

CLINICAL AND PATHOLOGICAL FEATURES OF AN INFECTION
CAUSED BY A NEW PATHOGEN OF THE GENUS
LISTERELLA *

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A new species of organism belonging to the genus *Listerella* was first obtained from a newborn infant in February, 1933. One year later a similar organism was recovered from the blood in 2 separate cases of fatal illness in infants, and soon thereafter a fourth organism of the same type was isolated at autopsy from the meninges and viscera of an adult. A brief clinical, epidemiological and pathological presentation of the findings in these 4 cases follows.

CASE REPORTS

CASE I. A-2810. The patient, a white male infant, was born at home at 1.00 A.M. on Feb. 17, 1933. It was the seventh child of apparently healthy parents. All the other children were living and well. It was said, however, that the mother had had a cold several days before delivery, but she had apparently recovered at the time of the birth of this child. Labor lasted for 20 hours, but it was a normal spontaneous delivery, occurring 2 hours after the rupture of the membranes. At birth the baby was cyanotic and did not cry immediately but had to be stimulated to breathe. Difficulty in breathing recurred later in the day and was accompanied by cyanosis, with the result that the physician sent the child to the hospital.

On admission the patient was moribund, breathing irregularly, gasping for air, and appeared cyanotic. The temperature was 101° F. The anterior fontanelle was open and not bulging. There was no evidence of injury to the head. Jaundice was not present. Heart sounds were poor in quality. There were numerous, fine crepitant râles heard over both lungs. Blood and lung cultures yielded a hemolytic Gram-positive bacillus.

The infant did not react to stimulation and expired within the hour.

Pathological Findings

Postmortem examination performed 12 hours after death presented the following significant findings.

The body was well developed, weighing 3175 gm., and was 53 cm. in length. The only gross evidence of change observed was the

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presence of atelectasis involving all of both lungs except the anterior margins.

Histologically the walls of the larger umbilical vessels showed some infiltration with small lymphocytes and a few polymorphonuclear leukocytes. Small areas of focal pneumonia and bronchiolitis were observed in both lungs. The sinusoids of the spleen were markedly congested and there were small areas of extravasated blood. Small focal areas of necrosis distributed throughout the liver parenchyma (Fig. 1) were infiltrated with polymorphonuclear leukocytes, red blood cells and large mononuclear cells.

Permission for examination of the central nervous system was not granted.

Cultures procured from the heart's blood and all the viscera yielded a hemolytic Gram-positive bacillus. The ileum and colon also contained this organism. In addition, *Pneumococcus* Group IV and *Hemophilus influenzae* were isolated from the throat.

The unusual nature of the clinical, anatomical and bacteriological findings made it necessary to attempt to determine the source of the infection. The infant's parents proved to be healthy; throat cultures yielded the usual mouth flora and no organisms resembling the one infecting the infant could be isolated. Vaginal examination of the mother 8 days after the birth of the child showed no unusual bacteria. Three of the four children were carefully examined and found to be well. Their throat cultures were entirely negative for pathogenic organisms. No evidence of agglutinins could be found for the organism obtained from the infant with the serum of the mother and father. A pet rabbit found in the house was emaciated and had snuffles, but a more detailed examination of it was refused.

CASE 2. A-3063. The patient was a white, female infant born 3 weeks before the expected date at 8.50 A.M., Feb. 17, 1934, on the outside obstetrical service of the New Haven Hospital. The mother was a 27 year old multipara. This was her fifth pregnancy. There are three children living and well. A spontaneous abortion occurred between the birth of the first two children. Normal spontaneous birth of this child was completed 27 hours after the onset of labor. Repeated stimulation was necessary to elicit regular and continued breathing, after which the child's color became good. However, during the course of the day episodes of labored breathing and cyanosis recurred and the child appeared drowsy. Later, on the 2nd day, after a somewhat prolonged attack similar to those occurring on the 1st day, it was brought to the New Haven Hospital.

On admission the child was drowsy and difficult to rouse. Respirations were irregular and slow. Cyanosis was present. The percussion note was impaired on both sides of the chest anteriorly with dullness in the left axilla. Breath

sounds were poorly transmitted and occasional râles were heard. The heart sounds were of poor quality; the rhythm was regular.

The child continued to have episodes of irregular respirations with complete cessation for short periods and the heart ceased beating in one of these attacks.

Pathological Findings

Postmortem examination was performed one-half hour after death. The body of the infant weighed 2050 gm., and measured 45.5 cm. There was no evidence of skull injury. Both lungs were atelectatic. The spleen was swollen and congested.

