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ON FROIN'S SYNDROME, AND ITS RELATION TO ALLIED CONDITIONS. IN THE CEREBROSPINAL FLUID.

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THE study of the cerebrospinal fluid is a field of investigation which during the present century has yielded a rich harvest to the neurologist. It has enabled him to diagnose certain progressive diseases of the nervous system at a stage when the patient is hardly aware that he suffers from any disability, and to distinguish with certainty between diseases which may present identical clinical pictures. Among the many changes which the cerebrospinal fluid may undergo, certainly the most striking to the clinical observer is a yellow coloration associated with the formation in the fluid, soon after it is received into a test-tube, of a coagulum, which may be so firm as to allow of the tube being turned upside down without a drop of fluid escaping. This combination of appearances was described first by Froin in 1903, and in French literature has since gone under the name of "syndrome de coagulation massive et de xanthochromie" or "syndrome de Froin". The rarity of appearance of this syndrome, the various nature of the cases in which it has been found, and the occurrence of all gradations of change from normal fluids to those presenting the typical syndrome, have combined to confuse our knowledge of its etiology and significance. And as far as British work is concerned, no attempt has been made to establish its pathogenesis or diagnostic value; in fact, beyond passing references in

text-books and papers on the cerebrospinal fluid, I have been unable to find any allusions to the subject in British publications. American schools have taken up the study of the cerebrospinal fluid with greater keenness than has been shown by the British schools, and several papers have recently appeared there on the syndrome of Froin which show intimacy with the continental work on the subject.

During the past ten years I have seen several spinal fluids which have presented the typical appearances of the syndrome of Froin, as well as a very considerable number in which changes of less degree, but similar character, were present. These fluids have been found in a great variety of forms of nervous disease, and in many of the cases I have been able to establish the diagnosis by following the case to operation or autopsy. This experience has been sufficient to enable me to test the value of current theories on the evolution of the syndrome, and to form some opinion as to its diagnostic value.

The present time is ripe for a critical review of the subject, in that some recent American work on the circulation of the cerebrospinal fluid has solved questions which have long been in dispute, and has thus made it more possible to understand the changes in the fluid which result from abnormalities in its circulation. At the same time it must be confessed that the causation of certain of these changes remains hidden in an obscurity which can only be cleared away by work in the more general field of chemical physiology.

I.—HISTORY OF THE SUBJECT.

In surveying the literature dealing with the syndrome of Froin, it has been considered useless and tedious to detail every case in which the syndrome has been encountered either in a complete or a modified form. This has, in fact, recently been done by Lantuéjoul, who has brought up to date the cases in which the syndrome was typically present, and by Raven, who has collected a large series of cases of spinal compression in which the cerebrospinal fluid showed similar changes. I have therefore considered it more helpful to a proper understanding of the subject to trace the growth of knowledge and theory with regard to it, recording only the first cases of any special affection in which the syndrome was encountered.

Early Observations.—The presence of fibrinogen in the cerebrospinal fluid of cases of acute meningitis was observed by Fürbringer and Netter in the closing years of last century, but it was not until 1903 that it was found in more chronic affections of the nervous system. In that year Jean Lépine first drew attention to

the formation of a coagulum "involving about half the fluid" in the tube, in a case diagnosed as lumbar rheumatism.

Froin in the same year published three cases which he described as "Inflammations méningées avec réactions chromatique, fibrineuse, et cytologique du liquide céphalorachidien".

One of his first cases was that of a woman of 36 years, who had a paraplegia apparently of syphilitic origin. Four lumbar punctures were performed on her. The first gave a golden-yellow fluid coagulating solidly in the tube within a few minutes; the second, twelve days later, a slightly yellow fluid with less dense coagulum; the third, a fortnight after the second, gave a fluid which was only slightly yellow and formed a spider's-web coagulum after two hours. The fourth puncture, performed two months after this, gave a fluid with a very faint yellow tinge and only a few flakes of fibrin. The albumin and globulin contents of the fluids obtained at the first two punctures were greatly increased.

In the same year, 1903, Babinski described a case of spastic paraplegia which he diagnosed as due to "Méningite hémorragique fibrineuse". It was probably of syphilitic origin, and was cured by mercury. Lumbar puncture performed by him gave a greenish-yellow fluid which coagulated *en masse* soon after being withdrawn. It showed numerous lymphocytes. The fluid obtained on the following day by a second puncture was stirred with a glass rod immediately it was drawn, and did not clot. A week later a third puncture was performed, and paler fluid was obtained which did not clot. A fortnight later still the fluid obtained by a fourth puncture was clear, gave no coagulum, and contained fewer lymphocytes. Fifth and sixth lumbar punctures were also performed. He considered that the condition of the fluid was due to a special form of meningitis, which was improved by repeated punctures. He drew attention to the diminution in the quantity of fibrinogen in the fluid obtained by the second and successive punctures.

In the following year (1904) Cestan and Ravaut reported similar changes in the fluid of a case of flaccid paraplegia. At the autopsy they found a meningomyelitis affecting the sacral enlargement of the cord. The meningitis at this level had matted the membranes and nerve-roots together, producing a "véritable symphyse fibreuse des méninges et de la moelle". They considered that the changes in the fluid were due to hæmorrhage complicating meningomyelitis.

Occurrence of the Syndrome in Landry's Paralysis and Polyneuritis.—Several writers, however, found that the syndrome might occur in other conditions than meningomyelitis. Julius Donath, in 1905, reported a case diagnosed as 'Landry's paralysis'

in which these changes in the cerebrospinal fluid were found. The first lumbar puncture was performed during the height of the malady. The fluid came out at first rose-red, but later was colourless. This latter half, on standing, set solid in the tube like gelatin, "so dass die Eprouvette gänzlich umgekehrt werden konnte". The second lumbar puncture, a fortnight later, gave a clear, slightly yellow fluid which flowed down the sides of the tube like gelatin. It contained albumoses.

A similar case, in a young miller of 19, diagnosed as alcoholic polyneuritis, was described by Claude in 1909. Two lumbar punctures performed at an interval of six days gave slightly yellow clear fluids which coagulated 'massively' in the tube. They contained some red cells and a few leucocytes.

Renon and Monier-Vimard in the same year described a case of Landry's paralysis with similar changes in the cerebrospinal fluid.

These three cases of polyneuritis, or Landry's paralysis, made it recognized that the syndrome of Froin could appear in these conditions. The significance of this seems to have been missed by the later writers on the subject, notably by Mestrezat, in whose theory of the etiology of the syndrome there seems to be no place for polyneuritis.

'Cavité Close' Conception of the Etiology of the Syndrome.—Sicard and Descomps, in 1908, described a case in which similar changes were found in the cerebrospinal fluid. They noted that a second lumbar puncture, performed within a few days of the first, gave a much less albuminous fluid which did not coagulate. A fortnight later the fluid had resumed the characters of that obtained at the first puncture. A fourth lumbar puncture, two days later, again gave a clear fluid without coagulum. At the autopsy they found a mass of fibrous and caseous tissue in the epidural space at the level of the 11th and 12th thoracic vertebræ, with thickening of the dura and of the soft membranes from the 10th thoracic to the 2nd sacral vertebræ. The dura was adherent to the arachnoid in some places, but not everywhere. The condition appeared to be tuberculous in origin, but no tubercle bacilli could be found in sections.

Reviewing the changes in the cerebrospinal fluid, in relation to the condition found at autopsy, they considered the meningeal inflammation to be a necessary but not sufficient cause for the syndrome, the other necessary factor being a process of adhesion whereby the plasma and corpuscular elements resulting from the inflammation were retained in a limited space. Vascular compression and local œdema they considered adjuvant causes of the syndrome. They explained the alterations in degree of the changes in

the cerebrospinal fluid at the several punctures by supposing that fresh cerebrospinal fluid from above filtered through the adhesions after the fluid below them had been drawn off. They laid stress on the value of the syndrome as an indication of meningitis rather than of tumour; but this was soon proved to be erroneous.

Indeed Rindfleisch, in 1904, had reported three cases of diffuse sarcomatosis of the meninges in which changes in the cerebrospinal fluid were found. In two of his cases the fluid was yellow, contained albumin in increased quantity (0·24 per cent and 0·1 per cent), and gave a deposit of tumour-cells. In the third the fluid was highly albuminous, but colourless, and showed very few cells. None of the fluids showed massive coagulation.

