

ON THE MODE OF INFECTION IN EPIDEMIC CEREBRO-SPINAL MENINGITIS *

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The *Diplococcus intracellularis* was identified as the specific excitant of epidemic cerebrospinal meningitis by Weichselbaum in 1887. The procedure of lumbar puncture as a means of obtaining cerebrospinal fluid and attaining an etiologic diagnosis in cases of meningitis was introduced by Quinke in 1891.

The studies of meningitis made possible by this means have established beyond question the relationship of the meningococcus to the epidemic type of meningitis which has presented itself in various parts of the world during the last decade. As this relationship has been made clear, the problem of the control of this dreaded disease has focused itself about the life of the specific organism, its distribution in the body of those affected by the disease, its paths of exit from the body, its viability, and the mode by which the infection might be conveyed to others. Most of the points of interest and importance in these relations have been quite thoroughly cleared up.

The meningococcus has been found not only in the cerebrospinal fluid of those suffering from the disease but in the conjunctiva and the eye, in the nose and throat, in the pleura and lungs, in the pus of joints, in the throat, and in the blood. So far as our present knowledge leads us, the organism may be excreted from the body by the purulent discharges from an active conjunctivitis or by the secretions of the nose, throat and bronchi. While the organism has been found in the conjunctival secretions by Koplik,¹ Robinson,² and others, and the possibility of contagion from that source must be recognized, active conjunctivitis is not a frequent accompaniment of the disease and infection from that source must be rare.

In like manner, as Jakobitz³ has shown, the meningococcus may be found in the lungs both in those suffering from cerebrospinal meningitis, with or without definite pulmonary complications, and in rare instances in pneumonias and bronchial catarrhs occurring independently of meningitis.

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1. Koplik: Osler's Mod. Med., ii, 499.

2. Robinson: Am. Jour. Med. Sc., 1906, cxxxi, 603.

3. Jakobitz: Ztschr. f. Hyg. u. Infections-krankh., 1907, lvi, 175.

The greatest interest and importance, however, attach to the presence of the meningococcus in the nose and throat, because its presence in these passages may not only be a ready means of disseminating the organism outside the body of the patient, but also suggests the possibility of direct infection of the meninges from this source.

Since von Lingelsheim directed attention to the fact that the organism was to be sought not in the nares but in the nasopharynx, the reports of its discovery in cases of meningitis have shown increasing positive results. With the question of the identification of the *Diplococcus intracellularis* we need not here concern ourselves. The work of Councilman, Mallory and Wright,⁴ Albrecht and Ghon,⁵ and von Bettencourt and Franca⁶ has made the differentiation of the meningococcus so certain that reports conforming to the established standards can be accepted as reliable.

From reports of the occasional finding of the specific organism in the nasal or nasopharyngeal secretions, we find more and more positive results recorded. Thus Goodwin and von Scholly⁷ obtained positive results from the nasal mucus of twenty-seven out of fifty-two (50 per cent., plus) cases examined during the first two weeks of the disease and Dieudonné four positive findings in six cases (67 per cent.) and von Lingelsheim⁹ under favorable conditions forty-six positive results in forty-nine examinations (93.8 per cent.). It seems probable that the organism is present in the nose or nasopharynx of most of the cases of epidemic meningitis during the early stages of the disease.

But it has also been found in the same site in well persons, especially in those who have been in contact with cases of meningitis and also in many in whom no knowledge of exposure can be obtained. Thus Goodwin and von Scholly found the specific organism in the nasal secretions of 10 per cent. of forty-five "contacts;" Dieudonné obtained five positive results in thirty-nine trials, and Fraser and Comrie¹⁰ ten in sixty-nine trials, of contacts.

In the effort to control the inroads of the disease in the German army, similar investigations have been made on a large scale in regiments exposed to the disease, with most interesting results. Hübener and Kutscher¹¹ report that in 400 men of one battalion they found eight

4. Councilman, Mallory and Wright: Epidemic Cerebrospinal Meningitis, Rep. Mass. St. Bd. Health, Boston, 1898

5. Albrecht and Ghon: Wein. klin. Wchnschr., 1901, xiv, 984.

6. Von Bettencourt and Franca: Ztschr. f. Hyg. u. Infectious-krankh., 1904, xlv, 463.

7. Goodwin and von Scholly: Jour. Infect. Dis., 1906, p. 21.

8. Dieudonné: Centralbl. f. Bakteriologie, 1906, xli, Pt. 1, 418.

9. Von Lingelsheim: Klin. Jahrb., 1906, xv, 400.

10. Fraser and Comrie: Scottish Med. and Surg. Jour., 1907, xxi, 18.

11. Hübener and Kutscher: Deutsch. militär-arzt. Ztschr., 1907, xxxvi, 639.

coccus carriers although there were no cases of meningitis in the regiment itself at the time, and Vagedes¹² in 1,703 men examined under like conditions found ten carriers.

