

## THE CHRONIC FORM OF MENINGOCOCCUS MENINGITIS \*

ALFRED GORDON, M.D.

PHILADELPHIA

Cerebrospinal meningitis with a prolonged course presents two varieties. In one we observe only recurrences or episodic meningeal manifestations. Here the patient during the intervals appears to be in perfect health. Nevertheless, suddenly or insidiously the symptoms return either in a slight or grave form. The intervals may last either a few days or a few weeks.

The other variety which is the subject of the present contribution, concerns cases of cerebrospinal meningitis the evolution of which is continuous. While in the literature are mentioned a few such isolated cases under different captions, nevertheless their chief characteristic features have not been sufficiently emphasized by various authors with the exception of Robert Debré, pupil of Netter. In 1845 Tungal<sup>1</sup> for the first time speaks of disturbances in the brain tissue proper in the course of a prolonged case of cerebrospinal meningitis. The next two earliest records we find by Rilliet<sup>2</sup> and Merkel.<sup>3</sup> They both speak of chronic hydrocephalus following a very prolonged course of cerebrospinal meningitis. Since then a number of records have accumulated in the German, French and American literatures indicating various isolated complications in the central nervous system. The present contribution is based on a study of ten cases of meningitis of the meningococcus type kept under observation for several years. Eight of these cases came to necropsy, so that in the largest majority of the series, clinical as well as anatomic data were available for consideration. The cases are very briefly as follows:

### REPORT OF CASES

CASE 1.—M. S., man of 27, mason, had a typical attack of epidemic cerebrospinal meningitis. The meningococcus was found. The spinal fluid presented polynucleosis and increase of albumin. The acute stage lasted eight days. There was a remission, but some rigidity of the neck remained. There was an exacerbation during five days, with remission again and a gradual deterioration, and muscular atrophy with a paretic condition, ataxia of all extremities,

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1. Tungal: Cited by Ebstein, *Deutsch. Arch. f. klin. Med.*, 1908, **93**, 241.

2. *Arch. Gén. de Méd.*, 1847.

3. Merkel: *Deutsch. Arch. f. klin. Med.*, 1866, **1**.

knee jerk diminished, decubitus, pain in the legs, mental dulness, deafness; spinal fluid almost clear, with mononucleosis. The patient lived five months. Necropsy report is given later.

CASE 2.—O. O'B., man 31, a laborer, had the usual acute onset. He had nine exacerbations during six months. In the intervals he developed amyotrophy with contracture of the limbs in flexion. There was decubitus in the occipital region, incontinence of sphincters; no spinal fluid was obtainable. There was deafness, palsy of internal recti in both eyes, mental hebetude, an occasional delirious state. The patient died in convulsions. No necropsy.

CASE 3.—M. S., girl, aged 25. Typical form. The patient had five exacerbations during ten months. There was amyotrophy with paresis of the lower extremities, contracture in flexion, incontinence: reflexes (tendon) diminished; deafness; impaired vision; palsy of left external rectus. Very little spinal fluid was obtainable, which was very slightly turbid. There was mononucleosis. The meningococcus was not found. The patient assumed a stuporous state. Necropsy.

CASE 4.—B. G., man aged 25, a watchmaker. Typical form. He had three exacerbations in four months; amyotrophy; paresis of all limbs; tendon reflexes much diminished; decubitus; pain in the lower extremities; deafness; vision impaired; incontinence; mental hebetude. Very little spinal fluid was obtainable on lumbar puncture and no meningococci were found. No necropsy.

CASE 5.—S. D., a man aged 29 years. Typical form. He had six exacerbations in thirteen months. The condition following each successive exacerbation was worse than the preceding. All the characteristic symptoms were pronounced, namely, amyotrophy, decubitus, contracture in flexion; knee jerks plus; deafness; palsy of left external rectus. No spinal fluid could be obtained after several attempts. Mental dulness. Necropsy.

CASE 6.—A. G., a boy, aged 19. Typical form. He had three exacerbations in six months: amyotrophy with flexion contracture of the legs was so pronounced that the knees touched the chin. The knee jerks were lost. There was incontinence of urine and feces and decubitus; spinal fluid very slightly turbid; mononucleosis; meningococcus not found; mental hebetude. Necropsy.