Blanchetière and Lejonne, in 1909, seem to have been the first to describe the full syndrome of Froin in a case of spinal tumour. Their case was one of slowly-developing paraplegia, with sensory loss below the level of the 7th thoracic segment, in a man of 66. The first lumbar puncture gave a lemon-yellow fluid coagulating *en masse*, but containing very few lymphocytes. Later punctures extending over a period of sixteen months invariably gave exactly similar fluids, with no reduction of the tendency to coagulate. At the autopsy a tumour was found lying under the dura mater and compressing the cord at the level of the 7th, 8th, and 9th thoracic segments. There seemed to be some adhesions between the dura mater and the dorsal surface of the cord, but the membranes stripped off the cord easily and there was no meningitis. The tumour, which was of the form and size of a large olive, gave the histological appearances of a very vascular round-celled sarcoma.

In the same year Derrien, Mestrezat, and Roger published a case of spastic paraplegia with anæsthesia and sphincter trouble, diagnosed as being due to subacute meningomyelitis in the lumbar region of the cord. The first lumbar puncture gave fluid which came out very slowly and stopped completely after 4 to 5 c.c. had escaped. It had a bright golden-yellow colour, and on standing set *en masse*. The serum from this gave only a slight fibrin web, until fresh guinea-pig serum was added, when it set again. On centrifugalization, the fluid gave a deposit of red blood-corpuscles and some lymphocytes. A second puncture a week later gave fluid at higher pressure, and less yellow, which did not clot until serum had been added. It contained 0·96 per cent albumin. The fluid obtained by a third puncture eight days later was only slightly yellow, and gave a thin fibrin clot. It was found to contain fibrin 0·03 per cent and albumin 0·6 per cent. A fourth puncture a week later gave almost colourless fluid containing 0·4 per cent albumin and no fibrinogen. A fifth puncture, a fortnight later, again gave

a fluid containing a trace of fibrinogen, but with no spontaneous coagulation. The fluids obtained by the sixth and seventh punctures were similar, but that from the eighth puncture—between which and the seventh an interval of a month had been allowed to elapse—was more definitely yellow and coagulated spontaneously, giving a spider's web of fibrin. It contained 1·08 per cent albumin. In these fluids the glucose content was often increased, two readings being as high as 0·08 per cent and 0·09 per cent. They considered that their case was due to a hæmorrhagic meningitis similar to that diagnosed by Froin, Babinski, and Cestan and Ravaut.

In commenting on Blanchetière and Lejonne's case, they held to the theory of 'cavité close' formulated by Sicard and Descomps, and considered the changes in the fluid in that case due to transudation of the principles of the plasma from the sarcoma. As adjuvant factors, they postulated obstruction of the perivascular sheaths, and compression of the cord by the tumour. These several factors, taken together, would transform the terminal part of the subarachnoid space into an isolated pouch, in which the transuded plasmatic elements would be retained.

This theory was insisted on by Mestrezat in his monograph on the cerebrospinal fluid published in 1912. He considered two factors necessary for the production of the syndrome: (1) That the lumbar cul-de-sac should be shut off from communication with the fluid around the upper part of the cord by meningitis, tumour, or disease of the bones of the spine; and (2) That there should be congestion of the spinal veins below the level of this block, or alteration of the vessel-walls by inflammatory processes. He did not insist on the necessity of a process whereby the perivascular channels were sealed up, but noted that substances such as iodides, nitrates, and collargol, when injected into the lumbar theca, did not escape from it. He also drew attention to the fact that in all the cases which had been followed to autopsy the level of the block was low down in the thoracic region of the cord, or at the lumbar enlargement. As has been noted above, his theory, being based only on cases where the pathological process had actually been seen at operation or autopsy, did not take any account of the cases of polyneuritis or Landry's paralysis in which the syndrome had been found. Cases of these affections which have come to autopsy have given no evidence of any process which would divide the subarachnoid space surrounding the cord into upper and lower portions, or which would prevent free circulation of the cerebrospinal fluid to the lowest parts of the lumbar cul-de-sac. But it is conceivable that œdema of the cord or slight inflammation of the meninges might have this effect. If so, the block must be only a temporary

one, as it has been seen that the fluid in these conditions rapidly loses its pathological characters.

Changes in the Cerebrospinal Fluid in Pott's Disease.—In 1910 Sicard, Foix, and Salin drew attention to the characters of the cerebrospinal fluid in Pott's disease. They gave four cardinal signs in the fluid which, if present together, they considered pathognomonic of the disease. These were (1) yellow coloration, (2) excess of albumin without increase of cells ('dissociation albumino-cytologique'), (3) the presence of albumoses, (4) the presence of hæmolysin to rabbit's red cells; the fluid by itself might not be hæmolytic, but might require the addition of fresh guinea-pig serum. They laid chief emphasis on the presence of albumoses, which they considered to have the same significance as Bence-Jones albumose in the urine, and to indicate disease of the bones of the spine. They did not insist that this should be necessarily tuberculous, but considered that albumoses might also occur in malignant disease of the spine. On the other hand, they pointed out that albumoses were only found in the fluids which showed the greatest changes, and then only at the first puncture. Mestrezat, in his monograph, considered that they were due to autolysis of the albumin stagnating in an isolated cul-de-sac, a theory which would explain why they were found only in the fluid drawn off by the first puncture. It should be noted that Mestrezat's technique for the detection of albumoses was rather more delicate and perhaps less free from error than that adopted by Sicard and his fellow workers.

In the same year Cooper published in America the report of a case of localized segmental lesion of the cord from which he obtained clear fluid "of a yellowish-brown colour" which gave "a well-marked cobweb coagulum". An operation was performed at which an angiomasarcoma was found pressing on the cord, and he noted "a strongly marked œdema of the membrane below the site of the tumour. The transudate character of the fluid was thus explained". This appears to be the first case published in the English language in which such a condition was found, and the writer does not seem to have had any knowledge of similar cases published by French observers.

Nonne's 'Compression Syndrome'.—Nonne, in 1910, detailed six cases of tumour compressing the spinal cord in which his 'Phase-I-reaktion' (Nonne-Apelt reaction) was strongly positive in the cerebrospinal fluid without any lymphocyte increase. He did not give any details as to albumin percentages, or the presence or absence of fibrinogen, but considered that excess of globulin, with no excess of lymphocytes, was diagnostic of spinal compression.

The authority of his name gave this new syndrome an importance in German literature to which it was by no means entitled, and it is unfortunate that the term 'syndrome of Nonne' or 'compression syndrome' should have been applied to fluids of this character, which had previously been found to occur also in other conditions, such as polyneuritis.

In 1912 Raven, in Nonne's clinic, collected forty-seven cases in which this 'compression syndrome' had been found. He paid little attention to the presence or absence of fibrinogen, but noted that a coagulum formed in some cases. He agreed with the theory of Derrien, Mestrezat, and Roger, that the local compression of the cord isolated the fluid distal to it from that on its proximal side, and considered the increase of albumin due to transudation from the blood-vessels in the pia arachnoid, which were congested as a result of the blockage ("Stauungshyperämie"). The yellow colour was considered as probably due to multiple small hæmorrhages, but the stagnation of the fluid in the lower part of the subarachnoid space might contribute to it. He observed also that the yellow colour in the compression syndrome was often much more intense than that resulting from cerebral hæmorrhage.

Punctures Above and Below the Level of the Lesion.—In two of his own cases Raven observed that he got by lumbar puncture a fluid of a deep yellow colour giving a heavy coagulum with the Nonne-Apelt reaction, whereas the fluid obtained by puncture above the site of compression of the cord showed no abnormality either in colour or in globulin content.

In 1913 Marinesco and Radovici published four cases observed in Bucharest in which Froin's syndrome was found. In the first, which was diagnosed as syphilitic meningomyelitis, three successive punctures made in the lumbar region gave yellow fluid which coagulated spontaneously. A fourth, made between the 11th and 12th thoracic spines, gave fluid of similar character; but a puncture between the 2nd and 3rd thoracic spines gave clear fluid which did not coagulate. They explained the yellow colour as due to a 'local bile-formation', from blood-corpuscles entering the subarachnoid space in minute hæmorrhages, and considered that the albumin was also derived from such hæmorrhages.

