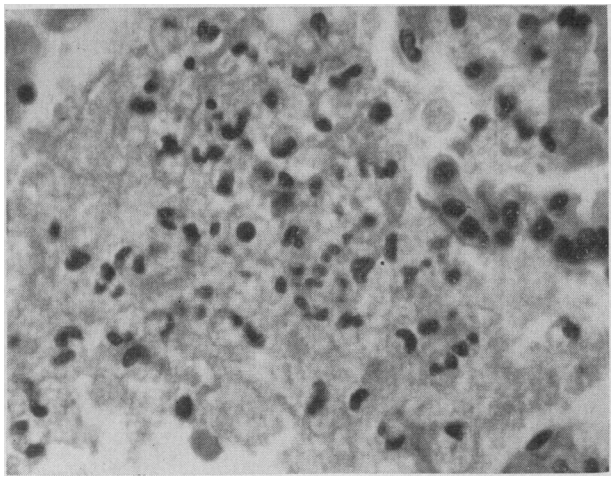

Fig. 13.—Exudate in alveoli. Note the relative paucity of polymorphonuclear leukocytes. (Hematoxylin-eosin, × 288.)

Admitting that the specimens of tissue taken for histological study from the eight cases autopsied may not have been fully representative, it is of interest to note that the central nervous system, adrenals and lungs were involved in all eight cases; the liver in seven; the gastrointestinal tract in six; the spleen in four; the kidneys and bone marrow in three; the thymus and pancreas in two, and the urinary bladder and peribronchial lymph nodes in one case. As mentioned previously, hepatomegaly was recognized clinically in almost 50% of the cases. However, when the weight of the liver and spleen was reviewed in relation to body weight,[25] every case showed hepatomegaly and half the cases showed splenomegaly.

The portal of entry in man has not been established, and different opinions[24, 26, 27] have been expressed as to the mode of entry of listeriosis in newborns. The most likely route is a transplacental hematogenous spread with secondary involvement of all organs. The infection of amniotic fluid appears to be secondary, with possible reinfection of lungs and gastrointestinal tract by means of aspiration and swallowing of the fluid. However, opinions differ considerably as to the importance of this particular feature.[24, 26, 27] That the aspiration of infected amniotic fluid may at times be the primary event in a generalized infection of the fetus is illustrated by Case 10. The very marked involvement of the respiratory tract, with only one or two early microscopic foci in the liver and adrenal, contrasts so much with the other cases of the series that the probable explanation of that type of involvement is that primary infection of the lungs occurred owing to aspiration of the infected amniotic fluid. One has to admit, however, that further study of Case 10 raised more questions than could be answered. Although LM was cultured from the vagina of the mother who gave a history of a "cold" with cough prior to delivery, the placenta was not available for study, and the possibility of an

ascending vaginal infection with primary involvement of the fetal membranes and the amniotic fluid cannot be excluded. The present series did not reveal any evidence to support Flamm's theory of retrograde infection of the mother.[28]

The mode of infection of mothers and of older children and adults with meningitis remained obscure, and no opinions can be offered. It is quite obvious that the pathogenesis of the disease in these cases is not uniform and much remains to be explained. Since many of the older children showed initial symptoms and signs of acute respiratory tract infection, it is conceivable that the respiratory tract may be the portal of entry, with subsequent hematogenous spread to the meninges. Direct lymphatic spread cannot be excluded in all instances, since Case 12 presented as otitis media of some days' duration.

No opinions can be offered in relation to Case 20 (septicemia other than in the newborn). The case of acute tonsillitis and pharyngitis (Case 21) representing localized organ infection probably resembles those described in the literature under oculoglandular and cervicoglandular forms.[2]

BACTERIOLOGY

Although there is some controversy as to the systematic classification of LM,[29] it appears that the majority of authors accept that given in Bergey's Manual.[30]

LM is a short Gram-positive, non-sporulating, non-encapsulated, aerobic to microaerophilic, motile rod, usually measuring half a micron in width and one to two microns in length in young cultures. Although the morphology is rather uniform at first, considerable pleomorphism is noted in older cultures, long filamentous forms predominating. The peritrichous flagellae are responsible for the motility, which is best demonstrated at room temperature and serves as a very important criterion in differentiating it from diphtheroid bacilli and *Erysipelothrix rhusiopathiae*. The so-called tumbling motility seen in hanging drop preparations appears to be rather characteristic of LM.

The colonies when first isolated on a blood agar plate are small, translucent, glistening and with entire edges. On further incubation the colonies tend to become greyish-white in colour, opaque and surrounded by a zone of beta hemolysis. The degree of hemolysis may vary and in young cultures may be present only in the medium directly underlying the colonies. Both smooth and rough forms occur, and many colonial variants have been observed.[31] The colonies may closely resemble those of streptococci. The cultures have a rather characteristic acid smell.

