MENINGOCOCCUS SEPTICEMIA WITH STERILE CEREBRO-SPINAL FLUID; IRIDOCYCLITIS; FLEXNER'S SERUM; RECOVERY *

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The specific relation of the diplococcus of Weichselbaum to epidemic cerebrospinal meningitis is established beyond question. Investigations of the last few years have aimed to solve the mystery as to the sources of infection and the route taken by the invading organism in reaching its objective point in the meninges of the brain and cord. The first light on these questions came from the discovery of Albrecht and Ghon¹ that organisms morphologically identical with the Diplococcus intracellularis could be found in the nasal secretions of some of the patients. This observation was quickly followed by the proof that, while some of these organisms resembling the diplococcus of Weichselbaum belonged to other species, there was no doubt that the specific excitant of meningitis could be found in the nasal fossæ of some of the patients and also of others who have not had the disease but had come in touch with patients. Thus Flügge² found the meningococcus in the nasal secretions of patients 4 times in 44 trials, von Lingelsheim³ 182 times in 787 examinations, while Koplik⁴ quotes Goodwin and Sholly to the effect that the organism can be found in the nasal mucus in 50 per cent. of patients during the first two weeks of the disease and in 10 per cent. of those who come into contact with the patients. It seems therefore established that the respiratory tract, especially the nasal fossæ, is the usual avenue of entrance for the organism. The route by which the bacteria make their way from this outpost into the cranial cavity has thus far been the subject of speculation. The popular theory has been that the meningococcus makes its way directly through the sphenoidal or ethmoidal sinuses or the ethmoidal plate to the base of the brain. The facts, so far as they are at present known, lend support to that theory. Evidence is, however, accumulating that it is possible that a general meningococcus septicemia may occur in the absence of a meningitis and that the systemic circula-

^{*}From the Service of Dr. F. P. Kinnicutt in the Presbyterian Hospital.

^{1.} Albrecht and Ghon: Wien. klin. Wchnschr., 1901, xiv, 984.

^{2.} Flügge: Klin, Jahr., 1906, xv, 353,

^{3.} Von Lingelsheim: Klin. Jahrb., v, 373.

^{4.} Koplik: Osler's Modern Medicine, ii. 499.

tion may, at least in some cases, be the pathway by which the organism reaches and lodges in the meninges.

That the meningococcus may be found in the blood in certain cases of epidemic cerebrospinal meningitis has been known for some time. In a recently published article Duval⁵ reports such a finding and has collected from the literature a number of others. The first positive blood finding is credited to Gywn in one of Osler's patients. Warfield and Walker have reported 1 case, Lenhartz 2, Robinson 1 in 6 cases examined, Möller 1, Martin and Rhode 1, and Elser, in 41 cases of cerebrospinal meningitis, found the specific coccus in the blood in 10. On the other hand, Bettencourt and Francis⁶ report 6 cases in which the blood examination during life was negative and 3 in which the organism was found in the heart blood, and Councilman, Mallory and Wright, in 35 cases, made cultures from the heart blood with negative results. Flügge² and Rautenberg⁷ each report failures to cultivate the meningococcus from the blood.

In addition to these reports collected by Duval, I have been able to find 2 positive findings made by Cochez and Lemaire,⁸ 2 by Jacobitz.⁹ 1 by Kutscher,¹⁰ and 1 by Jäger.¹¹

In a number of other cases the specific coccus has been found in locations indicating a systemic infection. Thus Fronz¹² found the organism in the meningeal exudate and in the right ankle, and Osler¹³ some years ago reported a similar observation. Gradwohl,¹⁴ in a postmortem examination of a pregnant woman who had died on the third day of her illness, found the meningococcus in the meninges of both the patient and the 7 months fetus, and also in pus from the mother's ear, although cultures from the lungs, blood, placenta and uterus were negative. Jäger¹¹ reports finding the organism in the urine in one case during life. A general distribution of the organism throughout the body is reported by only two observers. Jäger found it in the pericardium, pleural exudate, liver, spleen and pus in the pelvis of the kidney in 1 case, and Duval isolated it from the eye, pericardium, heart's blood, meninges and cerebrospinal fluid. Wintersteiner and Tooke (see Duval⁵) each recovered the organism from the spinal fluid and found it present in smears

^{5.} Duval: Jour. Med. Research, 1908, xix, 258.