Histologically the lungs showed areas of focal pneumonia and bronchiolitis. The liver parenchyma, also, contained foci of necrosis similar to those described in Case 1. However, a few of these foci showed evidence of repair, as manifested by an increase in the fibroblasts within these areas. Both adrenals (Fig. 2) showed histologically evidence of focal necrosis and exudation.

The gross findings in the brain revealed an extensive fresh hemorrhage in the ventricles which extended to the aqueduct of Sylvius and into the fourth ventricle.

Microscopically the blood vessels of the brain were tremendously engorged. There was no evidence of meningitic or encephalitic foci in the cerebral parenchyma.

Clinical postmortem cultures procured at the time of death yielded a hemolytic Gram-positive bacillus from the heart's blood.

CASE 3. A-3074. The patient, a white female infant, was delivered by the outside obstetrical service of the New Haven Hospital on Feb. 17, 1934. It was the fourth pregnancy of apparently healthy parents. The infant was delivered at full term and was born in a normal spontaneous manner, following a labor of 3 hours. She cried and breathed spontaneously and presented no evidence of birth injury. She did well until the 8th day when she rather suddenly refused food. A diarrhea developed in the following 24 hours.

On admission to the hospital there was no evidence of cyanosis, but the patient appeared expressionless and drowsy. The anterior fontanelle was not sunken. Both ear drums were red and bulging but without discharge. The heart and lungs showed nothing unusual. The reflexes showed marked irregularity and at times were absent. Kernig's sign was negative.

The white blood cells increased to 15,450 on the 2nd day after admission, of which 93 per cent were polymorphonuclear leukocytes. There was no evidence of anemia. Repeated daily blood cultures always showed the presence of a hemolytic Gram-positive rod. Spinal fluid, both by direct smear and cultural methods, was positive for the same organism found in the blood stream. Cultures made from the nose, throat, vagina, umbilicus and stools failed to demonstrate the presence of this organism at these sites.

On the 4th day after admission active movements of the extremities devel-

oped which were followed by tonic convulsions. Increasing periods of apnea and cyanosis appeared, the temperature became subnormal, and the child expired on the 5th day of its residence in the hospital and the 14th day of its life.

Pathological Findings

The postmortem examination performed 4 hours after death presented the following findings.

The body was that of a well developed infant weighing 3155 gm., and measuring 54 cm. A few petechial hemorrhages were observed beneath the pleural surfaces of both lungs. Otherwise there was no gross evidence of other change within the lung tissue. The spleen was large, swollen and markedly congested.

Histologically, similar focal zones of necrosis, such as were observed in the previous autopsies, were widely distributed throughout the liver parenchyma. The sinusoids of the spleen were engorged with blood and large hemorrhages were present. The umbilical cord showed no histological evidence of infection.

On gross examination of the brain a thick green exudate was observed in the subarachnoid space covering the medulla, pons and parietal lobes. Both lateral ventricles were filled with a similar type of exudate which extended into the aqueduct of Sylvius (Fig. 3) and completely occluded the lumen. A suppurative ependymitis was observed in both lateral ventricles.

Histologically there was an extensive suppurative meningitis, ependymitis and choroiditis. The process extended into the cerebral parenchyma from the arachnoidal and ependymal linings by way of the vascular sheaths. These vessels were surrounded by an exudate comprised of polymorphonuclear leukocytes, lymphocytes and plasma cells. Hemorrhage was present in all sections. A gliosis (Fig. 4) involving all the glial elements occurred in association with the necrotizing process.

At postmortem a hemolytic Gram-positive bacillus was cultured and demonstrated by stained smears in the heart's blood and viscera, including the brain.

The epidemiological studies of the family showed the mother to have had a cold several weeks before birth of the child. The father and five children were healthy and free of respiratory infection. However, cultures prepared from the posterior pharynx of all the family yielded a few colonies of *Streptococcus hemolyticus* and *Hemophilus influenzae*, besides the usual mouth flora. Likewise,

serological examinations of the family revealed no agglutinins for the organism isolated from the infant. No significant findings were obtained by examination of water and milk used in the household or of the saliva and feces of the pet dog.

CASE 4. A-3167. This patient was a 53 year old, white male who was brought to the New Haven Hospital on June 27, 1934. The immediate illness began in March, 1934, when he developed a bilateral otitis media. Two weeks before admission the left ear became very painful and the patient had a severe headache which persisted until he came to the hospital.