In the same year Marie, Foix, and Robert found a similar disparity in the fluids removed from above and below the lesion in two cases of tuberculous disease of the spine. In a third case, diagnosed as intramedullary tumour, no such difference was found. Marie, Foix, and Bouttier returned to the subject of 'double puncture' in the following year, and in one case found that the fluid removed from above the lesion was five times as rich in albumin as

that obtained by lumbar puncture. They considered that this result verified the theory of the 'cavité close' put forward by Sicard and Descomps, and by Derrien, Mestrezat, and Roger.

During the discussion of their case, Vincent stated that he had found yellow, highly albuminous fluids in several cases of tumour of the pontocerebellar angle. If in such a case a second puncture were performed within the next few days, the fluid obtained would be normal or almost so; but, if a third puncture was performed after an interval of some weeks, the fluid would again be found to be highly albuminous. He considered that these facts proved that the fluid altered its character after it was secreted.

It must be remembered that tumours of the pontocerebellar angle are sometimes associated with tumours of spinal nerve-roots, and it may have been to some such cases that Vincent referred. At the same time it is not impossible that these changes might be present in the fluid of cases of solitary eighth-nerve tumour, though I have not personally encountered this.

Froin's Syndrome in Epidemic Cerebrospinal Meningitis.—In 1915 Duncan Forbes and Adam reported an unusual type of cerebrospinal fluid in some fatal cases of epidemic cerebrospinal meningitis. They said that "sometimes in chronic cases which are evidently becoming worse . . . one finds the usual cloudy fluid replaced by a yellow, at times clear, fluid in which organisms may apparently be absent. This yellow fluid becomes like a jelly on standing even for a short time. . . . In no case, in which such fluid has been found, have we had a recovery".

Recent American literature has contained several references to the syndrome of Froin. Mix, in 1915, gave a clinical lecture on a case of spinal tumour in which the syndrome was found; in this he reviewed, fairly completely, the French work on the subject.

Hanes, in the following year, reported five cases of the syndrome. Two of these are of special interest. In the first case, which was that of a child of nine months with spastic paraplegia, the fluid obtained by lumbar puncture was the colour of picric acid and coagulated massively. It contained great protein excess, and 16 cells per c.mm. Hydrocephalus developed later, and fluid of a normal character was drawn from a ventricle. At the autopsy he found a ring of tubercular thickening of the meninges round the medulla. In the second case laminectomy disclosed a cyst of the pia arachnoid at the level of the 7th thoracic vertebra, below which the arachnoidal veins were seen to be greatly distended and tortuous. In this case a normal fluid was obtained by lumbar puncture six weeks after the operation.

Experimental Production of the Syndrome.—In 1913 Salin and Reilly, in the course of some experiments on the passage of antibodies from the blood into the cerebrospinal fluid, reproduced the syndrome of Froin experimentally. They injected a few drops of an emulsion of tubercle bacilli into the epidural space of dogs, and produced a tuberculous inflammation round the dura mater. At various intervals they tested the blood and cerebrospinal fluid for antibodies to the tubercle bacillus, by means of the Bordet-Gengou reaction. In the first experiment they found that the fluid drawn from the cisterna magna became albuminous without developing a corresponding increase in cells. It was found to contain antibodies. In their second experiment they obtained fluid both from the cisterna magna and by lumbar puncture, a month after the injection of tubercle bacilli. The fluid from the cisterna magna showed a slight increase in albumin, while that from the lumbar theca was very highly albuminous. A similar result was got from a third experiment.

More recently an attempt was made by Ayer experimentally to reproduce the conditions of pressure on the cord in which the syndrome of Froin may be encountered. He injected 1.5 c.c. of melted paraffin (melting point 55° C.) into the epidural space of cats, and removed fluid from the cisterna magna and lumbar region of the theca at varying intervals thereafter. Yellow fluid, coagulating spontaneously, was obtained by lumbar puncture within twenty-four hours of the operation in two of these experiments. But after the lapse of several days or weeks the cerebrospinal fluid obtained from both situations was normal. The result of his injections was to cover the outside of the theca for a considerable distance with a layer of paraffin which was never more than 3 mm. thick, and to produce a local myelitis of the cord at the site of injection. The latter effect was probably due to the high temperature of the 'injection mass', and was associated with the presence of polymorphonuclear leucocytes in the subarachnoid space.

In a recent paper (1920) Raven collected 145 cases of compression of the spinal cord by tumour or by disease of the vertebræ or meninges. From an analysis of these he came to the following conclusions: (1) The presence of increase of globulin content without any change in colour is uncommon in intramedullary tumours, and is more common in extra- than in intradural tumours. (2) Although xanthochromia is not limited to cases in which the site of the tumour is low in the spinal canal, it is more commonly found with tumours of this region than with those compressing the cervical region of the cord. Cases of increase of the globulin content without other change in the fluid decrease in frequency as the site of the

tumour is lower in the spinal canal. (3) Xanthochromia is no indication whether the tumour is intra- or extramedullary. (4) Rapidly increasing severe compression is more likely to cause xanthochromia than more slowly progressive forms of compression. In this connection he quotes a case of dislocation of the cervical spine in which a yellow fluid, in which no red blood-corpuscles could be seen, was obtained by lumbar puncture twenty-four hours after the accident. (5) Spontaneous coagulation is found equally in extra- and intramedullary tumours. (6) The nature of the compression is without bearing on the intensity of the changes in the fluid. (7) The character of the tumour is without influence on the development of the 'compression syndrome'.

In 1920 Lantuéjoul and Souques described a case of syphilitic meningomyelitis presenting the typical syndrome of Froin, in which very high percentages of albumin and of fibrin were found. The albumin was estimated in two puncture fluids at 4·285 per cent and 4·205 per cent; the fibrin at 0·275 per cent and 0·155 per cent. At the same time as the second lumbar puncture, another puncture was made between the 9th and 10th thoracic spines. This gave cerebrospinal fluid under slightly increased pressure which contained only 0·045 per cent albumin, the albumin contents of the fluids from the dorsal and lumbar punctures thus being in the proportion of 1 to 93.

In this year also Lantuéjoul, in the course of a review of the syndrome of Froin, found only thirty-eight pure cases in the literature, excluding all but those in which the fluid coagulated spontaneously and massively. He noted that not only had lumbar punctures on successive days given, in certain cases, fluids of different composition, but in two cases the colour and nature of the fluid had altered considerably as it flowed out of the needle; the yellow, highly-albuminous fluid which came first being followed by paler or colourless fluid showing little departure from the normal. It appeared as if, during the puncture, the lower, abnormal fluid had been progressively diluted by normal fluid from above.

II.—PERSONAL OBSERVATIONS.

During the past two years I have examined three cerebrospinal fluids which gave the typical appearances of Froin's syndrome, as well as numerous others which resembled these in yellow colour and notable increase of albumin, but which either did not coagulate at all or not sufficiently *en masse* to justify their presentation as true cases of the syndrome. They are recorded here in order to illustrate the type of disease in which the syndrome occurs, and to throw what light they may on the etiology of the changes found in it. For the

clinical notes of these cases I am indebted to the clinical staff of the hospitals in which they occurred.

1.—TYPICAL CASES OF FROIN'S SYNDROME.

Case 1.—Paget's disease of the spine.

V. C., male, age 63, was admitted to the National Hospital under Dr. Kinnier Wilson in March, 1920, with complete spastic paraplegia, which had come on gradually during the previous two years.

On March 17 lumbar puncture was done and a very small quantity of yellow fluid was obtained. This coagulated solid in the tube, so that on inversion of the tube it did not escape. The amount of fluid was too small (less than 1 c.c.) for any examination except that for cells, of which only

FIG. 1.—Low-power microscopic view of section of laminae from *Case 1*, showing very loose structure of the bone and, in the lower part, an area of red marrow.

red blood-corpuscles could be seen. The Wassermann reaction performed on the blood at the same time was negative.

On May 11, 1920, an operation was performed at the level of the 1st to the 4th thoracic vertebrae. No tumour was found, but there was a diffuse thickening of the laminal arches. No pulsation was visible in the dura mater covering the cord until after the laminectomy had been increased upwards.