^{6.} Bettencourt and Franca: Ztchr. f. Hyg., 1904, xlvi, 463.

^{7.} Rautenberg: Veröffentl. a. d. Geb. d. Mil.-San.-Wes., 1905, No. 31, 34.

S. Cochez and Lemaire: Baumgarten's Jahresbericht, 1902, xviii, 91.

^{9.} Jacobitz: Munchen. Med. Wchnschr., 1905, lii, 2178.

^{11.} Jäger: Die Epidemische. Meningitis als Heereseuche, Berlin, 1901, pp. 196, 198.

^{12.} Fronz: Wein. klin. Wehnschr., 1897, x, 351.

^{13.} Osler: Boston Med. and Surg. Jour., 1898, exxxix, 64.

^{14.} Gradwohl: Philadelphia Med. Jour., 1899, iv, 445.

from the eyes, in which iridocyclitis was present, but could not obtain it in cultures from the latter site. Von Drigalska¹⁵ cultivated the organism from herpetic vesicles on the ear, although he could not obtain it from the blood of the patient.

It thus appears that in a certain number of cases of cerebrospinal meningitis the meningococcus may be found not only in the spinal fluid, but in the blood or in various sites which indicate systemic infection. The number of such systemic infections thus far recorded is small, however, and we must regard them as rare. Duval, summing up his study, notes this fact and adds that there is at present no authentic case on record in which the meningococcus has produced lesions outside the meninges in the absence of a pre-existing meningitis.

In 1902, however, Salomon¹⁶ reported the following case:

The patient, a laborer's wife, aged 32, was seized on July 30, 1901, with pains and swellings in her hands, elbows, and knees. On the following day she had a chill, followed by fever, and an eruption on the hands and feet, and became weak and faint. She was admitted to hospital on August 3. She was then suffering from a high fever, and the constitutional symptoms of a severe infection without focal signs, and had a profuse eruption resembling erythema exudativum. The fever and other symptoms persisted. On August 7 a blood culture yielded the meningococcus. From this time on there was no radical change in the patient's condition, the fever continuing, and new crops of the eruption appearing from time to time, until the end of September, when she developed signs of meningitis and lumbar puncture gave vent to a characteristic turbid fluid containing meningococci. The patient finally recovered in December. She had been sick for two months before the advent of the meningitis, and the meningococcus had been found in the blood nearly two months before the lumbar puncture, but as there is no record of a lumbar puncture having been made before the development of the symptoms of meningitis, the possibility of the presence of a meningitis early in her disease is not excluded in this case.

The following case, reported in October of this year by Liebermeister,¹⁷ is free from that objection:

A laborer, aged 59, was admitted to hospital Feb. 25, 1908, complaining only of pain and stiffness in both shoulders. The beginning of his trouble he could not definitely place. The patient showed a high fever with signs of severe infection but no focal symptoms. There was a roseola resembling that of typhoid. On March 1 a blood culture yielded organisms later proved to be Weichselbaum's diplococcus. On March 7 lumbar puncture gave a clear fluid, under normal pressure, and containing no sediment. On March 18, 20 and 31 cultures from the blood still gave meningococci. On April 8 and 18 further cultures were negative-During all this time the fever of septic type continued, the eruption developed in repeated crops, and the patient had pains about various joints and some rigidity of the extremities. He had, however, no rigidity of the neck, no Kernig, no signs of involvement of the cranial nerves, so that there appears no good rea-

17. Liebermeister: München med. Wchnschr., 1908, lv, 1978.

Von Drigalski: Deutsch. med. Wchnschr., 1905, xxxi, 982.
Salomon: Berl. klin. Wchnschr., 1902, xxxix, 1045.

son for assuming that the patient had meningitis, especially in view of the negative results of the lumbar puncture (2). In May the patient developed an abscess on one arm, in which the common pyogenic organisms were found, but no meningococci. Finally the fever gradually subsided, the general condition improved and the patient recovered toward the end of June. In view of the evidence this case must, it seems, be accepted as a meningococcus septicemia without meningitis. As will later appear, I do not record this as proved by the negative results of the lumbar puncture alone; but the absence of the clinical signs of meningitis during the many weeks of observation and the normal spinal fluid constitute as strong evidence as can be had, so long as the patient recovers.