CASE 7.—C. S., a man, aged 32. Typical form. Had five exacerbations in ten months. Amyotrophy with contractures of lower limbs; decubitus; mental dulness, with periods of improvement; incontinence; spinal fluid clear, no meningococci, but mononucleosis; palsy of internal recti in both eyes; mental dulness. Necropsy.

CASE 8.—A. P., girl, aged 22. Typical attack. She had three exacerbations in five months. Amyotrophy with mild contracture of legs and parietic condition; knee jerks diminished; incontinence; deafness; impairment of vision; mental hebetude, but at times total lucidity; delirium with each exacerbation and a mild confusional state at times in the intervals; spinal fluid clear; mononucleosis. Died suddenly. Necropsy.

CASE 9.—J. O'H., boy, aged 13. Typical form. He had five exacerbations in two and a half months. Amyotrophy with contracture of legs; incontinence; decubitus; impairment of vision; spinal fluid clear, but with a yellowish tint; mononucleosis; mental dulness, with occasional mild delirium. Necropsy.

CASE 10.—S. H., girl, aged 7. Typical form. Six exacerbations in four months; amyotrophy with contracture of legs in extension; extreme emaciation; incontinence; mental dulness with occasional complete lucidity; spinal fluid clear, with a yellowish tint; mononucleosis; impairment of vision; palsy of the right external rectus; died in convulsions. Necropsy.

A detailed analysis of these cases brings out the following important anatomic and clinical facts.

*Pathology.*—The anatomic-pathologic findings in the eight cases that came to necropsy are as follows: The condition of the meninges could be characterized as one of diffuse pachymeningitis: irregularly distributed patches of thickened membranes could be seen, especially along the larger blood vessels and mostly at the base of the brain and near the cerebellum. The blood vessels appeared congested. Purulent areas were not frequent but if they occurred, were seen particularly at the level of the chiasma. Adhesions between the dura and the pia-arachnoid, as well as between the latter and the cortex, were occasionally seen, but more frequently the pia could be detached from the cortex without tearing the tissue of the latter. In several of the cases small cystic collections were found at the level of the pons.

The brain itself appeared on palpation somewhat softer than normal. It was due to dilatation of the lateral ventricles. In all the eight cases they were filled with considerable quantities of turbid fluid, and in two of these cases it was frankly purulent. There was apparently little or no communication between the various ventricles, as they were all overfilled with fluid. The histologic examination revealed in the meninges the usual findings of a chronic inflammatory state, namely, large masses of fibrous tissue with leukocytic infiltration of the walls of the blood vessels. In the cortex besides an edematous condition there was also infiltration of the blood vessels and proliferation of neuroglia. A certain degree of chromatolysis was evident throughout.

In the spinal cord, thickening of the meninges with meningeal adhesions in isolated areas were seen over the posterior aspect of the cord and especially at the level of the cervical and lumbar segments. The spinal fluid was less turbid than that of cerebral ventricles and sometimes very clear. The tissue of the cord suffered only at the periphery close to the altered meninges. Leukocytic infiltration with dilatation of some blood vessels was observed. Of special interest are the alterations found in the roots, more in the posterior than in the anterior ones, and in the nerve trunks. Leukocytic infiltration of the latter's blood vessels and actual degenerative changes in the nerve fibers were in evidence. Specimens were taken at the level of the cervical and lumbosacral segments. Portions of individual nerves of the brachial and sacral plexuses were examined. Chromatolysis was present in the posterior spinal ganglia.

The cerebrospinal fluid deserves special mention. I have already spoken of the appearance of this fluid and of its greater turbidity in the ventricles than in the subdural space of the spinal cord. In the latter I found it to be somewhat yellowish in two cases, but in the majority of the cases it was clear. Other writers observed the change of turbid to clear fluid in prolonged cases, although it is not so in every

case. Hajek,<sup>4</sup> for example, observed during an epidemic of cerebro-spinal meningitis in Milan clear fluid at first, then later purulent and then again clear. Netter and Debré<sup>5</sup> in their extensive studies also report such occurrences in rare cases. Albumin was found in the earlier stages of the disease in large quantities; in the later periods, three and four months after the onset, the albumin content was negligible. The polymorphonuclear cells of the early periods disappeared and mononucleosis was almost exclusively found weeks later. The same condition was found with regard to the meningococci. While they were abundant in the beginning, their number gradually became smaller and smaller, and several weeks later they were very rare. Cultures made in three cases from the spinal fluid, respectively six, eight and nine weeks later, failed to reveal the presence of the micro-organism. The disappearance of the meningococcus ran parallel with the clearing up of the spinal fluid. Other authors, however, reported the occasional presence of the micro-organism in perfectly clear fluids. Hajek<sup>4</sup> made daily punctures in a child of 3 during eight days; the spinal fluid was invariably clear and still a few meningococci were found, but curiously enough they were extracellular instead of being included in the cells.