The patient died shortly after the operation. An autopsy limited to the spine was performed about twelve hours after death. At the level of the laminectomy the vertebral laminae looked rather thicker and cut more easily than normal. Below this level the thickening and increased softness of the laminae became progressively more evident, so that in the lower dorsal and upper lumbar regions the bone could be picked away with dissecting-forceps. The thickening of the bone caused narrowing of the

spinal canal, the dura mater being everywhere in contact with the bone, to which it was also abnormally adherent all over. The cord was removed and appeared normal. It was then seen that a small nodule projected backwards from the lower part of the body of the 8th thoracic vertebra. A smaller nodule of similar character was seen on the body of the 6th thoracic vertebra. At the lower end of the 10th thoracic vertebra the spine had a sharp concavity as though the body of the 11th thoracic vertebra had been displaced forwards. This body was shorter than those of the other vertebrae. Below this level the contour of the spine was rather irregular. No sign of thickening of the tibiae or femora could be made out, and no thickening or bossing of the skull, but a dissection of these parts was not allowed. Microscopically the laminae showed great rarefaction of the bony trabeculae, with numerous large osteoclastic cells in contact with them (*Fig. 1*). The tissue spaces were abnormally wide, and were filled with myxomatous cells with oval or elongated nuclei and long, fine, branching processes. There was also a sprinkling of small rounded lymphocyte-like cells through the interstitial tissue, and in some places collections of blood-forming marrow cells. The appearances seemed to be those of osteitis deformans.

Case 2.—Carcinoma of the spine.

Annie F., age 45. Admitted to the National Hospital on Sept. 6, 1919, under Dr. Holmes, complaining of loss of power in the legs of one year's duration.

On examination, she showed a nodular tumour of left breast, with a gland in the axilla. She was paraplegic in flexion, with involuntary flexor spasms, and very slight power of movement.

On Sept. 9 lumbar puncture was performed, and a yellow fluid obtained which coagulated spontaneously into a fairly dense jelly. It contained albumin, 1·2 per cent. Only a very few lymphocytes were seen in films. The Wassermann reaction was negative in blood and cerebrospinal fluid.

On Sept. 20 laminectomy was performed by Mr. Sargent, who found diffuse malignant disease of the lumbar vertebrae, which proved on histological examination to be a scirrhus carcinoma.

Case 3.—Intradural myxoma. Operation. Recovery.

Alfred W., age 42, admitted to the National Hospital on Oct. 22, 1920, under Dr. Hinds Howell, complaining of pain in the left side and paralysis of both legs. The pain had come on in the summer of 1918, but he had not felt his legs weak until July, 1920.

On examination, he was found to suffer from spastic paraplegia, with anaesthesia over the lower limbs.

On Oct. 26 a lumbar puncture was performed, and golden-yellow fluid escaped which coagulated solid in the tube in a few minutes. No cells were found in it. It contained 0·75 per cent albumin. No opacity was produced on 28 per cent or 33 per cent saturation with ammonium sulphate,

FIG. 2.—Macroscopic appearance of tumour removed from Case 3: 'myxo-endothelioma'.

but half saturation gave a very heavy precipitate. The Wassermann reaction was found to be negative in the blood and cerebrospinal fluid.

On Nov. 9 a laminectomy was performed by Mr. Sargent on the lower thoracic and upper lumbar regions of the spine. A large, soft, oval, gelatinous tumour, in shape and size like a pigeon's egg, was found on the left side of the cord opposite the cut arches of the 11th thoracic vertebra. It lay under the arachnoid membrane, to which, however, it was very loosely attached, and indented the cord considerably on its left posterior surface. Before the theca was opened, it was observed to pulsate normally above the tumour but not at all below it. The tumour was removed. It measured 2.5 cm. in length and 2 cm. in transverse diameter, and weighed 5 gm. On section, it was found to be composed of myxomatous tissue, with very few branching cells, the processes of which reached for long

FIG. 3.—Microscopic appearance of tumour removed from *Case 3*.

distances and contained in their meshes clear, serous fluid; a few groups of endothelial cells were also seen in the tumour (*see Figs. 2, 3*).

The patient made a rapid recovery.

2.—INFLAMMATORY DISEASES OF THE MENINGES WITH HIGHLY ALBUMINOUS YELLOW FLUIDS.

Case 4.—Acute myelitis of unknown origin.

Gertrude S., age 23, was admitted to the National Hospital in November, 1920, under Dr. Taylor, for paralysis of the lower limbs which had come on suddenly four months previously. The history of the onset was that on July 15, 1920, she woke with pain over the left eye, and the same evening had pain in the legs and back, with headache, and was feverish. During the night she lost the sight of her left eye, and within a few hours that of the right eye also. On the next day she could not distinguish

light from darkness, and had complete loss of power of both legs, and loss of sensation up to the face. She also had retention of urine and faeces. On July 18 she had a profuse red rash. After a fortnight of total blindness her sight improved gradually, so that on admission to hospital she could see well.

On examination, she was found to have a complete paraplegia of both lower limbs, which were swollen, oedematous, and quite flaccid, with incontinence of urine and faeces. All forms of sensibility were completely lost below the waist, as were also both deep and superficial reflexes.

Lumbar puncture on Nov. 29 gave a clear lemon-yellow fluid with no coagulum. It contained 0.6 per cent albumin, and with 28 per cent saturation with ammonium sulphate gave a slight opalescence indicating fibrinogen. No cells were found in it. The Wassermann reaction was negative in both blood and cerebrospinal fluid.

The diagnosis appeared to be acute meningomyelitis of the lower thoracic region, which had completely abolished conductivity in the cord.

Case 5.—**Staphylococcal meningitis, limited by adhesions in pia arachnoid to region above 10th thoracic segment.**

Pte. B. C. O., age 30. Admitted to Tooting Military Hospital on Feb. 12, 1919, with the history of four days' headache, and pains around the chest and the lower part of the back. He had vomited frequently since the onset; he was very constipated, and had at first had retention of urine.

On examination, he was found to have weakness of the neck muscles and head retraction. All movements of the arms were possible but weak. Only slight extension movements of the lower limbs were possible; there was no power of flexing the legs. Both plantar reflexes were in extension.

Lumbar puncture was performed on Feb. 16. Clear, dark-yellow fluid with a greenish tinge was removed. It showed 7 small lymphocytes per c.mm., and contained 3 per cent albumin, 0.65 per cent chlorides, and sugar in diminished quantity.

On Feb. 17 he had a fit at 8.0 a.m., with at first an opisthotonic position. There was tremor of both arms, with clutching movements of the right arm and hand. Shortly after the fit an attempt was made to puncture the cisterna magna by inserting a lumbar puncture needle between the atlas and the foramen magnum. When this was done, thin yellow pus came out in large quantities under increased pressure. This was full of polymorphonuclear cells, with numerous intracellular staphylococci which on culture proved to be *Staphylococcus pyogenes aureus*. After the pus settled, the fluid above it was clear and colourless. It contained 0.1 per cent albumin and 0.63 per cent chlorides. Glucose was absent.

The patient died at 3.20 p.m. on the same day, and an autopsy was performed on the following day. The brain was covered on its inferior surface with purulent exudate which filled the basal cisterns but did not run up over the outer aspect of the cerebrum. Punctate haemorrhages were seen over the inferior surfaces of the frontal lobes. The cord, from its upper end to the 10th thoracic segment inclusive, was covered both anteriorly and posteriorly with pus. Below the 10th thoracic segment this stopped suddenly, and the surface of the cord appeared perfectly normal.

Except for chronic tuberculosis at the apices of both lungs, with a recent peribronchial spread of miliary tubercles, no disease was found in the other viscera.

Case 6.—Cerebrospinal syphilis.

F. G., male, age 35, was admitted to the National Hospital under Dr. Hinds Howell on May 12, 1919. In 1917, when in the army, on board a transport to India, he started putting on much weight, and arrived in India about three stone heavier than when he left England. On arrival he became unable to speak, and was sent to hospital and treated with thyroid gland extract. As he was unfit for service, he was sent back to England and discharged.

On examination, he was a very stout man and extremely slow in his mental processes. He presented no definite physical signs of disease of the nervous system, but the plantar reflexes gave a somewhat suspicious response.