Under ordinary conditions the meningococcus quickly perishes outside the human body. It therefore seems highly probable that the spread of the disease depends on the presence of the specific organism in the nasal passages or respiratory tract of those sick with the disease and also of many persons in good health. The respiratory tract, and especially the nasopharynx, appears to be the usual portal of entry.

These facts being accepted, how does the organism from the nasopharynx or other part of the respiratory tract reach the meninges and there set up its specific inflammation?

The proximity of the nasopharynx to the meninges naturally suggested the possibility of direct infection. Of many contributions to the discussion of this subject, that of Westenhoeffer¹³ is based on the study of the most ample material and is of most interest.

As the results of his anatomic observations, Westenhoeffer lays emphasis on the following facts:

1. The meningitis begins at the base of the brain, in the region of the optic chiasm and about the hypophysis cerebri, and from this point spreads in all directions.
2. There is a suppurative exudate about the gasserian ganglion and in the sheaths of the several motor nerves of the eye.
3. Constant redness, swelling and hypersecretion of the nasopharyngeal tonsil and adjacent parts with an ascending otitis media.
4. The sphenoidal sinuses are constantly affected in all patients over 3 years of age. They were found markedly affected in twelve out of thirteen cases.
5. The antrum of Highmore is less often involved.
6. The ethmoidal sinuses are rarely and but slightly affected.
7. In all cases there is some swelling of the cervical lymph-nodes.

From these observations it seemed probable that there might be direct infection of the meninges from this nasopharyngeal focus through the sphenoidal sinuses. Especial emphasis is laid on the perihypophysial inflammation because of the close relation of the hypophysis to the sphenoidal sinuses and the known fact that in fetal life the sella turcica communicates with the throat through a hypophysial passage.

Two lymphatic paths are open for infection of the meninges from the nasopharyngeal process.

1. The infectious agent may make its way along the nerve sheaths, especially the several branches of the gasserian ganglion, as staphylococci,

12. Vagedes: *Deutsch. militär-arzt. Ztschr.*, 1907, xxxvi, 647.

13. Westenhoeffer: *Klin. Jahrb.*, 1906, xv, 657.

streptococci and typhoid bacilli have been shown by Homen to rise along the lymph channels of the sciatic nerve to the spinal cord. The inflammatory deposits surrounding these nerves are, however, readily shown to be secondary to the meningitis and descending, not ascending, processes.

2. The path of invasion may be along the carotid sheath to the region of the hypophysis.

However, investigation shows that the same perihypophysial inflammation is found in both otitic and tubercular meningitis. In the latter at least of these the infection undoubtedly reaches the meninges through the blood-stream and not by lymphatic channels. The value of the perihypophysial inflammation as evidence of the lymphatic transmission of the infection is therefore slight.

In the end Westenhoeffer admits the impossibility of proving the lymphatic transmission and assumes that the infection must reach the meninges through the blood-stream.

He even suggests that the whole throat affection may be secondary, although this seems improbable, inasmuch as it appears too early, in some cases before the onset of the meningitis, and also because the specific organisms are known to be often found in the throats of persons in good health (carriers).

Lymphatic transmission having apparently failed of proof, Westenhoeffer regards the infection as carried by the blood and probably by the arteries, inasmuch as no extensive thromboses are regularly present in cerebrospinal meningitis.

The cocci, as he says, are known frequently to be found in the blood, in some cases in the earliest stages of meningitis. In two or three cases lasting less than twenty-four hours, an endocarditis of the mitral valve and purulent myocarditis produced by the meningococci have been found.

Göppert¹⁴ similarly summarizes his study of this question in these words:

The whole respiratory tract, from the nose to the pulmonary alveoli, shows in the early stages of epidemic cerebrospinal meningitis more or less severe inflammatory changes. These may precede the onset. Chance brings one or the other—the pharyngitis, tonsillitis, pneumonia or bronchial catarrh, otitis media—of these conditions into the foreground. None of these affections is obligatory and therefore the opinion may be advanced that sometimes this, sometimes that point of the respiratory mucous membrane becomes the portal of entry of the meningococcus. Therewith must we accept the fact that the meningococcus may reach the brain through the blood channels, a conception which obtains support from the presence of the meningococcus in the blood.

Thus these two observers, disagreeing at the outset as to the importance of the local lesions of the respiratory tract, come in the end to agreement as to the probable route of infection of the meninges.

14. Göppert: *Klin. Jahrb.*, 1906, xv, 527.

At this point the problem of demonstrating a meningococcus septicemia, either as an attendant feature of epidemic cerebrospinal meningitis or independently of it, becomes of great interest.

That the meningococcus may be found in the blood in certain cases of epidemic meningitis has been known for some time. Gwyn¹⁵ first reported such a finding in a patient of Osler, and since then similar observations have been made by many others, Cochez and Lemaire,¹⁶ Jakobitz,¹⁷ Martini and Rohde,¹⁸ Lenhartz,¹⁹ Marcovitz,²⁰ Robinson²¹ and Duval.²² Elser,²³ in forty-one cases found the coccus in the blood in 10.25 per cent.; Dieudonné reports positive blood findings in four out of five cases, in one of which the nasal secretion was negative.