*Clinical.*—The clinical picture based on the ten cases presents the following chief characteristics: The onset shows nothing unusual worth mentioning. The initial symptoms gradually subside and to all appearances recovery is expected, but close observation reveals that it is only a remission, as there are still physical and mental manifestations sufficiently evident to consider the patient ill; some rigidity of the neck and of spine, some difficulty of walking are all present. Mentally the patient shows a diminution of attentive power, of the mnemonic faculty and of general intelligence. The remission may last various times. In my cases from nine to twenty-one days. In the midst of the apparent amelioration of the symptoms there is suddenly or rapidly a reappearance of the manifestations characteristic of the acute stage: the foregoing mental and physical symptoms become accentuated and fever is added. Again, this symptom group will gradually subside for a period of one or several weeks, but nevertheless will not totally disappear. The curve of accentuation and amelioration of the condition may repeat itself an indefinite number of times. Gradually one observes the development of special disturbances which are so constant that they may be considered as characteristic of the

4. Hajek: *Pediatrics*, January, 1909.

5. Netter and Debré: *Bull. Soc. méd. d. hôp., Paris*, July 29, 1899, and May 11, 1900.

chronic form of meningococcus meningitis. They are seen in the motor, sensory, trophic and psychic spheres.

The most conspicuous change takes place in the state of *general nutrition* and especially in that of the musculature of the body. It is diffuse and not confined to any one area. The limbs become extremely thin, the usual roundness about the shoulders and hips disappears and the bony processes are very conspicuous. The subcutaneous fat disappears and the bones appear to be covered with a thin and wrinkled segmental covering which is dry and without the usual elasticity. Erythematous and herpetic disorders readily develop. Decubitus in the sacral, in the occipital (one case) regions and also on the heels are common.

*Motor* disturbances are especially evident in a body affected with a marked amyotrophy. The neck becomes more rigid than formerly. The limbs are in a state of contracture and in flexion and thus the patient remains immobile. In Case 6 the contracture and rigidity were so pronounced that the patient was all doubled up, with his knees almost reaching the chin. In less contracted limbs (Cases 2, 3, 5, 9 and 10) movements are possible, but there is a distinct parietic condition with diminished reflexes, and the movements remind one of those which are observed in cerebellar affections, namely, ataxia or awkwardness. In only one case (5) the knee jerks were increased, but there was no ankle-clonus and no toe phenomenon. In all the other cases the knee jerks were diminished, and in Case 6, with extreme contracture, the patellar tendon reflex was not obtainable.

*Sensory* disturbances are observed chiefly in the subjective field. Rigidity, with pain in the neck, spontaneous paroxysms of pain, especially in the cervical and dorsolumbar regions radiating down in the limbs, severe headache, are almost constant. Hyperesthesia is a striking symptom. The least touch or change of position provokes pain. The special sensorium is not infrequently invaded. In every one of my cases there was more or less involvement of the hearing, in five there was impaired vision, although the ocular fundi remained intact. In four of the latter there remained some involvement of the eye muscles, which became paralyzed during one or another recrudescence of the original symptoms accompanied by fever.

In all the ten cases the *sphincters* of the bladder and rectum were involved; during the entire course of the disease incontinence was present, with this difference, however, that during the intervals between the periods of recrudescence, it was less marked. Nevertheless, toward the end, namely, many weeks after the onset, when no more phases of acute symptoms occurred, the incontinence remained unaltered and more and more disturbing.