A lumbar puncture was performed on May 19, and the fluid was examined by Dr. Nabarro, who found it to be a clear yellow fluid forming a heavy coagulum on standing. It contained 5 to 10 cells per c.mm., and 1.9 per cent albumin. The Wassermann reaction was strongly positive in the fluid, and less strongly in the blood.

A second lumbar puncture was made on June 30, when I found the fluid to be clear and yellowish without a coagulum. It contained 100 to 150 cells per c.mm., mainly of the lymphocyte type, with a few polymorphonuclear cells. The albumin totalled 0.75 per cent. The Wassermann reaction was again strongly positive in the fluid.

3.—PRESSURE ON SPINAL CORD DUE TO THORACIC ANEURYSM.

Case 7.—

H. N., male, age 53. Admitted to the National Hospital on Aug. 26, 1920, under Dr. Turner, with a history of pain in the back and hips for five months, and of loss of use of the legs for two months.

On examination, he was found to suffer from spastic paraplegia, with sensory loss over the thighs and loss of joint sense in the feet.

Lumbar puncture on Aug. 30 gave a yellowish clear fluid with no coagulum. It contained 15 cells per c.mm., most of them being large cells with a rounded nucleus, which were rather larger than the ordinary large mononuclear cell found in the cerebrospinal fluid. These cells were occasionally seen in groups. Albumin totalled between 0.5 per cent and 1 per cent, but owing to the small quantity of fluid obtained a more accurate reading was impossible. The Wassermann reaction was negative in blood and cerebrospinal fluid. A second lumbar puncture on Oct. 19 gave a clear colourless fluid containing no cells, with only 0.035 per cent albumin, and a weakly positive Nonne-Apelt reaction.

X-ray examination revealed a pulsating tumour on the left side of the thoracic spine, and an aneurysm of the descending thoracic aorta was diagnosed. This seemed to have eroded the vertebrae and produced pressure on the cord.

4.—THREE CASES OF POTT'S DISEASE AND PARAPLEGIA GIVING YELLOW HIGHLY ALBUMINOUS FLUIDS.

Case 8.—Pott's disease, paraplegia, and tuberculous meningitis.

Sam M., age 21, was admitted to the National Hospital under Dr. James Collier in May, 1919, with Pott's disease and paraplegia. Pain had commenced in the lower thoracic region of the spine in June, 1918,

but he was examined and passed "fit for service in France". In November, 1918, his back became curved, and in December his legs gave way under him.

On examination, he showed a kyphosis, almost angular in type, with the greatest prominence at the 8th dorsal spine. There was weakness of the lower part of the rectus abdominis, and complete paralysis of both lower limbs; with involuntary flexor spasms.

On July 12 an operation for the relief of pressure on the cord was performed by Mr. Sargent, who resected the laminae of the 6th to the 10th thoracic vertebrae and evacuated some cheesy pus from the body of the 9th thoracic vertebra. It was noticed that the perithecal fatty tissue was matted and infiltrated, but the dura mater looked normal.

After the operation he gradually regained slight power in his lower limbs. In October he developed a slight pleural effusion on the left side.

Towards the end of February, 1920, he showed signs suggesting meningitis, and on the 20th a lumbar puncture was performed which gave a yellow clear fluid. It did not coagulate, and showed only one cell per c.mm. It contained albumin (rather over 0.5 per cent), chlorides 0.75 per cent, and glucose about 0.04 per cent. Albumoses were also present. The Lange curve was 0.0.1.1.2.2.2.3.3.3.

The patient died on Feb. 24, 1920, and an autopsy was performed at which old-standing tuberculosis of the left lung and tuberculous pleurisy covering both lungs was found, but no evidence of recent spread in the chest. The spleen, however, showed many miliary tubercles under its capsule and elsewhere in its structure. The spine at the level of the laminectomy showed a right-angled bend over which the cord was stretched. A considerable quantity of pus escaped from the remains of the body of the 9th thoracic vertebra. The dura mater at this level was covered over and infiltrated with tuberculous granulations and pus, and was adherent to the cord. Above this level the cord and the base of the brain were covered with a thick gelatinous tuberculous exudate. Below it the surface of the cord was clearly seen, and the membranes looked perfectly healthy.

Case 9.—Pott's disease and paraplegia.

Cr., male, age 49, was admitted to the National Hospital on Feb. 10, 1920, under Dr. Risien Russell, complaining of pain in the neck and weakness of the legs. The pain in the neck had begun in May, 1919, and he noticed a lump in the back. He continued at work until Christmas, when he had to stop owing to pain spreading down from the shoulder, and to weakness of the knees. About three weeks before admission his feet felt cold, and he gradually lost power in them until he could not move them at all. About three days before admission he lost control of the bladder and rectum.

On examination, he showed a sharp angular curvature in the lower thoracic region, the 10th thoracic spine being the most prominent. Except for slight movement at the right hip and knee the lower limbs were completely paralyzed, and there was loss of sensibility to all forms of stimuli from the 10th thoracic segment downwards, increasing on passing towards the periphery.

On Feb. 16, lumbar puncture gave a clear yellow fluid which did not coagulate until after the addition of a drop of fresh blood. No lymphocytes were found in it, but it contained 1.5 per cent albumin. The Wassermann reaction was negative in blood and cerebrospinal fluid. On

Feb. 22 an operation for the relief of pressure on the cord was performed by Mr. Armour, who found a tuberculous cavity in the body of the 10th thoracic vertebra. The dura below the level of the curvature did not pulsate until after the removal of the laminae above, when pulsation returned.

Case 10.—Pott's disease and paraplegia.

Eben. H., age 17, was admitted to the National Hospital under Dr. Buzzard in April, 1920, with Pott's disease and paraplegia. He had suffered from spinal curvature since the age of 7, and from paralysis of the legs since January, 1919. This had come on gradually, and he could walk until August, 1919. The paralysis had improved slightly since November, 1919.

On examination, he showed a spinal curvature in the dorsal region in which scoliosis predominated over kyphosis, and the costal margins were approximated to the iliac crests. He had paraplegia in extension, with dropped feet. There was almost complete paralysis of the right leg, and considerable loss of power in the left.

Lumbar puncture performed on April 13 gave a clear lemon-yellow fluid which did not coagulate. It contained 1 lymphocyte per c.mm. and 0.8 per cent of albumin. The Wassermann reaction was negative.

These three cases are recorded as they showed very great increase of albumin in the cerebrospinal fluid. I have examined the fluids of several other cases of paraplegia due to Pott's disease, in which changes of a similar nature though of less degree were found.

5.—NINE CASES OF SPINAL TUMOUR WITH YELLOW HIGHLY ALBUMINOUS FLUIDS.

Case 11.—Recurrence of spinal tumour (?)

B., female, age 37, was admitted to the National Hospital under Dr. Tooth in October, 1919. She had commenced to develop paraplegia in June, 1906, and had previously been admitted to the National Hospital completely paraplegic in 1913. In January, 1914, a laminectomy had been performed, and a tumour found which completely blocked the spinal canal between the cut laminae of the 4th and 6th thoracic vertebrae. The tumour lay in the mid-line on the posterior surface of the cord, and was removed except for its attachment to the ribbon of cord lying in front of it.

On Nov. 2, 1919, a lumbar puncture was performed and yellow cerebrospinal fluid containing some blood admixture was removed. It formed a heavy coagulum on standing, and was found to contain 2.3 per cent albumin and 0.76 per cent chlorides. No cells were found in it. On Nov. 24 a second lumbar puncture again gave a yellow fluid, which this time did not clot. It was found to contain a large number of mononuclear cells and 3.6 per cent albumin. The Wassermann reaction was negative in the blood and cerebrospinal fluid. The lymphocytes in the fluid obtained by the second puncture were explained by the hemorrhage into the subarachnoid space caused by the first puncture.

Case 12.—Neurofibromatosis of cauda equina.

Fred. A., age 50, was admitted to the National Hospital under Dr. Kinnier Wilson on Oct. 23, 1920, with the diagnosis of lesion of the cauda equina. The history of his disability started in 1915, when his left leg became stiff and painful, and his heel tended to rise from the ground. This

became progressively worse, and during the summer of 1920 he developed numbness and weakness, first of the left leg and then also of the right leg.