All strains in the present series grew well on ordinary culture media and had very similar morphological and colonial characteristics. There were differences in the fermentation of certain sugars, these findings corresponding well to those described in the literature. None of the strains produced gas and all strains fermented glucose, maltose, salicin, rhamnose, xylose, levulose, and trehalose. No acid was produced in mannitol, arabinose, glycerol, dulcitol, inositol, sorbitol, adonitol and raffinose. Sucrose was fermented slowly by two strains only. Fermentation of lactose showed some irregularity and frequently it was delayed for 48 to 72 hours. However, two strains failed to ferment lactose and two additional strains showed traces of acid only after incubation for several days. Variability was also noticed in fermentation of melezitose, and Seeliger's[2] finding of certain biotypes within serotypes 1 and 4 could be partly confirmed. Only three out of 18 serotype 4b strains failed to ferment melezitose. All strains failed to utilize citrate on Simmonds' citrate agar, and all failed to reduce nitrates. All strains were negative for indole, hydrogen sulfate and urease. The Voges-Proskauer test and the methyl red test were positive in all instances and all strains were catalase-positive. Acid was produced in litmus milk, whereas gelatin was not liquefied. None of the strains survived 60° C. for one hour. Sodium chloride tolerance was tested only with half of the strains, and there was definite but feeble growth after 48 hours on mannitol-salt agar plates (Difco).

Serological studies were done as previously indicated, and with two exceptions all strains belonged to serotype 4b. The strain from Case 3 belonged to serotype 1, and Case 6 was due to a type 2. To our knowledge this is the first isolation of type 2 in Canada. The strains isolated from infants and their mothers corresponded to each other.

The monocytosis-producing agent (MPA) was discovered by Stanley.[32] Recently it has been suggested by Keeler and Gray[33] that MPA is contained either in the bacterial cell wall or membrane. The production of monocytosis in experimental animals, although highly suggestive, is not pathognomonic for LM.[2] The production of keratoconjunctivitis in rabbits and guinea pigs appears to be much more specific.

Antibiotic sensitivities by the disc-plate method revealed that all strains were fully sensitive to tetracycline, oxytetracycline, chlortetracycline, erythromycin, neomycin, kanamycin, ristocetin and vancomycin. All strains were resistant to polymyxin B, and most strains were resistant or not fully sensitive to nitrofurantoin. About half of the strains were not fully sensitive to penicillin, streptomycin, bacitracin and novobiocin. Only three strains were fully sensitive to chloramphenicol, the rest being not fully sensitive. A similar pattern was found with oleandomycin. The findings with chloramphenicol were surprising, since a very good therapeutic response was obtained in the treatment of meningitis with this drug. It may be that the age of the inoculum used in doing the tests (18 hours) was responsible for these results *in vitro*.

The results are similar to those found in the literature, and the choice of antibiotic for therapy should be based not only on results of *in vitro* tests, but should be guided by other aspects as well (diffusibility into meninges, and so on).

DISCUSSION

Ever since the cultural and serological similarity between human and animal strains of LM was established, numerous attempts have been made to relate human infections to contact with animals. This direct causal relationship has been proved in few cases, and we are still ignorant as to the exact epidemiology in most instances.

The present series failed again to supply additional information, and although a number of our cases probably had contact with animals, nothing definite could be elucidated. The portal of entry remained obscure and one can only speculate as to the factors which played a role in initiating the infection. Undoubtedly the host plays an important role, and a lowering of resistance may pave the way for the infection. This probably occurred in the two chronic alcoholics who developed meningitis.

Since LM is rather resistant to adverse environmental conditions and can survive for prolonged periods in hay, straw, soil, etc.,[13, 34] it would appear that it can exist as a saprophyte. The role of healthy human carriers has received scanty attention.[35]

Human-to-human infection appears to be very rare, but the low degree of communicability could be enhanced by environmental conditions, and it seems that listeriosis could assume epidemic proportions under certain conditions (overcrowded nurseries).[10, 36] Direct contact with infected animals may be an occupational hazard (veterinary personnel) and cutaneous manifestations may predominate in these cases.[2, 37]

Although the final diagnosis of listeriosis depends on cultural confirmation, we believe that the miliary type of lesion with its detailed histopathology is sufficiently characteristic to be recognized as such and to allow a diagnosis. Furthermore, Gram-positive rods could be demonstrated with ease in stained sections of the lesions and thereby almost fully confirm the diagnosis. The necrosis of parenchymal cells is suggestive of the effects of bacterial toxin(s), but clear-cut evidence to this effect is lacking, even though toxic substances have been isolated from cultures.[38]

Care has been taken to demonstrate that the earliest lesion in tissues is characterized by degenerative changes in parenchymal cells accompanied by mononuclear cell infiltrate. It appears that this mononuclear reaction depends on the lipoid fraction of LM (MPA of Stanley) and we believe that it is a constant feature of early lesions. The relationship of listeriosis to infectious mononucleosis is highly controversial. Although no cases resembling infectious mononucleosis have been traced to LM in our experience, a number of such cases have been reported and review articles have appeared in the literature.[2, 7, 39] The isolation of the organism from those cases may have two explanations: first, that LM is a saprophyte with no relationship to this syndrome; and secondly, that it is the causative agent of a syndrome indistinguishable from the viral disease. We agree with Krepler and Flamm[7] and believe that infectious mononucleosis is a syndrome caused by two or more etiological agents. The constant presence of localized mononuclear infiltrate in early lesions in tissues tends to support this, and it is quite conceivable that under exceptional circumstances the host will react to infection with LM not with well-marked localized lesions, but with a generalized reticuloendothelial response and a peripheral monocytosis.

