

# THE SPINAL-FLUID SYNDROMES OF NONNE AND FROIN AND THEIR DIAGNOSTIC SIGNIFICANCE.

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G. Froin<sup>1</sup> reported in 1903 three cases which upon lumbar puncture showed spinal fluids yellow in color (xanthochromia), containing numerous cells, and which, upon standing, coagulated spontaneously and massively, owing to their high fibrin content. The phenomena thus described were new to medical literature, and they have since been collectively designated "Froin's syndrome." Later observers, using more accurate methods of cell enumeration, have not confirmed Froin's finding of "numerous cells," and pleocytosis cannot be regarded an essential part of the syndrome. This point will be discussed later.

Some five years after Froin's publication, M. Nonne<sup>2</sup> reported three cases of cord tumor, the spinal fluids of which contained an excess of proteid (strongly positive phase I) with no leukocytosis (pleocytosis) of the fluids. Nonne was unable to interpret the dissociation of proteid excess and pleocytosis in his three cases, and did not feel from his limited experience that any positive diagnostic significance could be attributed to the syndrome in relation to spinal-cord tumors.

Since the appearance of these two contributions the literature has been augmented by several papers dealing with either one or the other of these two syndromes, but no one has suggested that they are closely related phenomena. In this communication we shall bring forward evidence, both from our own experience and the literature, with the object of proving that the syndrome of Nonne is simply the early manifestation of a process which in its later and terminal phases gives rise to the syndrome of Froin. We shall try, furthermore, to show that the Nonne-Froin syndrome when properly interpreted is of the greatest practical assistance in the differential diagnosis of spinal-cord lesions.

Xanthochromia, or yellow pigmentation of the spinal fluid, has been described by many observers, and cannot be regarded as a rarity. We have seen five instances of this condition in the past three years. It is such a striking and unexpected finding at lumbar puncture that it has assumed a larger share of importance than it deserves. It will be necessary to define clearly the exact condition which can properly be termed xanthochromia, for hemorrhage into the cerebrospinal fluid from ventricular apoplexy, traumatic rup-

<sup>1</sup> *Gaz. d. hôp.*, 1903, 000, 000.

<sup>2</sup> Quoted by Raven, *Deutsch. Ztschr. f. Nervenk.*, 1914, xlv, 380.

ture of meningeal vessels, or other causes leads to a condition which has been designated erythrochromia, and this hemorrhagic pigmentation has been frequently confused with xanthochromia. The two conditions possess certain characteristics which permit of their ready differentiation.

1. The color in erythrochromia varies from a bright red through varying shades of reddish-brown, reddish-yellow to a dark yellow color. Lumbar punctures made at intervals of several days on a case with hemorrhagic spinal fluid have shown a variety of color changes (Schwarz), whereas the color in xanthochromatic fluids remains the same from puncture to puncture. The shades in xanthochromia are described as amber, cream, or straw colored, and instances are recorded in which the color remained the same throughout several months.

2. In erythrochromatic fluids red blood cells or their shadows may be very numerous. In a case which we saw recently, in which the patient had fallen upon his head from a swiftly moving automobile, the spinal fluid was the color of arterial blood and red blood cells were present in very large amount. From this extreme picture lesser grades of erythrocytosis are found, and finally only shadows of red cells or a reddish-yellow pigmentation remains as evidence of former hemorrhage. Such fluids, however, yield positive chemical test for blood, although in later stages the spectroscopic may fail utterly to reveal characteristic bands. Furthermore, owing to the meningeal irritation of the products of red-cell destruction, a leukocytosis of the fluid develops. Schwarz reports such a case in which there were numerous shadows of red cells and 265 white cells (mostly lymphocytes) to the cubic millimeter of fluid. In xanthochromia the white cells are, as a rule, not increased; there are no red cells, and the fluid does not yield either chemical or spectroscopic evidence of hemoglobin derivatives. When the white cells are increased it is evidence of meningeal inflammation.

3. The fibrin content of xanthochromatic fluids is extremely high. The citron-yellow fluid, which is quite limpid, coagulates spontaneously, and in so massive a manner that the containing test tube can be inverted without loss of its contents. The coagulum is gray or white. This is not true of erythrochromatic fluids. They may contain fibrin to a certain extent, but they do not coagulate massively.

4. Both xanthochromatic and erythrochromatic spinal fluids contain proteid substances in very large amount, but whereas in xanthochromia a large excess of proteid is a constant and characteristic part of the picture, in erythrochromia the proteid tends to decrease in amount the further away in time from the hemorrhage the fluid is removed.

In purulent meningitis the spinal fluid may be colored yellow, brown, or green, but there is no danger whatsoever of confusing

such a finding with any other, owing to the presence of pus cells in enormous amounts and of bacteria.