On examination, the spine was slightly kyphotic in the lumbar region, and there was some tenderness in the same area. Sensibility was impaired over the area of skin supplied by the 2nd to 5th lumbar segments, with partial loss in the distribution of the 1st sacral, but none in that of the lower sacral segments. There was wasting of the glutei, especially on the left side, and of all the muscles below this level, especially those of the thighs. The abdominal reflexes were diminished below the umbilicus. Neither plantar reflex nor knee-jerk could be elicited. The right ankle-jerk was brisk, but the left feeble.

On Oct. 26 lumbar puncture was performed and 5 c.c. of amber-coloured fluid escaped. The flow then ceased abruptly. This fluid was of a deep golden yellow, without a coagulum. It contained 9 lymphocytes per c.mm., and about 1.5 per cent albumin. On fractional saturation with ammonium sulphate it gave a slight opalescence with 28 per cent saturation, which increased to a fairly heavy cloud at 40 per cent saturation. The Wassermann reaction in blood and cerebrospinal fluid was negative.

I am indebted to Dr. Oxley for a report on the examination of cerebrospinal fluid obtained by him by puncturing between the 12th thoracic and 1st lumbar spines on Oct. 11. This was a bright golden-yellow fluid with a large firm clot, which contained in its meshes a few cells. The total albumin apart from the clot was 0.95 per cent. There was thus very little difference between the fluids obtained by two punctures at a fortnight's interval.

On Nov. 9 a laminectomy was performed by Mr. Sargent in the lumbar region. The membranes were found distended by growth, and formed a sausage-shaped mass twice the normal diameter of the theca. The growth was a soft, gelatinous, hæmorrhagic mass, attached all round the cord and surrounding the nerve-roots at the conus medullaris and for about 3 in. above it. This was dissected off the nerve-roots as far as possible. Unfortunately the patient developed a very severe cystitis, to which he succumbed on Nov. 20.

A post-mortem examination was made, limited to the lower part of the cord and the kidneys. The area from which the tumours had been removed was represented by a cyst formed by the membranes and containing blood. On the right side of the lumbar enlargement at a higher level there was a soft fleshy piece of tumour about 1 in. long and $\frac{1}{4}$ in. wide lying among the nerve-roots, to which it was loosely attached. The tumours gave the typical microscopic appearances of neurofibromata.

Case 13.—Endothelioma pressing on the mid-thoracic region of the cord.

Dorothy F., age 19, was admitted in February, 1920, to the National Hospital under Dr. Tooth, suffering from inability to walk. Her symptoms commenced in August, 1918, when her legs became cold and numb. On examination, she showed complete paraplegia, with loss of sphincter control and of sensibility to all forms of stimuli below the 11th thoracic segment.

On Feb. 24, 1920, lumbar puncture gave a very slightly yellow fluid containing about 4 small lymphocytes to the c.mm. and 1.5 per cent albumin. It did not clot. No albumoses were found in it. The Wassermann reaction was negative in blood and cerebrospinal fluid.

A laminectomy was performed by Mr. Sargent on May 15, and

an intrathecal tumour of about the size of a walnut was found opposite the lower thoracic vertebræ. It was vascular, soft, and fleshy, and had to be removed in several pieces. Histologically it gave the appearances of a fibrous endothelioma containing many round areas of fibrous tissue, in some of which calcification was commencing.

Case 14.—Intramedullary tumour of the spinal cord.

Mrs. S., age 48, was admitted to the National Hospital under Dr. Buzzard, complaining of paralysis of the legs of one year's duration. In February, 1919, laminectomy had been performed at the South London Hospital by Miss Davis Colley, who found thickening of the meninges in the mid-dorsal region.

On June 20, 1919, laminectomy was performed, enlarging the previous operation downwards. The cord opposite the body of the 8th thoracic vertebra was swollen and pale, and below that level the membranes were matted. No tumour was found outside the cord. A shallow incision through the postero-median fissure gave exit to a single drop of glairy fluid.

A lumbar puncture on Nov. 20 gave a yellow fluid with a heavy coagulum. Albumin was about 1 per cent, and 2 large mononuclear cells were found per c.mm.

Case 15.—Granuloma of spine.

A., male, age 36. Admitted May 18, 1920, to the National Hospital under Dr. Buzzard, diagnosed as spinal tumour. Since November, 1919, he had weakness in his legs, which dragged when he tried to get about, and soon after Christmas he felt as though he were walking on a cushion. Since then walking had become impossible.

On examination, he showed complete spastic paraplegia, with no voluntary power below the waist, complete loss of all forms of cutaneous sensibility below the 1st lumbar segment, and diminution between this and the 10th thoracic segment.

A lumbar puncture on May 25, 1920, gave a clear cerebrospinal fluid of a pale lemon-yellow colour which contained 4 cells per c.mm. and about 1 per cent of albumin. No coagulum formed until after a drop of blood was added, and then only a very thin web. Albumoses and peptones were absent. The Wassermann reaction was negative in cerebrospinal fluid and blood.

On June 9 laminectomy was performed by Mr. Sargent, who found an extrathecal tumour adherent to the dura and infiltrating and eroding bone in the region of the 8th and 9th thoracic vertebræ. Numerous fragments of this growth were removed, weighing altogether about 8 gm. Microscopically the tumour appeared to be composed of vascular inflammatory tissue and fibrous tissue, the more cellular parts showing various forms of cells, among which small lymphocytes were most numerous; but polymorphonuclear and plasma cells were not rare, and a few larger endothelial cells were seen.

Case 16.—Intramedullary sarcoma in upper dorsal region.

William W., age 40, was admitted to the National Hospital under Dr. Risien Russell in October, 1920, with the diagnosis of spinal tumour. In 1917 he had had pains in the right hypochondrium which were diagnosed as due to gall-stones. In 1918 he began to have weakness and stiffness of his legs, and a tendency to retention of urine. Since August, 1920, he had become very weak on his legs.

On examination, he showed spasticity of both legs, with comparatively little loss of power.

Lumbar puncture on Oct. 25 gave a clear yellowish fluid without any coagulum. It contained 6 cells per c.mm. and 0.75 per cent albumin. Ammonium sulphate in 28 per cent saturation gave no opalescence; but at 33 per cent, and still more at 40 per cent saturation, there was definite opalescence. The Wassermann reaction was negative in blood and cerebrospinal fluid. On Dec. 18 a laminectomy in the upper dorsal region was performed and an intramedullary growth found, a small portion of which was removed for examination. It proved histologically to be a sarcoma of the perivascular type, being composed of a mass of small rounded cells grouped round blood-vessels, the walls of which were very thick and in places hyaline. At a certain distance from these vessels the tumour-cells tended to degenerate, so that the blood-vessels appeared to be surrounded by a collar of cells with a degenerated area outside this.

Case 17.—Intramedullary tumour.

Geo. B., age 28, was admitted to the National Hospital under Dr. Hinds Howell on July 11, 1919, with the diagnosis of lesion of the cauda equina. This history dated back to March, 1917, when his right leg became weak and he had pain in the lumbar region and in the right leg. In August, 1917, he had an attack of pyrexia associated with frequent involuntary jerks in the lower limbs. After this he could scarcely walk at all.

On examination, he was found to be almost completely paraplegic, with sensory loss to all forms of cutaneous sensibility up to the upper lumbar segments.

On July 15, 1919, lumbar puncture gave a yellowish clear fluid which did not clot even after the addition of a drop of blood. It contained 4 cells per c.mm. and 0.3 albumin. Glucose was present in about normal amount, and the chlorides were estimated at 0.71 per cent. On July 28 a laminectomy was performed by Mr. Sargent at the level of the 7th thoracic to the 1st lumbar spines. No tumour was found, but the dura mater was adherent to the pia mater, and the latter to the nerve-roots. The cord looked irregular and bulged through the dural opening. A shallow incision into the posteromedian fissure showed gliomatous matter, and a little fluid escaped.

Case 18.—Intradural hæmangioma.

Thos. P., age 51, was admitted to the National Hospital under Dr. Risien Russell in March, 1920, with symptoms of paralysis of the left arm and leg. The history of his affection commenced in August, 1919, with pain in the left shoulder. In November, 1919, the left arm began to lose its power, and by Christmas the left leg was awkward and stiff.

On examination, he presented the Brown-Séquard syndrome, having spastic weakness of the left leg, and loss of thermal and pain sensibility in the right half of the trunk and right lower limb.