The psychic status of the patients is characterized particularly by a general intellectual hebetude. The degree of the latter varies from one patient to another and in the same patient at various periods of his disease. They all appeared indifferent, seemingly unable to understand when spoken to. Questions have to be repeated before they show evidence of grasping their meaning. The apathy and indolence may be extreme. The emotional sphere is almost obliterated. When pain is brought on by a change of position, or by a movement of a limb, the facies will not exhibit much suffering. On the other hand, when the same manipulations are made during a period of amelioration of the mental condition, the suffering of the patient is intense. In Cases 3, 5, 7, 8 and 10, there were phases of considerable improvement in the intellectual faculties without a corresponding improvement in the somatic disturbances. Such an improvement may go even as far as to present complete lucidity (in Cases 8 and 10), but the latter is not permanent, and a return to the debilitating status does not fail to take place. In some cases during the periods of recrudescence, namely, when the symptoms become accentuated and present the same picture as during the acute stage, especially when the temperature rises, a delirious state with confusion and incoherence is observed. It disappears when the acute symptoms subside and the patient returns to the chronic course of his malady. In Cases 8 and 10 a mild delirium was observed two and three times, respectively, not during recrudescence of the symptoms, but without a febrile state and when the trophic disturbances became much pronounced. The delirium is then probably due to the state of inanition or exhaustion.

The *course* of the disease in my ten patients was variable. Some of them had more acute attacks than others. The elevation of the temperature during the latter varied also from case to case. The state of prostration which follows the acute attack differed from one patient to another. But what was common to all cases is that the state of mental and physical exhaustion after the individual attacks were more and more profound with each successive attack; also that the course of the disease is very insidious and that, at least in my cases, the termination was fatal. The longest case lasted thirteen months and the briefest two and a half months. In one case (2) the patient died in convulsions which lasted five hours. There was a status epilepticus, as every five minutes a seizure would occur. Patient 1 died suddenly. All others expired after a gradually increasing prostration.

As to the age, my patients were, with two exceptions, all adults. The two cases were children, of 7 and 13 years, respectively. The 13-year-old patient presented no different features from those of the

adults. In the 7-year-old girl the only peculiarity noticed was contracture of the limbs in extension different from that in adults, in whom flexion was the striking feature.

The *pathogenesis* of the chronic form of meningococcus meningitis was not difficult to determine in view of the anatomic findings. Ventricular dilatation with secondary intracranial hypertension; otherwise speaking, a hydrocephalus as a sequel of a meningococcus meningitis is the chief morbid condition. It will readily explain the chronic psychic state which is so conspicuous in the form of meningitis under discussion. Moreover, the trophic disturbances—the sensorimotor manifestations and the state of the sphincters, which all run a chronic course and are so pronounced—are due to the profound degenerative condition of the nerve roots and of the peripheral nerves. Although a recovery is hardly to be expected under such conditions, nevertheless occasionally such recoveries have been recorded.

*Diagnosis.*—From a diagnostic standpoint difficulties may be encountered, especially when cases fall under observation weeks or months after the onset. First of all, the spinal fluid at this period of the disease is, as we have seen, more or less cytologically mononuclear. Besides, the meningococcus is not to be found directly or culturally. One may think, therefore, of a tuberculous meningitis. In such cases the precipito-reaction of Vincent with tuberculin may be of assistance. On the other hand, the syndrome of intracranial hypertension, especially when visual disturbances are present, will direct us toward cerebral neoplasm. Finally, the subjective and the objective sensory disturbances, together with the motor manifestations, may make one consider polio-encephalitis, polyneuritis or poliomyelitis. The diagnosis must be based on the ensemble of the various individual phases of the disease.

*Treatment.*—The character of the lesions in the chronic form of meningococcus meningitis precludes the possibility of obtaining results from any form of treatment. In every one of my cases the lumbar punctures were tried for the purpose of injecting antimeningococcus serum. In some cases very small quantities of fluid were obtained; in one case (5) no fluid at all escaped through the needle on several attempts. The serum was injected into the canal at various intervals, but no favorable results were obtained, a fact which I fully anticipated. The pachymeningitis, various adhesions, absence of communication between the cranial and spinal cavities—are all circumstances which, on the one hand, prevented the spinal fluid from escaping sufficiently through the puncturing needle, and, on the other hand, prevented the injected serum from reaching the ventricles, the main seat of the meningococci. Ventricular punctures with injection of serum into

them are therefore directly indicated, but permission could not be obtained for such procedures in my cases. It is to be presumed that when attempts of this character are made during the early phases of the affection, when the tendency to chronicity is first observed, desirable results could be expected. The chronic form of cerebrospinal meningitis is one of the most serious affections. Since it usually follows the acute form which had not been sufficiently treated with anti-meningococcus serum, its recognition is of paramount importance.

1812 Spruce Street.