Andrewes,¹⁸ pathologist of St. Bartholomew's, in 1906, reported the following decisive experience:

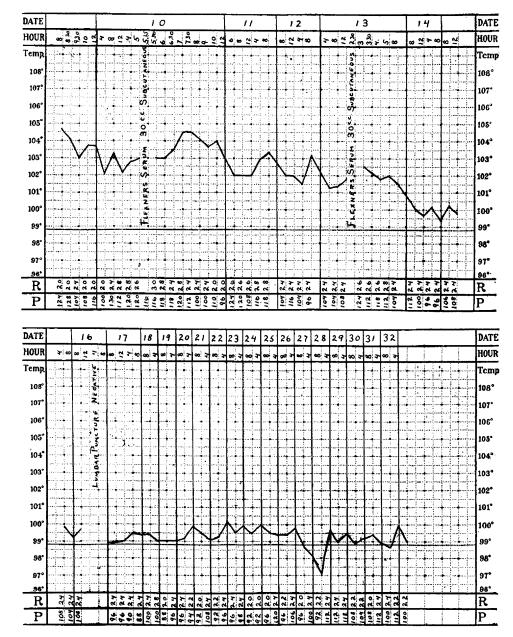
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A physician, aged 52, was suddenly taken sick on the morning of Feb. 12, 1906-A few spots appeared on the face at noon. By evening a profuse hemorrhagic purpura had developed. The patient was moribund. Temperature was 99.4, pulse imperceptible, respirations 34; intracellular cocci found in the polynuclear leucocytes of the blood, proved by cultural studies and pathogenicity to be the *Diplococcus intracellularis*. Autopsy showed no meningitis either in the gross or microscopically. Extravasated meningeal blood, however, yielded a more abundant growth of the diplococci than did that of the heart.

Andrewes concluded that the case was proved to be one of blood infection by the meningococcus without meningitis.

18. Andrewes: Lancet, London, 1906, i, 1172.

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Temperature Chart of a Case of Meningococcus Septicemia from October 5 to November 6.

In view of this evidence of the possibility of systemic infection by the meningococcus in the absence of meningitis, I wish to put on record the following case:

Patient.—S. P., aged 15, Russo-American, was admitted to the Presbyterian Hospital Oct. 5, 1908. Her family history was irrelevant. There was no contagious disease in the neighborhood; no meningitis among her friends.

History.—The patient was born in New York; lived under fair tenement-house conditions; had never menstruated. From birth up to the age of 2 she had frequent hemorrhages from the navel. Since then she enjoyed good health. She had had no previous illness except measles eight years ago, uncomplicated.

Present Illness.—On October 4 the patient was perfectly well. She went to a holiday dinner and was said to have greatly overeaten. About midnight she vomited three or four times. Vomitus consisted of green undigested food; vomiting was not projectile. The rest of the night the patient seemed to sleep quietly. On the morning of October 5 she complained of slight headache. The child did not seem very ill and the parents went to the synagogue, leaving her at home alone. At noon when they returned the child seemed as if dead, her face was yellow, and there were many dark spots on the body. She did not recognize her parents; the urine and feces were passed involuntarily. After that she was in a stupor; shook a little but had no real convulsions. She had no vomiting, and could swallow a little. The eyes were closed. She was brought to the hospital in an ambulance.

Examination.—A careful physical examination was made by Dr. Du Bois; only the important findings are here reported. The patient was a well-nourished but rather undersized girl of 15. She lay doubled up on her right side, unconscious, but could be roused enough to give her name and age. When left alone she was perfectly quiet; when disturbed she resisted a little with her hands. She was cyanotic, not anemic or dyspneic. She looked very seriously ill.

Tongue: Moist and coated with white fur and covered with thick mucus.

Eyes: Pupils small, equal, reacted slightly; no ocular palsies, no nystagmus. On the ocular and palpebral conjunctiva were several small petechial spots.

Neck: Not stiff; when moved forward of the median line, the patient was aroused and resisted a little.

Heart: No enlargement. Action 140 to the minute, regular, of good force. No murmurs heard.

Pulses: Equal, corresponded to apex, small, soft, walls of vessel not felt.

The other viscera apparently normal.

Extremities: Upper, no paralysis. Lower, no paralysis. No edema, knecjerks normal. Kernig: There was slight resistance when the leg was fully extended on the flexed thigh.