A lumbar puncture on March 9 gave a very slightly yellow fluid without coagulum or cells. It contained 0.15 per cent albumin, and gave a strongly positive Nonne-Apelt reaction. The Wassermann reaction was negative in blood and cerebrospinal fluid. On April 17 a laminectomy was performed on the cervical region of the cord. On exposing the dura mater it was seen to be very tense and non-pulsatile below the 4th cervical vertebra. On opening it, an oval sessile tumour measuring 15 by 5 mm. was found lying against the left side of the cord and slightly in front of it.

It lay under the ligamentum denticulatum and the posterior nerve-roots of the 3rd and 4th cervical segments. It was removed, and the patient made a good recovery.

Microscopically the tumour was composed of papillary outgrowths and irregular strands in which numerous large vessels ran. Between these strands were clear spaces in which here and there collections of serum containing a few leucocytes and red blood-corpuscles were seen. The tumour was composed partly of fully-formed connective tissue and partly of collections of fibroblasts and endothelial cells, and in some places there were collections of brownish granules, apparently composed of hæmatoidin pigment, some of which were contained in large endothelial cells while others apparently lay free in the tissue. The tumour appeared to be a hæmangioma.

Case 19.—Perivascular sarcoma of the conus medullaris.

Mary E. G., age 40, was admitted to the National Hospital on Oct. 22, 1920, under the care of Dr. Farquhar Buzzard. For the previous two years she had had weakness and wasting of the right leg, pain in the right thigh, and defective sphincter control.

On examination, the right leg below the knee was found to be $1\frac{1}{2}$ in. less in circumference than the left, and the wasted muscles had lost their faradic excitability. There was loss of sensibility to pin-prick over the area supplied by the 3rd, 4th, and 5th sacral segments on both legs, and there was diminution of the sensibility to cotton-wool over the same area, with confusion of hot and cold contacts. The knee-jerks were present, and the ankle-jerks both absent.

FIG. 4.—Macroscopic appearance of tumour in 'Case 19: 'perivascular sarcoma'.

Lumbar puncture performed on Oct. 26 gave a clear, slightly yellow fluid which did not coagulate. It contained 3 mononuclear cells per c.mm. and 0.08 per cent albumin, and gave a trace of opalescence on 28 per cent saturation with ammonium sulphate. The Wassermann reaction in the (unheated) fluid was positive, but in the serum negative. A second lumbar puncture a fortnight later gave a clear colourless fluid with no clot. It contained no cells and only 0.04 per cent albumin. Percentage saturation with ammonium sulphate gave no opalescence below 40 per cent, but a definite haze between 40 per cent and 50 per cent saturation. The Wassermann reaction was negative in both blood and cerebrospinal fluid.

On Nov. 26 a laminectomy was performed by Mr. Sargent, and a tumour was found lying posteriorly over the lumbar enlargement. Its upper end was free, but its lower end appeared to be attached to the lower end of the conus medullaris. It was removed as completely as possible. After removal, it was found to measure $1\frac{1}{2}$ in. in length by about $\frac{1}{2}$ in. in transverse diameter ($\frac{3}{4}$ in. at its widest part), and weighed 10 gm. It was pinkish-white in colour, nodular on the surface, and covered over by a smooth capsule in which veins and arteries ran. Microscopically it was

found to be composed of small rounded or oval cells, with round nuclei, which surrounded thick-walled blood-vessels, many of which were thrombosed. A small part of the lower end of the cord had been removed along with the tumour, and this showed infiltration by tumour-cells and much glial proliferation (*see Figs. 4, 5*).

FIG. 5.—Microscopic appearance of tumour in *Case 19*.

6.—TWO CASES OF MULTIPLE NEURITIS WITH YELLOWISH HIGHLY ALBUMINOUS FLUID.

Case 20.—

R. A., male, age 22. Admitted to the National Hospital under Dr. Collier, on Sept. 14, 1920. Paralysis of the legs, arms, and trunk commenced on Sept. 2, 1920, followed on the next day by some loss of visual accommodation. This came on a few days after a sore throat and nasal catarrh. On Sept. 5 he had some difficulty in swallowing, and two days later his voice was indistinct owing to difficulty in opening his mouth. The weakness of the legs and arms progressed, so that on Sept. 12 he was completely paralyzed in his legs except for some movement of his toes. His arms also became very weak, and he had a numb feeling over the hands.

On examination, he was found to be almost completely paralyzed in the limbs and trunk, and there was also some weakness of the diaphragm and of the muscles supplied by the fifth and seventh cranial nerves, especially on the left side. The pharyngeal reflex was diminished. There was some loss of sensibility to pin-prick over the arms, and some over-reaction to pin-pricks on the legs. Sense of position was defective in the legs. The co-ordination of the arms was good. All the deep reflexes were absent, and plantar stimulation gave the normal downward movement of the great toe.

Lumbar puncture performed on Sept. 17 gave a slightly yellow fluid,

which yielded on standing a fairly thick web of coagulum. Two lymphocytes per c.mm. were found in the fluid exuded from the clot. The total albumin content was found to be 0.25 per cent by the Aufrecht tube, and the Nonne-Apelt reaction was positive, but not very strongly; 0.72 per cent chlorides were found. The fluid gave a strongly positive Wassermann reaction in the unheated condition. A second lumbar puncture performed on Sept. 28 again gave a slightly yellow fluid with a thick web of coagulum. Examination showed it to contain about 1 cell per c.mm., and 0.35 per cent albumin by the Aufrecht tube. This time, after heating, the fluid and blood both gave a negative Wassermann reaction. Lumbar puncture was performed on Nov. 30 after the patient had improved considerably, and a clear colourless fluid was obtained. No cells were found in this fluid. The albumin was 0.07 per cent as measured by Mestrezat's method, and the Nonne-Apelt reaction was positive. The Wassermann reaction was again negative. The curve given by Lange's colloidal-gold reaction was 0.0.1.2.3.3.1.1.1.0.

Case 21.—

E. B., male, age 25, was admitted to the National Hospital under Dr. Toth on Feb. 18, 1921. He suffered from paralysis of the arms and legs which had come on about seven months before admission. It began with twitching of the muscles at the back of the left shoulder, and pain of a dragging and shooting nature down the arm. The right arm followed soon after, and then the legs were similarly affected. Aching pains in the paralyzed limbs had been a feature of the disease.

On examination, he was found to present slight weakness of the right side of the face. The tongue was tremulous, and wasted at the sides. The arms were almost completely powerless, the only movements possible being slight movements of the fingers and of the arms at the shoulder girdle. In the lower limbs the only movements possible were slight movements of the toes and of the thighs at the hips. No change in cutaneous sensibility could be found. All the muscles of the body were wasted and flabby. All the deep reflexes were absent, and plantar stimulation gave a slight downward movement of the toes. The sphincters were unaffected.

Lumbar puncture performed on Feb. 21 gave a slightly yellow fluid containing 0.24 per cent albumin (Aufrecht), with a positive Nonne-Apelt reaction. No cells were found in it. Lange's reaction gave a curve as follows: 1.1.2.2.3.3.4.3.2.1. A second lumbar puncture was performed on June 7 after considerable power had returned to the limbs. A small quantity of clear slightly yellow fluid was obtained, which did not coagulate. No cells were found in it. It contained 0.16 per cent albumin by Mestrezat's method. Ammonium sulphate gave a cloudy precipitate in 50 per cent saturation, but no opalescence with 33 per cent saturation. The Lange curve was 0.0.0.1.2.2.3.3.2.1.

Table I.—ANALYSIS OF THE FOREGOING 21 CASES.

