AN EPIDEMIC OF STREPTOCOCCUS HEMOLYTICUS SEPTICEMIA *

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The purpose of this report is to record an epidemic of streptococcus septicemia occurring late in November and early in December, 1921, in a ward of seventeen babies in a nursery home.

The age of these infants ranged from one month to 7½ months. They were housed in a new building in a commodious ward, well ventilated and well lighted, with a sun porch attached, where they spent the day in individual cribs and were returned to their beds in the ward at night.

Before the onset of the epidemic all the babies were in good general condition, gaining in weight and having no gastro-intestinal disturbance. All were bottle fed babies, on whole milk dilutions with water and sugar added. Two were receiving small amounts of breast milk in addition to their cow's milk formulas. The milk and water used was boiled three minutes.

Suddenly, as it were out of a clear sky—two of the youngest infants (aged 1 month and 2 months, respectively) began to have fever, one 103 F. and the other 104 F. For the next two days their temperatures ranged from 103 to 105 F., coming down to 102 F. on the fourth day—the day of their death.

Clinically, both children showed extreme prostration, an acutely inflamed pharynx, enlarged cervical glands; on the third day distention of the abdomen with paralysis of the intestines; stupor and death on the fourth day. One infant showed some retraction of the head on the third day. There was no vomiting and no diarrhea. Enemas were given daily. Both infants took their food eagerly until the day of death. There were no convulsions. Nothing abnormal was found on examination of the heart and lungs.

The necropsy findings were: Case 1: Septicemia; peritonitis; cloudy swelling of viscera; hypostatic congestion of lungs and pericardial effusion. Case 2: Septicemia; cloudy swelling of viscera; punctate hemorrhage of renal capsule with a little bloody fluid in the peritoneal cavity.

During the next two and one-half weeks, seven other infants developed symptoms and clinical findings similar to the above, but with the absence of the extreme prostration, the marked pharyngitis and

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cervical adenitis. Five of these seven infants died, and at necropsy the picture was the same as in the first two cases recorded. The degree of pathologic change seeming to be directly proportional to the duration of the illness (Table 1).

Blood was taken from the longitudinal sinus in six of the cases and cultured in sugar agar and sugar bouillon. The *Streptococcus hemolyticus* was recovered in five cases. No attempt was made at further classification of the streptococcus other than to note that it

TABLE 1.—NECROPSY FINDINGS

	Case							
	1	2	3	4	5	6	9	
Septicemia.....	+	+	+	+	+	+	+	
Peritonitis.....	+	..	+	+	+	+	+	
Cloudy swelling of viscera.....	+	+	+	+	+	+	+	
Bronchopneumonia.....	..	..	+	..	..	..	+	
Hyperemia of lungs.....	+	..	..	+	+	..	..	
Edema of brain.....	..	..	..	..	..	+	+	
General lymphoid hyperplasia.....	..	..	+	+	+	+	..	
Pericardial effusion.....	+	..	..	..	..	..	+	
Punctate hemorrhage of renal capsule.....	..	+	..	..	..	..	..	

belonged to the hemolytic group. Of the two infants who eventually recovered, one showed a positive and the other a negative culture. All of the seven infants that died and came to necropsy gave positive cultures of the *Streptococcus hemolyticus* from the heart's blood. In one case (Case 4) cultures taken from the heart's blood, pericardial fluid, pleural fluid and peritoneal exudate showed the *Streptococcus hemolyticus* in pure culture.

TABLE 2.—CLINICAL DATA

Case	Name	Age in Mo.	Fever	Prostration	Pharyngitis	Adenitis, Cervical	Distended Abdomen	Retraction of Head	Late Stupor	Leucocytosis	Blood Culture	Duration of Disease Days	Result
1	Gordon	1	+	+	+	+	+	+	+	..	..	4	Death
2	Marion	2	+	+	+	+	+	0	+	..	..	4	Death
3	Lena	1½	+	+	0	0	+	+	+	Slight	..	4	Death
4	Eleanor	3½	+	0	0	0	+	0	+	+	+	9	Death
5	Dean	4½	+	0	0	0	+	0	+	+	+	13	Death
6	William	4½	+	0	0	0	+	0	+	+	+	10	Death
7	Leo	4	+	0	0	0	0	+	0	+	0	6	Recovery
8	Martin	3½	+	0	0	0	0	0	0	+	+	10	Recovery
9	Norma	7½	+	0	0	0	+	+	0	+	+	5	Death