Surface: Over the whole surface, but most abundant on the abdomen, was a profuse eruption of irregular purpuric (purple) spots varying in size from a pinpoint to 2 cm. in diameter. They occurred in the face, conjunctivæ and pharynx. Clinical Diagnosis: Epidemic cerebrospinal meningitis, fulminant.

Course of Disease.—October 7: Temperature 100 to 101. Lumbar puncture. at 9 p. m., October 5, withdrew normal fluid at normal pressure. High leucocytosis. Urine normal. Patient was very noisy and irrational, at times unusually bright. She seemed somewhat hysterical. She could repeat her multiplication tables with few mistakes. The neck seemed a little stiff. No new spots appeared on the skin; the old ones were a little darker and were now a reddish purple, edges indistinctly defined; many of them had gray centers which seemed to be on the point of sloughing. These were slightly raised and distinctly tender. There were about 20 such spots on the buttocks, 3 on the right hand, 1 on the chin, 1 on the left shoulder, about 20 on the thighs and legs. There was a crop of herpes on the lips.

October 9: The patient was a little quieter; she was obstreperous but perfectly rational. She had no headache. The herpes vesicles on the lips were more marked. The tongue was splightly coated and red at the edges. The petechial spots on the soft palate were now white and sloughing. The right eye showed a severe conjunctivitis, the whole conjunctiva being intensely injected and swollen. The left conjunctiva was normal. The hearing was acute. The neck was a little stiff. The joints were held somewhat stiff, but not tender. Kernig: The patient complained of great pain when an attempt was made to extend the leg beyond 135 degrees. No new petechial spots had appeared. The spots which two days previously showed gray centers were indurated and tender, not broken down and seemed to be dissolving. Lumbar puncture October 8 was unsuccessful, only blood being obtained after several punctures.

October 11: The temperature rose to 102.5. The patient was quieter, and perfectly rational. She had pain in the feet and abdomen. Leucocytes continued high. Lumbar puncture withdrew only a small amount of dark clotted blood. Conjunctivitis in the right eye increased rapidly. October 10 it was found that the cornea was hazy, iris blurred and markings indistinct and that the anterior chamber contained much yellowish exudate. The eye was examined by Dr. F. J. Parker, who made the diagnosis of hemorrhage in the eye with iridocyclitis. This day there was no facial paralysis; hearing was acute; there was no headache; the neck was stiff and could not be bent beyond the midline. The mouth showed two small ulcers where the petechial spots had been located. Over the outer aspect of each ankle there was redness, slight tenderness, increased local heat. The right foot was more tender. All the smaller purpuric spots on the skin had practically disappeared and there were now only faint purplish mottlings. A few of the larger ones were still indurated with gray sloughing centers. The skin was not broken down over any of them. All the joints were stiff and a little painful on movement.

October 13: Temperature was 101 to 103. Meningococci were found in the blood culture taken October 9. The patient was very noisy and at times irrational. The whole anterior chamber of the eye was hazy; the exudate did not seem increased; the conjunctive not so much inflamed. The neck was very stiff. The spots were fading; there were now about fifty left. A few contained pus; none were broken down. Kernig: The legs could be extended to within 45 degrees of a straight line. The knee-jerks were faint. The feet were no longer swollen. The general condition was not so good. The patient talked incessantly in a loud shrieking voice. The cultures obtained from the blood were submitted to Dr. Flexner who corroborated the diagnosis.

October 14: On October 13 lumbar puncture in the third lumbar space, withdrew about 20 c.c. of claret-colored fluid not under increased pressure. It did not look purulent and no organisms or pus cells were found. Twenty c.c. of Flexner's meningitis serum were injected into the spinal canal and 25 c.c. more were given in an intravenous infusion just after a blood culture had been made. This latter proved sterile. Following this the temperature rose to 104.6 but fell a little to 103.4 on the morning of October 14. The patient was still very noisy. She did not seem irrational and could multiply 6 by 6 and 5 by 8 correctly. She seemed hyperesthetic when touched. The neck was not quite so stiff as on the 13th. The throat was clear except for white patches on the left tonsil and right cheek, where petechial patches were located. Right eye: Conjunctival sac deeply injected and swollen, although not so much as three days previously. The cornea was cloudy, the

pupil moderately dilated, iris cloudy. There was a white patch apparently in the middle of the anterior chamber. Knee-jerks active. Sensation: Patient could distinguish accurately between sharp and blunt end of a pin. Kernig: The right leg could be extended to within 35 degrees of a straight line. The left could be extended to almost a straight line. The joints were no longer stiff. The feet were only a little tender. No paralysis; eyes looked in every direction; the tongue did not deviate. General condition a little better.