The syndrome of xanthochromia with massive coagulation of the spinal fluid and high proteid content, with or without pleocytosis, is always produced by a localized obliteration of the pia-arachnoid space which divides it into two parts, an upper one in free communication with the pia-arachnoid spaces of the upper cord and brain and a lower cul-de-sac. In this lower cul-de-sac the fluid gradually changes in character from the normal limpid spinal fluid to the xanthochromatic type of fluid just described. The following briefly summarized case will illustrate perfectly the conditions leading to the xanthochromia-syndrome:

A child of nine months was admitted to the hospital suffering from spastic paralysis of both arms and legs. Upon the least stimulus the arms, legs, and trunk would pass into a tetanic spasm. Lumbar puncture revealed a fluid the color of picric acid, containing sixteen cells to the cubic millimeter, a very great excess of proteid, and the fluid coagulated massively on standing. After a few days it was observed that the child's fontanelles were bulging markedly, and to relieve the tension a needle was inserted through the anterior fontanelle and 30 cm. of perfectly normal limpid cerebrospinal fluid was withdrawn. This fluid contrasted strongly in every way with that removed by lumbar puncture.

The child died, and at autopsy a large mass of tuberculous granulation tissue was found completely encircling the medulla and quite obliterating the pia-arachnoid space at the level of the foramen magnum. The mass of new growth had completely separated the pia-arachnoid spaces of the cord from those of the brain.

Another instance of the syndrome under discussion was seen recently in a man, aged twenty-seven years, who for a year had suffered from a painlessly developing paraplegia which had terminated in an utter spastic paralysis of both legs. The history and physical findings indicated cord compression at the level of the seventh dorsal segment, and at operation a cyst of the pia-arachnoid was discovered which was completely obliterating the pia-arachnoid space and compressing the spinal cord. Below the site of this compression the veins of the pia were much engorged and tortuous. The cyst was drained, and six weeks after operation a lumbar puncture revealed a fluid normal in every respect. The paraplegia improved remarkably following operation.

Three other instances of the xanthochromia syndrome which we have studied were in cases of extramedullary spinal-cord tumors, situated at various levels of the cord. In every instance, however there was produced by the tumor a cul-de-sac below the site of cord compression, and following the removal of the tumor the spinal fluid regained its normal characteristics.

The literature of xanthochromia with massive coagulation has

been reviewed recently by Mix.<sup>3</sup> He says: "Whenever the spinal fluid is found to conform to this syndrome it means that there is an isolated cul-de-sac. It may be isolated by meningitis, which has sealed the meninges to the surface of the cord, or it may be due to a pachymeningomyelitis or to a tumor which compresses intradurally, and so "cuts off by pressure the cul-de-sac, or to an intradural tumor which acts as a ball-valve, plugging up the top of the lumbar enlargement of the spinal cavity." With this statement our own experience is in complete agreement, and from this clear description of the mechanism of production of the syndrome the great practical diagnostic importance of the finding will readily be appreciated. Any pathological alteration of the vertebrae, dura mater, or pia-arachnoid which leads to partial or complete obliteration of the pia-arachnoid space and the formation of a cul-de-sac is capable of producing the syndrome of xanthochromia with excess proteid and massive coagulation. If the pathological change is associated with inflammation of the meninges there will be a leukocytosis of the fluid, but when the compression is due to non-inflammatory growths it is our experience that no pleocytosis is present. When cellular elements are present in more than normal amount, syphilis or tuberculosis should be strongly suspected.

The origin of the pigment in xanthochromatic fluids has led to some discussion. It has been suggested that the color in the last analysis is due to blood pigment from multiple small hemorrhages (Schwarz,<sup>4</sup> Kafka,<sup>5</sup> Raven<sup>6</sup>). We believe from our observations that the xanthochromia syndrome is produced by transudation of blood serum into the pia-arachnoid cul-de-sac, owing to stasis produced by pressure upon the veins of the pia at the site of cord compression. The high content of such fluids in fibrin and proteids, and the presence in them of few cells, supports the view that we are dealing in these cases with a transudate which is perfectly analogous to pleural transudates due to venous compression. One has only to recall the circulatory conditions in the spinal cord to realize how pressure upon the venous return flow would naturally lead to stasis with transudation. Multiple small hemorrhages, on the other hand, would produce the condition of erythrochromia, which, as we have pointed out, possesses characteristics which distinguish it from the xanthochromia syndrome.

At the beginning of this paper we stated that the findings of Nonne—namely, high proteid content with no pleocytosis—in three cases of cord tumor were closely related to Froin's syndrome of xanthochromia, with massive coagulation. It remains to make clear this connection.

<sup>3</sup> Murphy's Clinics, 1915, iv, 187 (full literature).