The leukocyte counts varied markedly in different patients and during the course of the disease in the same patient, without bearing any remarkable relation to the duration of the disease, the amount of prostration, or the ultimate outcome. These counts varied from 10,000 to 44,000 per cm. The average leukocyte count during the disease, as shown by thirty counts taken from seven patients was 22,650 per cm.

The average differential count taken soon after the onset of the cases was: Polymorphonuclear neutrophils, 52.6 per cent.; basophils,

0.3 per cent.; eosinophils, 0.3 per cent.; small mononuclears, 40.1 per cent.; large mononuclears, 3.1 per cent.; transitionals, 3.3 per cent.

A composite clinical picture of the disease may be summed up as follows:

An infant of the average age of 3½ months, previously well, has a sudden rise in temperature, moderately inflamed pharynx, leukocytosis of about 22,000, a blood culture positive for the *Streptococcus hemolyticus*, a distended abdomen, stupor occurring late (or not at all) and death intervening on about the sixth day of the disease. Cervical adenitis and retraction of the head may also be present (Table 2).

Other babies in the ward showed slight variation from the normal in their temperature records, but not enough to be classed clinically as having the disease. Only one blood culture in this group was taken and it was negative.

At the onset of the epidemic, throat cultures were taken from four of the sick infants and a pure culture of *Streptococcus hemolyticus* was recovered from three while the fourth showed a short gram-negative bacillus together with the *Streptococcus hemolyticus*. A vaccine was prepared from these throat cultures and administered as a preventive to the well babies and in the treatment of the sick.

The entire nursery was put under quarantine and a strict isolation of the sick was instituted at the onset.

Treatment was, in the main, symptomatic. Sodium-bicarbonate was given both by mouth and by rectum. Stimulation with camphor in oil, caffeine and digitalis was used. Salt solution was not administered intraperitoneally owing to the ever present abdominal distention and the complicating peritonitis. In one case stock antistreptococcus serum (20 c.c., subcutaneously, in two doses) was given without any apparent change in the clinical course of the disease. Both the well and the sick received small doses of the autogenous vaccine every other day. Its effect on the sick was not striking, but it is possible that the giving of this vaccine to the well babies may have aided them in building up an immunity to the disease.

An effort was made to determine the source of the infection. The milk cultured showed no *Streptococcus hemolyticus*. In addition it was the custom to boil all the milk and water used in feeding for at least three minutes.

Cultures were taken, separately, from the throat and nose of each adult (twenty-two in all) connected with the institution. They showed about the usual incidence of *Streptococcus hemolyticus* in the throats of normal adults. Only two persons showed an abundant growth of the *Streptococcus hemolyticus* from both the nose and throat. These two adults had no part in directly caring for the infants of this par-

ticular ward nor did they come in contact with their food supply. However, they mingled, when off duty, with those in direct charge of these infants at the onset of the epidemic. One of these "carriers" was removed from the nursery for a period of two weeks. Since her return (more than three months ago) there has been no new case. In fact, the whole epidemic from the beginning to the end was of only three weeks' duration.

To sum up the more striking features:

1. *The suddenness of the onset of an epidemic of Streptococcus hemolyticus septicemia in a ward of seventeen babies all of whom were previously in good physical condition.*—In 1918, when the *Streptococcus hemolyticus* came in for such strong incrimination as the great etiologic factor in respiratory infections, there were, as a rule, predisposing diseases of various sorts, such as measles, influenza and pneumococcus pneumonia, which broke down the resistance of the body and prepared the way for the invading streptococcus (MacCallum,¹ and Blake²). In the cases here reported no predisposing disease was present.

2. *The absence of vomiting and diarrhoea.*—These symptoms are frequent complications of all acute infective processes in infants, yet in this group of cases they were entirely absent.

Epidemics of diarrheal diseases due to the streptococcus have been reported (Wilson³).