October 19: This was the fifteenth day since the onset. The patient was improving steadily. On October 17 30 c.c. of Flexner's serum was given subcutaneously. After that the temperature fell from 101.5 to 100. The leucocytes were decreasing. The patient was very noisy and irrational at times, but this seemed to be largely hysterical. This morning she was rational and laughed and complained of no pain. The eye was still hazy and there was an opacity apparently on the anterior surface of the lens, but this was decreasing in size. The pupil was dilated and a little irregular. The conjunctivitis was less marked.

October 20: Lumbar puncture gave clear fluid at first; later a little blood; pressure was low; fluid rose in tube to 11 cm., and when patient was crying ranged between 11 and 27 cm., returning to 11 cm. when patient became quiet.

November 5: The temperature remained below 100. The patient was up in a chair without fatigue; had no headache, no earache, no pain in the eye. Vision with left eye seemed normal, with right eye absent. Intraocular tension was very low, pupil dilated and a little irregular. Far back in the posterior chamber was a gray mass. Iris was dull, conjunctivæ slightly injected. Sloughs on tonsils and inside of cheeks had entirely healed. Otherwise the patient was well.

November 25: The patient had made a steady improvement; was now able to be up and about. The right eye was still blind. Beyond a moderate anemia the patient showed no other consequence of her illness.

TABLE OF LEUCOCYTE COUNTS, LUMBAR PUNCTURES, ETC.

Day of Date. Disease	Leuco-	Hour.	
10/51	e. Cytes.	12:30 a. m.	Onset with vomiting.
10/51		9 p. m.	Lumbar puncture—clear fluid.
10/ 6 2	27,500	-	-
10/82	$28,\!600$	5:20 p. m.	Lumbar puncture—small amt, blood,
10/95		3 р. т.	Lumbar puncture—dark blood clot.
10/95		5:20 p. m.	Blood culture—pure cult. meningococci.
10/128	19.400		
10/139		4 p.m.	Lumbar punc.—clear blood-tinged fluid.
		4 : 15 p. m.	Flexner's serum—20 c.c. intradurally.
		4:30 p. m.	Blood culture—sterile,
		4 : 50 p. m.	Flexner's serum—25 c.c. intravenously.
10/1410	18.000	5:15 p. m.	Flexner's serum, 30 c.c. subcutaneously
	18,200		
10/1511	18,400		
10/1612	13,800		
10/1713	13,100	2:30 p. m.	Flexner's serum, 30 c.c. subcutaneously.
10/18 14	13,000		
10/1915	9,000		
10/2016	11,100	6;25 p. m.	Lumbar puncture—clear fluid.
10/21 17	10,400		· · · · · · · · · · · · · · · · · · ·
10/2218	9,800		
10/2420	10,100		
10/2622	23,500		
10/2723	$17,\!600$		
10/30, 26	14,100		
11/ 2 29	14,700		

DIFFERENTIAL COUNTS OF LEUCOCYTES

•	Daily Percentages.											
Oct. 6. Polynuclears	Oct, 12 .	Oct. 14.	Oct. 17.	Oct. 27. 64.								
Transitionals 3.7	2.7	.2	2.3	1.3								
Large mononuclears 8.	9.6											
Lymphocytes 6.	15.	-27.8	19.	34.								
Basophiles	0.	1.	0.7	0.								
Eosinophiles 0.	0.	.7	0.7	0.7								
Platelets few	few	few	few	few								
*300 leucocytes counted.												

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Oct. 9-Blood culture on broth. Pure culture of meningococcus (Cecil).