On admission he was uncoöperative and at times irrational. A purulent discharge from the left ear was manifest. There was marked tenderness over the left mastoid. No stiffness of the neck could be elicited. Reflexes were absent and there was a loss of sense of position of the feet. An X-ray examination of the mastoid showed bilateral mastoiditis with evidence of marked destruction of the petrous bone on the left. On the 6th postoperative day, following a mastoidectomy (left), the patient developed signs of meningitis. A second operation revealed an abscess of the petrous apex from which *Pneumococcus* Type III was obtained. The laboratory findings were compatible with an acute infection. The blood became positive for *Pneumococcus* Type III and death occurred on the 9th day after the operation.

Pathological Findings

Postmortem examination performed 2 hours after death presented the following findings.

The body was that of an emaciated white male, weighing 52 kilos and measuring 178 cm. A serosanguineous exudate drained from the operative incision of the left ear. The superficial lymph nodes were enlarged. Both lungs were voluminous because of congestion and edema. Histologically both lungs showed evidence of focal pneumonia and bronchiolitis.

The cortical surfaces of the brain were covered by a thick green exudate within the subarachnoid space. Microscopically this exudate was comprised of polymorphonuclear leukocytes, but showed no extension into the cerebral parenchyma.

The heart's blood and viscera, including brain, contained a *Pneumococcus* Type III. In addition, a hemolytic Gram-positive bacillus was procured from the brain, liver and both kidneys, but not from the heart's blood or spleen. This bacillus was demonstrated in the meningeal exudate by stained smears.

DISCUSSION

The clinical and anatomical findings in the 4 cases described above have several factors in common. A new pathogen belonging to the

TABLE I
Summary of Clinical and Postmortem Findings

No. of Case	Age	Presenting symptoms and signs	Physical examination	Blood culture	Total duration of disease	Autopsy findings				Postmortem bacteriology		
						Lungs	Liver	Spleen	Brain	Heart's blood	Liver	Brain
2810	1 day	Labored breathing, cyanosis, normal delivery	Temp. 101° F., irregular breathing, cyanosis, no jaundice	Hemolytic Gram-positive bacillus	24 hrs.	Focal pneumonia, bronchiolitis, atelectasis	Focal necrosis	Congestion and hemorrhage	Not examined	+	+	-
3063	1½ days	Irregular and weak respiration, cyanosis, drowsy, normal delivery	Temp. 98° F., irregular breathing, cyanosis, no jaundice	Hemolytic Gram-positive bacillus	36 hrs.	Focal pneumonia, bronchiolitis, atelectasis	Focal necrosis	Congestion	Hemorrhage in ventricles	No cultures procured at postmortem		
3074	14 days	Diarrhea, onset on 8th day after birth, normal delivery	Temp. 101.8° F., cyanosis, no jaundice, drowsy, expressionless, apnea	Hemolytic Gram-positive bacillus	6 days	No change	Focal necrosis	Congestion and hemorrhage	Suppurative meningitis	+	+	+
3167	53 yrs.	Bilateral otitis media, operation (mastoidectomy), meningitis	Temp. 98.6° F., tenderness of mastoid, meningitis — 6 days postoperative	Pneumococcus Type III	6-8 days?	Diffuse pneumonia	Focal necrosis	Congestion and hemorrhage	Meningitis	o	+	+

+ = hemolytic Gram-positive bacillus.
o = no growth in bouillon.
- = not cultured.

genus *Listerella* has been readily obtained from the heart's blood or viscera in all 4 cases. The organism has been grown by the usual culture methods and has been demonstrated readily by the Gram stain in the various tissues. Cultural, serological and pathogenic properties of these strains are described in another communication.¹

In all 4 cases the anatomical lesions involved the liver and in the 3 cases in which the central nervous system was examined lesions were revealed in the tissues. Otherwise, there were no clinical or anatomical manifestations that would permit a differentiation of this infection from other infectious processes without careful bacteriological studies made either during the clinical course of the disease or at postmortem.

Confusion in a bacteriological diagnosis may arise from two standpoints. First, since this bacillus is markedly hemolytic on blood agar plates and in blood broth, and since it has a tendency to form short chains in meat infusion broth, particularly when freshly isolated from the tissues, it may be mistakenly called a *Streptococcus hemolyticus*. Second, it has some of the characteristics of the diphtheroids and consequently may be overlooked as a non-pathogenic organism. Since careful morphological, cultural and pathogenic studies are required for identification of this new pathogen, a more detailed comparative study with some related organism will be forthcoming in a later communication.