No additional information could be obtained about the relationship of repeated abortions to listerial infections. This causal relationship, although suspected for some time, has been based on serological evidence only[2, 40] and has been denied by others.[41] Important observations were reported by Rappaport *et al.*[42] from Tel Aviv, who isolated LM from the cervical canal in 25 of 34 women with histories of repeated abortions. No positive cultures were obtained from a control group of 87 women. These observations are important, and although it is too early to draw conclusions, they warrant further study. The overall incidence of listerial infections in relation to pregnancies and perinatal mortality has received little attention, and it would be interesting to compare the mortality figure of 0.154% reported by Breuning and Fritzsche[43] with those from other centres.

During the study no difficulties were encountered in growing the various strains of LM. One wonders, however, how many times the organism may have been missed because it failed to grow. There is universal agreement that few difficulties are encountered once the strains have been isolated. However, potential difficulties have been noted in isolating the organism from tissues. Many attempts have been made to overcome these difficulties, and the refrigeration method described by Gray[44] has proved to be reliable, although time-consuming in an ordinary diagnostic laboratory. The use of selective media has been suggested,[45-47] as well as the use of a scanning microscope with obliquely transmitted light for rapid identification of colonies.[48] According to Potel,[49] examination of meconium is most important in establishing the diagnosis in the newborn. In cases of granulomatosis infantiseptica, a direct smear stained by Gram's method will frequently reveal masses of Gram-positive rods, whereas normal meconium contains few bacteria.[2, 7] Conclusive diagnosis would naturally depend on cultural confirmation. In view of the high mortality in cases of granulomatosis infantiseptica, the earliest possible diagnosis is imperative and such examination of meconium might help. Although no such

examinations were made during life in our cases, Gram-positive rods were seen with ease in the lumen (meconium) of the infantile gastrointestinal tract in all sections taken for study.

Available data indicate that great caution should be exercised in interpretation and evaluation of the results of serological studies. Apart from the fact that many bacteriologically proved cases fail to develop demonstrable agglutinins, it has been shown that some strains of enterococci, beta hemolytic streptococci and staphylococci share common antigens with one or more Listeria serotypes.[2, 50]

Since no cases of listeriosis had been recognized prior to 1951, a preliminary histological review of autopsy material from The Hospital for Sick Children, Toronto, was undertaken to ascertain whether any cases had been misdiagnosed. Although the survey included material as far back as 1939, only one suspicious case was found. This was not included, because of insufficient data. No explanations can be offered for the apparent increased prevalence between 1951 and 1960.

Since animal experiments have shown that cortisone enhances the susceptibility of animals to listerial infection,[51] it is advisable to refrain from using the various hormone preparations in the treatment of these cases.

The apparent increase of listerial infections indicates that these are not rare, and with increased awareness more cases will be recognized. It should be re-emphasized that LM resembles "diphtheroid bacilli", and this may result in mistaken identity, with subsequent discarding of the culture as a contaminant. In view of this, it is not permissible to regard Gram-positive rods in smears of cerebrospinal fluid as contaminating diphtheroid bacilli. The fact that more than 80% of our cases belonged to the neonatal period suggests the importance of the problem to pediatricians and obstetricians and the need for an increased awareness of the disease by the medical profession generally.

SUMMARY

Twenty-one cases of listeriosis seen in Greater Toronto during the past 10 years have been described. Eleven cases (52%) belonged to the group of listeriosis of the newborn. Eight cases (38%) had listeriosis of the central nervous system. The remaining two cases represented localized organ infection (tonsillitis) and septicemia other than of the newborn type. Emphasis has been placed on the non-specific clinical picture of the disease in the newborn period and on its severity (mortality 91%). The clinical and laboratory aspects of cases of meningitis resemble those of other types of bacterial meningitis. The histopathology of the basic lesion in tissues, although not altogether pathognomonic, is sufficiently characteristic to permit a tentative diagnosis with a very high degree of accuracy. The final diagnosis must depend on cultural confirmation. The biochemical reactions of the strains have been discussed and compared with the reports in the literature. Evidence to suggest that LM is one of the causes of repeated abortions has been reviewed and emphasis has been placed on factors responsible for the misconception that human listeriosis is a rare disease.

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