- Oct. 13—Blood culture on broth. Both sterile.
- Oct. 12—Smears from right conjunctiva. Pus: fibrin. Very few micro-organisms (Meakins).
- Oct. 11—Culture from right eye (blood agar). Smears show mucus and pus; Gram cocci and bacilli. Cultures give *Staphylococcus albus* and *B. xerosis* (Cecil).
- Oct. 13—Smears and cultures from purpuric spot (sheep serum agar). Smears show a few scattered pus cells but no bacteria. Cultures sterile (Cecil).
- Oct. 12-Smears from vagina. Many organisms and epithelial cells (Meakins).
- Oct. 13—Smears from posterior fornix of vagina, 12 hrs. after douche. Moderate number of pus cells negative (Cecil).
- Oct. 5—Spinal fluid. Twenty c.c. perfectly clear fluid. No sediment. No coagulum. Smears negative. Culture sterile (Cecil).
- Oct. 9—Spinal fluid. About 1 c.c. of serum containing a large blood clot. Smears show blood but no pus. No micro-organisms. Cultures sterile (Cecil).
- Oct. 13—Spinal fluid. 15 c.c. of blood-tinged fluid. Dark red sediment. Smears show blood but no pus. Cultures sterile (Cecil).
- Oct. 16—Spinal fluid. 25 c.e. blood tinged. Dark red coagulum. Smears show blood, no pus, no bacteria. Cultures sterile (Cecil).
- Oct. 20—Spinal fluid. 30 c.c. of clear colorless fluid. No coagulum. No sediment. Smears entirely negative. Cultures sterile (Cecil).
- Oct. 7.—Urine, 24 hours; alkaline; sp. gr., 1014; no albumin, no sugar, no indican. Quantity 1076 c.e. Uric acid, 0.403 gm. Total phosphates, 2.09 gm. (Granat).

As it is established that meningococcus septicemia is possible without meningitis, the question naturally arises whether the case here recorded belongs in that category.

On the admission of the patient the clinical diagnosis was entered as cerebrospinal meningitis. In the light of the negative lumbar puncture, and the marked hemorrhagic symptoms, together with the absence of conclusive signs of meningitis, purpura hemorrhagica was later suggested. The blood culture cleared up the question of diagnosis. We are not yet entirely satisfied as to the presence of meningitis. On admission the patient was stuporous, but without notable stiffness of the neck or extremities, or other definite evidences of invasion of the cord or brain. Later the stupor gave place to a fretful and irritable mental condition, in which the patient appears to have been mentally more active than since her recovery, with definite rigidity of the neck, Kernig's sign and general hyperesthesia. The apparent Kernig may have been due to the involvement of the knees. Rigidity of the neck is seen, as all know, in conditions free from meningitis, such as typhoid fever or pneumonia, and Kernig's sign is not by any means limited to meningitis, but taken together these symptoms certainly point to a definite involvement of the cord. On the other hand, five successive lumbar punctures yielded a quantity of cerebrospinal fluid which must have shown the meningococcus if the cord had been involved in the inflammatory process; on each occasion, however, the fluid proved sterile.

The chief source of cerebrospinal fluid, it is agreed, is the chorioid plexus. The maintenance of a normal supply of the fluid about the cord implies an uninterrupted circulation of the fluid from the ventricles of the brain through the foramen of Magendie to the spinal canal. The quantities of fluid obtained at lumbar puncture, 20 c.c., 1 c.c., 15 c.e., 25 c.c. and 30 c.c. seem to show clearly that there was no obstruction to the normal course of the fluid, or the later tappings would have been "dry." The inability to obtain more than 1 c.c. on the second puncture was evidently due to the presence of considerable blood at the usual point of puncture. When the needle was later inserted in the third lumbar space the larger quantities were readily obtained. The normal pressure reading obtained at the puncture of October 20 is another strong argument for the presence of normal circulatory conditions in the spinal canal. Involvement of the cord can, therefore, it would seem, be excluded.

The possibility remains that there was a meningitis limited to a part or the whole of the cerebral surface but cut off from connection with the surface of the cord, or of such nature that the usual purulent exudate was lacking. For either of these suppositions no support can be found in the pathology of epidemic cerebrospinal meningitis. Involvement of the cord seems always to be found. In the thirty-five autopsies of Councilman, Mallory and Wright the process always invaded the surface of the cord to some extent, and so far as I can learn such extension of the disease is constant. It is well known that in the early stages of the meningitis the pathologic process may be limited to a congestion of the pia-arachnoid with very little exudation, so that an early lumbar puncture may be negative, but in cases protracted for two weeks or more the typical exudate always appears and the spinal fluid sooner or later shows pus and cocci. It is also true that in a series of punctures one or more may be sterile while the others yield the specific organism, but I can find no reference to an experience such as ours, in the presence of a definite meningitis.