One might suppose that harboring virulent streptococci in the throat, on swallowing these organisms a definite gastro-enteritis would result. Davis,⁴ investigating experimentally the fate of the *Streptococcus hemolyticus* in the gastro-intestinal canal, showed that this organism does not develop appreciably in the intestine, nor does it readily gain a permanent foothold there.

3. *The absence of any apparent localized infection or site of primary infection.*—Exception to this is made in the case of the first two cases reported; both babies showed marked pharyngitis and cervical adenitis.

Fox and Hamburger,⁵ reporting a streptococcus epidemic following measles, note that it would seem more likely that the process was a primary septicemia, although the infection atrium is clear in no case.

4. *The absence of pulmonary involvement, at least until very late in the disease.*—This, in spite of the fact that bronchopneumonia, as MacCallum¹ and Longcope⁶ have reported, was so prevalent in the streptococcal epidemics in the Army camps in 1918.

1. MacCallum: J. A. M. A. **71**:704 (Aug. 18) 1918.

2. Blake: Ann. Otol., Rhinol. & Laryngol. **28**:361, 1919.

3. Wilson: War Med. **2**:556, 1918.

4. Davis: J. Infect. Dis. **26**:171, 1920.

5. Fox and Hamburger: J. A. M. A. **70**:1758 (June 8) 1918.

6. Longcope: War Med. **2**:566, 1918.

5. *The generally good appearance of the patient until very near the end, thus belying the seriousness of the disease.*—Clinically, this possibly was the most striking feature, and were it not for the fact that positive blood cultures had been obtained, a good prognosis might have been given on the physical findings, when in reality the patient was near death. It leads us also to believe that many of our so-called ordinary "flu" infections are in reality septicemias.

6. *The uniformity with which positive blood cultures were obtained.*—In six patients, with clinical evidence of the disease in which blood cultures were taken, five, or 83 per cent., gave positive cultures for the *Streptococcus hemolyticus*.

Blanton, Burhans and Hunter⁷ state:

The infrequency of septicemia accompanying other localizations of streptococci in the body has frequently invited remark. On many occasions organisms have been recovered from blood at necropsy which repeated cultures had failed to reveal during life.

Davis and Rosenow,⁸ reporting the Chicago epidemic of streptococcus sore throat in 1912, found that blood cultures were almost always negative.

Keegan,⁹ reporting a hospital epidemic of streptococcic sore throat with surgical complications, obtained negative results from blood cultures.

Only one case of streptococcus septicemia was encountered by Nobécourt and Gimbert¹⁰ with bacteriologic examination of the blood in 600 cases among 3,000 soldiers in more than a year.

Abderhalden¹¹ obtained 57 per cent. positive blood cultures in fifty cases of septicemia.

Longcope,⁶ pointing out the relation of the *Streptococcus hemolyticus* to pneumonia in the troops in the United States, says that blood cultures gave no growth.

However, Wilson³ reports obtaining the streptococci from blood cultures in twenty out of twenty-three cases.

7. *The marked uniformity with which peritonitis was encountered.*—Clinically this was manifested by a distended tympanitic abdomen, with late paralysis of the intestine, but without the characteristic vomiting and tenderness. It did not appear as an "acute abdomen."

MacCallum¹ says, in regard to the pathology of the epidemic of streptococcal bronchopneumonia in the Army camps, that "peritonitis occurred only twice."

7. Blanton, Burhans and Hunter: J. A. M. A. **72**:1520 (May 24) 1919.

8. Davis and Rosenow: J. A. M. A. **58**:773 (March 16) 1912.

9. Keegan: J. A. M. A. **72**:1434 (May 17) 1919.

10. Nobécourt and Gimbert: Bull. Soc. méd. d. hôp. de Paris **41**:1037, 1917.

11. Abderhalden: J. A. M. A. **67**:236 (July 15) 1916.

Irons and Marine,¹² reporting on streptococcal infections following measles and other diseases, cite two cases occurring in the course of measles with primary peritonitis.