Especial interest, however, attaches to the presence of the meningococcus in the blood in patients free from meningitis. In 1908 I²⁴ reported the case of a girl of 15 years who presented some of the symptoms of cerebrospinal meningitis, but whose spinal fluid remained free from meningococci, while the organisms were found in the blood. At that time I was able to find in the literature three other reports of meningococcus septicemia without meningitis, these being recorded by Salomon,²⁵ Liebermeister²⁶ and Andrewes.²⁷ Netter has since recorded the case of a woman suffering from diarrhea, fever and general malaise, whose blood agglutinated two strains of meningococci, but whose blood culture was not taken. The patient's sister had cerebrospinal meningitis at the time.

Cecil and Soper²⁸ have collected from literature four cases of meningococcus endocarditis, two of these being the cases of Westenhoeffer already referred to, and add an observation of their own. The patients of Warfield and Walker²⁹ and Cecil and Soper gave no evidences of meningitis.

The occurrence of meningococcus septicemia both in conjunction with the cerebrospinal meningitis and independently of it, lends support to the view that the infection of the meninges is brought about through the blood, the primary focus being in the respiratory tract.

15. Gwyn: Bull. Johns Hopkins Hosp., 1899, x, 112.
16. Cochez and Lemaire: Baumgarten's Jahres., 1902, xviii, 91.
17. Jakobitz: München. med. Wehnschr., 1905, lii, 2178.
18. Martini and Rohde: Berl. klin. Wehnschr., xlii, 997.
19. Lenhartz: Deutsch. Arch. f. klin. Med., 1905, lxxxiv, 81.
20. Marcovitz: Wein. klin. Wehnschr., 1906, xix, 1312.
21. Robinson: Bull. Ayer Clin. Lab., 1903, i-iii, 27.
22. Duval: Jour. Med. Research, 1908, xix, N. S. xiv, 258.
23. Elser: Jour. Med. Research, 1905, O. S. ix, 89.
24. Bovaird: Arch. Int. Med., 1909, iii, 267.
25. Salomon: Berl. klin. Wehnschr., 1902, xxxix, 1045.
26. Liebermeister: München. med. Wehnschr., 1908, lv, 1978.
27. Andrewes: Lancet, Lond., 1906, lxxxiv-ii, 1172.
28. Cecil and Soper: Arch. Int. Med., 1911, viii, 1.
29. Warfield and Walker: Bull. Ayer Clin. Lab., 1903-6, i-iii, 81.

Elser and Huntoon³⁰ summarize the evidence of hematogenous infection in these words:

The early appearance of the meningococcus in the blood in a considerable number of cases, the appearance of general sepsis suggested by some patients early in the disease, the lesions in parts far removed from the central nervous system found at autopsy of individuals who succumbed to the disease within twenty-four hours of its inception, and finally the appearance of characteristic lesions in the eye synchronously with manifestations referable to the central nervous system, all point to an early generalization of the meningococci, but are not competent to prove that such an infection antedated the meningeal involvement.

The experimental study of this problem has not yet yielded decisive results. Bettencourt and Franca⁶ failed to produce meningitis in monkeys either by rubbing cultures of the meningococcus into the nasal mucous membrane or by intravenous injection.

Flexner³¹ succeeded in producing meningitis in monkeys by intraspinal injection, the resulting meningitis having in this case also the basal distribution thought suggestive of nasopharyngeal infection.

Elser and Huntoon, by intravenous injections of *Streptococcus mucosus* in rabbits succeeded in producing a meningitis which in its onset and the distribution of lesions resembled the meningococcus meningitis of man.

Finally, we may say that the evidence at our command at present strongly suggests that the primary infection in epidemic cerebrospinal meningitis is respiratory, in most cases nasopharyngeal, and that the meningeal infection is developed through the blood.

Protection of the community therefore will demand not only the isolation of those sick with the epidemic disease, but the detection of the many unaffected "carriers." To what extent this may be practicable remains to be seen. In the restricted fields offered by regimental organizations, the German military officers have already applied these methods with apparent success.

The efforts to free carriers from their infection (nasopharyngeal) have, so far as I can learn, proved ineffective. Various applications, douches and insufflations have been tried without success. In this regard the experience seems to repeat that with diphtheritic infections of the throat. In time the infection appears to die out in most cases, but treatment does not hasten that desired end.

Our present knowledge would suggest the desirability of treating these persons by serum or vaccines. The possibility of protecting the exposed by like means naturally presents itself, but thus far I have not been able to learn of any work along these lines.

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30. Elser and Huntoon: Jour. Med. Research, 1909, xx, 373.

31. Flexner: Jour. Exper. Med., 1907, ix, 142.