The involvement of the eye to the extent described may be regarded as good evidence of the presence of a meningitis. Councilman, Mallory

and Wright report the histologic examination of two eyes presenting the lesions of iridocyclitis as a complication of cerebrospinal meningitis. In one of these they were able to trace the meningococci along the optic sheaths from the brain to the eye, apparently showing that the inflammation of the eye developed by direct extension from the pia-arachnoid. On the other hand, it must be granted that, the organism being present in the blood, it may readily lodge in any part of the body, affecting the eye quite as easily as the joints.

In view of the conflict of evidence it is impossible to reach an entirely satisfactory conclusion, but it seems easier to explain the clinical symptoms as expressions of a general bacteriemia than to assume the presence of a meningities in the face of the strong evidence against it. In the title of this report, however, only the proved facts have been stated: a meningococcus septicemia with sterile cerebrospinal fluid.

Apart from the difficult problem of diagnosis the case here reported presents interesting features.

The eruption was a very remarkable one in the size of the petechial areas and the sloughing which took place in the centers of the larger patches.

In Salomon's and Liebermeister's patients also the eruptions were striking features of the illness. They describe the lesions as a roseola, resembling that of typhoid, or like flea-bites. The multiform character of the eruptions seen in cerebrospinal meningitis is too well known to merit comment. It is perhaps suggestive that in those cases in which, as in the present case, the meningococcus was present in the blood, the eruptions were so marked. Is the eruption in these cases the expression of an embolic or thrombotic process set up by the lodgment of the specific organism in the capillaries of the skin? It is of interest that in Andrewes' cases, as well as in the one here recorded, the appearance of the eruption marked the onset of the disease; and if we take this view of its pathogenesis, we have another argument for primary blood infection in the case just reported.

Liebermeister notes that his case enables us to determine the accessory symptoms of meningitis—that is, those due to the general infection and not to the focal lesion; and he enumerates these as hectic fever, pain in the joints, and contractions of muscles, slight mental dullness, emaciation and roseola-like rash. The fever, eruption and arthritis with resulting muscular contractions are all found in Salomon's case, as well as the one here reported.

All but two of the ten cases in which Elser found the meningococcus in the blood proved fatal; and in almost all the other cases of menin-

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gococcus septicemia here mentioned the outcome was the same. It is therefore notable that the patient whose case has just been recorded made a prompt recovery. Liebermeister's was in the hospital for four months, Salomon's for more than that period. The patient here reported was quite well at the end of one month, and is now, at the end of the second, able to return home at any time she wishes. In fact, whether she had meningitis or not, the rapidity of her recovery was remarkable, all the more so if it be granted that she had meningitis as well as the blood infection. In what degree this rapidity of recovery was determined by the energetic administration of the Flexner serum one can not say, but from clinical observation we (the hospital staff) were satisfied that the serum played an important part in the improvement of the patient.

It has been noted that the blood culture taken immediately before the first dose of serum, as well as those cultures made later, all proved sterile, but it would not be justifiable to assume from this fact that the organisms had altogether disappeared from the blood before the introduction of the serum. The efficacy of the serum has been too well proved in cases of meningitis to make it desirable to pursue this point further.

Special mention must finally be made of the ocular complication. Beginning as a conjunctivitis, this quickly developed into a panophthalmitis, with hemorrhage in the vitreous humor. The affection increased rapidly and seemed to threaten the destruction of the eye. Following the use of the serum, improvement began which, in Dr. Parker's opinion, was most remarkable. From that time on the condition changed rapidly for the better, and the preservation of the eye, though without vision, seems assured. Dr. Parker considered the condition as typical of metastatic infective inflammation of the eye. The cases of Tooke, Wintersteiner, and Duval were apparently of like kind. It is notable that these were all fatal cases. The complication is not a frequent one and the cases just mentioned are the only ones in which Duval could find mention of it. Koplik speaks of it as a complication of fatal cases only. The fortunate recovery of our patient is, therefore, all the more noteworthy and constitutes a strong argument for the efficacy of the serum.

The cases here grouped together fairly establish the possibility of a primary meningococcus septicemia and suggest the clinical picture. Doubtless with more frequent bacteriologic examination of the blood during life we shall find such cases not very uncommon.

My thanks are due to Dr. Kinnicutt for the privilege of reporting this case, and also to the house physician, Dr. DuBois, for the very careful clinical notes recorded from day to day.

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