The only clear cut account of a case in a child found in the literature is that of a girl, 6½ years old, reported by MacLennan and McNee¹³ in 1913, who had a primary *Streptococcus hemolyticus* peritonitis with septicemia. This occurred after an attack of measles and presented the clinical picture of an "acute abdomen." Operation was performed and a general peritonitis was found with a normal appendix. No localizing cause for the peritonitis was revealed. Pus from the abdomen and blood culture showed the *Streptococcus hemolyticus*. The patient recovered.

8. *The epidemiologic study.*—That pathologic streptococci of the hemolytic group can be conveyed by milk is common knowledge (Davis,¹⁴ Jones,¹⁵ Salter¹⁶ and others). Milk was apparently not a factor in the spread of the present epidemic as a great many more children taking the same milk were not affected. Also, the cases did not have their onset simultaneously, and, finally, the milk used was always boiled and when examined bacteriologically gave negative cultures for the *Streptococcus hemolyticus*.

Davis¹⁷ states that there is no evidence to indicate that strains of streptococci pathogenic to man can even resist the usual temperature for pasteurization (145 F. for thirty minutes).

Reviewing the recent literature which is fairly well saturated with bacteriologic studies of the *Streptococcus hemolyticus*, one is impressed with the frequency which the organism inhabits the throats of not only persons suffering from acute infectious diseases, but the throats of normal persons (Otteraaen,¹⁸ Smillie,¹⁹ Pilot and Davis,²⁰ Havens and Taylor,²¹ and Pilot and Pearlman²²).

In fact, Davis²³ states that cultures taken at short intervals sooner or later reveal the presence of hemolytic streptococci in the throats of virtually all normal adult persons. True, they are found less frequently

12. Irons and Marine: J. A. M. A. **70**:687 (March 9) 1918.

13. MacLennan and McNee: Brit. J. Dis. Child. **10**:258, 1913.

14. Davis: J. Infect. Dis. **23**:559, 1918.

15. Jones: J. Exper. M. **31**:347, 1920.

16. Salter: Am. J. Hyg. **1**:154, 1921.

17. Davis: Am. J. Pub. Health **8**:40, 1918.

18. Otteraaen: J. Infect. Dis. **26**:23, 1920.

19. Smillie: J. Infect. Dis. **20**:45, 1917.

20. Pilot and Davis: J. Infect. Dis. **24**:386, 1919.

21. Havens and Taylor: Am. J. Hyg. **1**:192, 1921.

22. Pilot and Pearlman: J. Infect. Dis. **29**:47, 1921.

23. Davis: J. Infect. Dis. **29**:524, 1921.

in the normal throat after tonsillectomy, as reported by Tongs,²⁴ Bryan,²⁵ Nichols and Bryan,²⁶ Van Dyke,²⁷ Pilot and Davis,²⁸ and Meyer, Pilot and Pearlman.²⁸

However, Bloomfield,²⁹ reporting on the significance of bacteria found in the throats of healthy people, states that hemolytic streptococci of the typical beta type (pathogenic) were not obtained in any case.

This is of interest, as the cultures were made from people who were in intimate contact with patients suffering from sore throats due to these organisms. We believe that their presence in normal throats, as reported by some writers, indicates the recent presence of widespread infection among large groups of people with a virulent type of the germ.

These facts lead one to suspect that in the epidemic under study we were dealing with a different strain of hemolytic streptococcus than the ordinary throat inhabitant, or that the virulence of one of the streptococcus strains inhabiting the normal throat became activated and by contact infection (mainly hand infection, in the present case) was spread to other members of the ward.³⁰

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24. Tongs: J. A. M. A. **73**:1050 (Oct. 4) 1919.

25. Bryan: Ann. Otol., Rhinol. & Laryngol. **28**:337, 1919.

26. Nichols and Bryan: J. A. M. A. **71**:1813, 1918.

27. Van Dyke: J. A. M. A. **74**:448 (Feb. 14) 1920.

28. Meyer, Pilot and Pearlman: J. Infect. Dis. **29**:59, 1921.

29. Bloomfield: Johns Hopkins Hosp. Bull. **32**:33, 1921.

30. At the present time (April 1922) Portland is having an epidemic of septic sore throat, undoubtedly due to contaminated milk. There have been several deaths among infants due to streptococci septicemia with terminal peritonitis.