<sup>4</sup> Deutsch. Ztschr. f. Chir., 1913, cxxiv, 346.

<sup>5</sup> Ztschr. f. d. ges. Neurol. u. Psychiat., 1912.

<sup>6</sup> Loc. cit.

Raven,<sup>7</sup> a pupil of Nonne, has contributed a very valuable paper from Nonne's clinic reviewing 47 cases of cord tumor—20 from the experience of the clinic and 27 from the literature—in which the proteid content (phase I) of the spinal fluids was high with low cell count (no pleocytosis). His article is deficient in that he does not state how many of these cases showed xanthochromia and massive coagulation. That some of his cases did show these phenomena is obvious from his discussion and conclusions. In his series the findings ranged from slight proteid increase without coloration of the fluid to frank outspoken xanthochromia with great excess of proteid and massive coagulation. Although he clearly recognizes that cord compression is the cause of the proteid increase, xanthochromia, etc., he fails to make clear the all-important fact that xanthochromia with massive coagulation is but the terminal picture of a process which begins with an increase of proteid without pleocytosis as its sole distinguishing feature. In a series of spinal fluids from cord-compression cases every gradation can be traced from proteid excess alone to marked xanthochromia with an enormous excess of proteid and massive coagulation.

Mestrezat in his monograph on the cerebrospinal fluid (Paris, 1912) reports nine cases which illustrate the early stages of the Nonne-Froin syndrome. He speaks of them as "*les cas frustes*," or imperfectly developed examples of the xanthochromia—syndrome. Some of these cases failed to show xanthochromia; others showed no pleocytosis, though yellow in color and coagulating spontaneously; still others exhibited variations in the formation of a coagulum. As one reads these cases in the light of what has been said previously in this paper, one has no hesitancy in classing them among the type of cases reported by Nonne; they represent stages more or less advanced in the Nonne-Froin syndrome.

Under the title "*Dissociation albumino-cytologique an cours des compressions rachidiennes*," Sicard and Foix<sup>8</sup> have published interesting observations upon the spinal fluids of patients suffering from active Pott's disease. They found the albumin content of such fluids abnormally high, but with no accompanying pleocytosis, and, as indicated in their title, they attribute their findings to cord compression by the tuberculous vertebrae. They likewise mention that twelve cases of cord tumor showed increase of albumin with no pleocytosis. It is thus evident that compression of the cord from whatever cause leads to an excess of proteid in the spinal fluid, and that when the meninges are not involved, there is no abnormality in the cell count.

We are convinced that the prominence which Froin's syndrome of xanthochromia with massive coagulation has assumed in the

<sup>7</sup> Loc. cit.

<sup>8</sup> Sicard and Foix, *Presse méd.*, 1914, xx, 1013.

literature is due to the fact that the striking yellow color and spontaneous coagulation of the fluid cannot possibly be overlooked, whereas proteid increase alone requires laboratory experience for its demonstration and interpretation. It is perfectly obvious though that if evidence of cord compression is to be obtained from the spinal fluid, it is important to elicit this evidence before the terminal phase of xanthochromia with massive coagulation is established. Proteid increase without pleocytosis has the same significance in the early stage of cord compression that the full-blown xanthochromia syndrome has in the later stage of more or less complete paraplegia. Indeed, the stage of xanthochromia with massive coagulation may never be reached, and only the early phase of proteid excess without pleocytosis exist as evidence of cord compression.

**CONCLUSIONS.** 1. Compression of the spinal cord and its meninges from whatsoever cause leads to the formation of a cul-de-sac, more or less complete, distal to the site of compression. This leads to characteristic changes in the spinal fluid.

2. The earliest characteristic change has been described by Nonne as an increase of proteid (phase I positive) without cell increase (pleocytosis).

3. As the condition of cord compression persists, the fluid gradually becomes yellow in color (xanthochromia), the proteid content increases enormously, and the fluid, when removed, coagulates spontaneously (Froin's syndrome). Pleocytosis may or may not be present, depending upon whether or not the meninges are inflamed by the pathological process causing the compression.

4. Xanthochromia of the spinal fluid must be distinguished from staining of the fluid by hemoglobin derivatives (erythrochromia).

5. The spinal-fluid syndrome of Nonne-Froin is very helpful and reliable in the diagnosis of spinal-cord lesions. When present it always indicates a compressive lesion of the cord.

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## CHYLOTHORAX. REPORT OF A CASE.

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**INTRODUCTION.** Chylothorax is a condition in which the pleural cavity contains chyle. This condition may be due to a rupture of the thoracic duct or its radicles, or to some pathological condition of their walls, whereby the contents may be transuded into the pleural cavity. Chyle is lymph derived from the walls of the alimentary tract.