The literature contains isolated reports in which Gram-positive bacilli or diphtheroids have been described in association with meningitis. The description of the cultural and pathogenic properties of many of the strains is inadequate but in a few instances sufficient data are available to exclude identification with the organism under consideration. In an epidemic of meningitis occurring in infants, Atkinson² isolated a Gram-positive bacillus which may be similar to the one herewith described, although a more detailed cultural, serological and pathogenic study would be necessary before relationship could be established. Schultz, Terry, Brice and Gebhardt,³ however, have recently described the isolation of an organism from a non-fatal case of meningo-encephalitis occurring in an adult, which has proved to be identical morphologically, culturally and serologically with the hemolytic Gram-positive bacillus isolated from these 4 cases.

The latter fact is of importance since it is hardly a coincidence that

the same organism should be isolated in 4 separate fatal cases here, and also by observers in California. Moreover, Jones and Little,⁴ of Princeton, and Seastone⁵ recently isolated and described a similar organism associated with a suppurative meningitis in cattle. Through the courtesies of these investigators,^{3,4,5} it has been possible to study transplants of their strains and they have been found to be identical, both culturally and serologically, with those isolated from the 4 cases included in this report. A possible source of the infection in man through the milk supply is suggested in view of the isolation of the same organism in suppurative meningitis of cattle.

SUMMARY

A hemolytic Gram-positive bacillus of the genus *Listerella* has been isolated from each of 4 fatal human infections. Three of the individuals were newborn infants and the fourth an adult.

The clinical symptoms and anatomical changes presented by the fatal cases are briefly described.

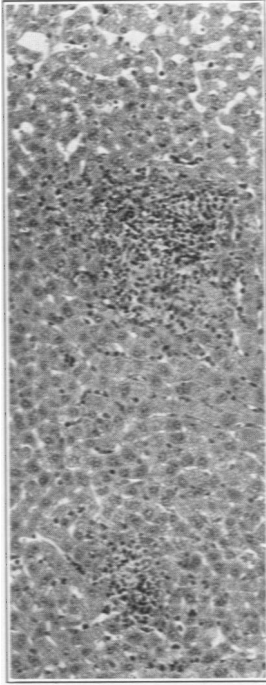
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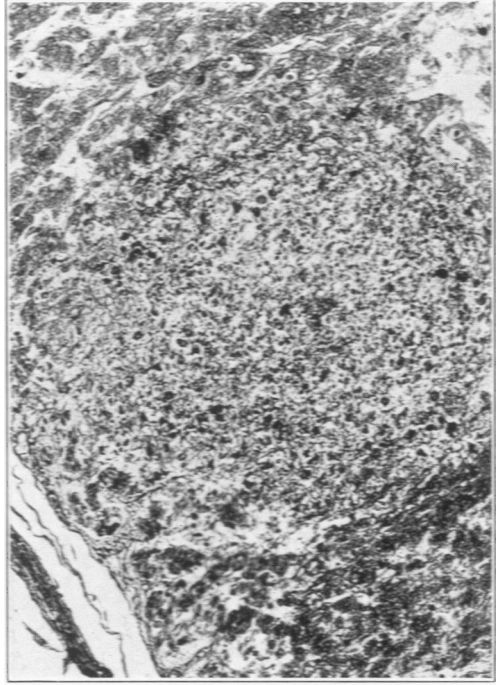
DESCRIPTION OF PLATE

PLATE 39

- FIG. 1. Case 1. Focal zone of necrosis in liver. $\times 70$.
 FIG. 2. Case 2. Focal zone of necrosis in adrenal. $\times 70$.
 FIG. 3. Case 3. Suppurative meningitis with occlusion of fourth ventricle. $\times 70$.
 FIG. 4. Case 3. Suppurative meningitis with marked glial proliferation. $\times 70$.



1

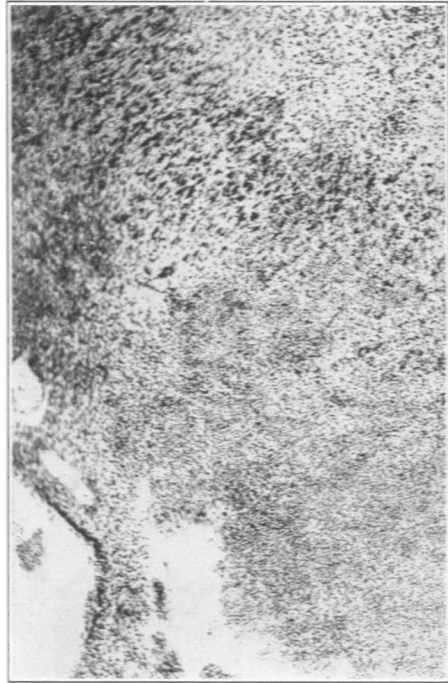


2



3

Burn



4

New Pathogen of Genus *Listerella*