NO. OF CASE	NATURE OF CASE	CEREBROSPINAL FLUID			CELLS
		Colour	Fibrin	Albumin per cent	
1	Paget's disease of the spine	Yellow	Solid clot	?	None
2	Carcinoma of spine	Yellow	Solid clot	1·2	A few lymphocytes
3	Intradural myxoma	Yellow	Solid clot	0·75	None
4	Acute myelitis	Lemon-yellow	No coagulum, but fibrin present	0·6	None
5	Staphylococcal meningitis	Dark greenish-yellow	No clot	3	7 lymphocytes per c.mm.
6	Cerebrospinal syphilis	Yellow	Heavy coagulum	1·9	5 to 10 per c.mm.
7	Thoracic aneurysm	Yellowish	No coagulum	0·5 to 1	15 large mononuclears per c.mm.
8	Pott's disease and tubercular meningitis	Yellow	No coagulum	0·5 (Albumoses present)	1 per c.mm.
9	Pott's disease and paraplegia	Yellow	Fibrin web after addition of a drop of blood	1·5	None
10	Pott's disease and paraplegia	Lemon-yellow	No coagulum	0·8	1 per c.mm.
11	? Recurrence of spinal tumour	(1) Yellow	Heavy coagulum	2·3	None
		(2) Yellow	No coagulum	3·6	Many mononuclear cells
12	Neurofibromatosis of cauda equina	Golden-yellow	No clot. Fibrin present	1·5	9 per c.mm.
13	Endothelioma of cord	Slightly yellow	No clot	1·5	4 per c.mm.
14	Intramedullary tumour of cord	Yellow	Heavy coagulum	1	2 per c.mm.
15	? Granuloma of spine	Pale lemon-yellow	Thin web after a drop of blood	1	4 per c.mm.
16	Intramedullary sarcoma of cord	Yellow	No clot. Fibrin present	0·75	6 per c.mm.
17	Intramedullary tumour of cord	Yellow	No fibrin	0·3	4 per c.mm.
18	Intradural hæmangioma	Very slightly yellow	No coagulum	0·15	None

Table I.—ANALYSIS OF THE FOREGOING 21 CASES—*continued.*

No. OF CASE	NATURE OF CASE	CEREBROSPINAL FLUID			CELLS
		Colour	Fibrin	Albumin per cent	
19	Perivascular sarcoma of the conus medullaris	(1) Slightly yellow	No coagulum. Fibrin present	0·08	3 per c.mm.
		(2) Colourless.	No fibrin	0·04	None
20	Peripheral neuritis	(1) Slightly yellow	Thick web of coagulum	0·25	2 per c.mm.
		(2) Slightly yellow	Thick web of coagulum	0·35	1 per c.mm.
21	Peripheral neuritis	(1) Slightly yellow	No fibrin	0·24	None
		(2) Slightly yellow	No fibrin	0·16	None

III.—ETIOLOGY OF THE CHANGES IN THE CEREBRO-SPINAL FLUID IN THE SYNDROME OF FROIN.

A survey of these cases makes it clear that the essential feature of the syndrome of Froin is a notable increase in the percentage of albumin in the cerebrospinal fluid, and the presence of types of albumin normally absent, notably fibrinogen. Along with this there is usually some yellow coloration of the fluid of greater or less intensity; but it must be recognized that this is not a necessary concomitant of the syndrome, although fluids which coagulate sufficiently for the tube to be turned upside down without any escape of fluid constantly show some yellow colour. It is therefore necessary to consider whence this great protein increase is derived.

1. Obviously in tumours of the arachnoid and in cases of meningitis and myelitis the albumin may be transuded directly from the tumour or the focus of inflammation into the subarachnoid space. But tumours vary in vascularity, and, as Raven has shown, it is not by any means the case that vascular tumours are constantly associated with a greater protein percentage in the lumbar fluid than less vascular tumours. Again, the percentage of albumin usually found in the acutest forms of meningitis rarely rises above 0·3, and very seldom above 0·5, whereas the percentages found in the syndrome of Froin are frequently above 1 and sometimes in the region of 3 or even 4.

A survey of several cases of vascular tumour which obviously transuded serum into the cerebral ventricle or basal cisterns lends additional light to this problem (*see Table II*). In all of them the fluid was abnormally albuminous, and in one case contained fibrinogen, giving rise to fine fibrin coagulum; in most it had a yellow colour, but although a large surface of tumour growth was in relation to the cerebrospinal fluid, and seemed to be able to transude serum directly into it, the percentage of albumin was never above 0.2.

Table II.—FOUR CASES OF CEREBRAL TUMOUR WITH YELLOW CEREBROSPINAL FLUID.

NO. OF CASE	NATURE OF TUMOUR	COLOUR	FIBRIN	NONNE-APERT REACTION	ALBUMIN PER CENT	CELLS
1	Gumma involving left basal ganglia and walls of ventricles	Yellowish	None	—	0.06	10 large and small mono-nuclears per c.mm.
2	Glioma of posterior half of left cerebral hemisphere extending into the lateral ventricle	Yellowish	None	Weakly positive	0.045	21 large and small mono-nuclears per c.mm.
3	Carcinoma secondary to growth in stomach growing from tentorium cerebelli and invading the cerebellum and temporal lobe	Pale yellow	Fine web	Faintly positive	0.06	No cells seen
4	Glioma involving right optic thalamus, right corpus mamillare, and anterior part of fornix	Slightly yellowish-green	None	Strongly positive	0.18	12 large and small mono-nuclears

There must therefore be some factor other than transudation concerned with the abnormal increase of albumin found in cases of tumour of the cord or its coverings, disease of the bony walls of the spinal canal, meningitis, and myelitis, which have been quoted. And it will have been seen that in almost every case there was a partial or complete closure of the subarachnoid space round the cord at some level above that at which the fluid was drawn off. In the case of staphylococcal meningitis in my series (*Case 5*) it was possible to compare the fluids drawn from above and below this level, and although the fluid from the cisterna magna was purulent and frankly inflammatory in every respect, it contained only one-thirtieth of the percentage of albumin found in the lumbar fluid. Raven, Marinesco and Radovici, Marie, Foix, Bouttier and Robert, and Lantuéjoul have quoted many cases where fluid was drawn off the subarachnoid space round the cord at various levels; the lower punctures gave fluids which showed the syndrome of Froin in a more or less typical

form, whereas the higher punctures gave fluids which differed little from the normal. There seems therefore to be no room for doubt that the syndrome depends primarily on the damming off of the fluid in the lumbar cul-de-sac from communication with the ventricular fluid. This hypothesis was advanced first by Sicard and Descomps, who considered that two factors entered into the etiology of the syndrome: first, the shutting off of the lumbar fluid from communication with the fluid derived from the ventricles; and, secondly, increased transudation from the meninges owing to congestion of the veins in the lumbar subarachnoid space. Other writers (Derrien, Mestrezat, and Roger) have suggested that a third factor is at work, namely, some process which seals up the perivascular channels and prevents the escape of subarachnoid fluid into them; for it has been noted that although in cases presenting the syndrome lumbar puncture usually gives a fluid under very low pressure, occasionally it is found that the fluid spurts out under considerably increased pressure, even when the patient is lying with his head and spine horizontal.

Physiological Considerations.—In order to form any estimate of the importance of these several factors, it is necessary shortly to review our knowledge of the physiology of the circulation of the cerebrospinal fluid.

There is no longer any doubt that the cerebrospinal fluid is formed entirely by the choroid plexus in the lateral, third, and fourth ventricles. But there is still some uncertainty as to the route whereby it is reabsorbed into the general circulation. Leonard Hill found that it passed out of the cranial cavity chiefly by the blood-stream, and to a less extent by the lymphatic channels of the neck. Injecting a solution of methylene blue into the cisterna magna, he found the urine coloured in less than twenty minutes, whereas the lymphatics of the neck were only seen to be coloured about one hour after the injection. The original work of Key and Retzius on the arachnoidal villi in relation to the absorption of the fluid was largely discounted by the French workers on the subject (Sicard and Cestan, Milian, Mestrezat, Cathelin), who considered that the fluid was absorbed into the blood chiefly by way of the perivascular lymphatic spaces in the cord and subarachnoid space.

The question of resorption of the fluid has recently been taken up by Cushing's school of workers, and Weed and Dandy have added considerably to our knowledge. Weed was able to show that the spinal resorption of the fluid was negligible in comparison with the intracranial resorption. He injected a readily diffusible coloured fluid into the cisterna magna, and judged the rapidity with which it returned to the blood-stream by estimating with the colorimeter the amount secreted in the urine at various periods after the injection.

He then tied the dura mater tightly in the cervical region of the cord, and, repeating the injection under otherwise similar conditions, found that the quantities of pigment recovered from the urine did not differ appreciably from those in the control experiment. Dandy formed a similar conclusion from a totally different series of experiments. Having found that the fluid did not escape through the floor of the third ventricle after blockage of the iter of Sylvius, he attempted to find out which was the chief area of resorption. He therefore surrounded the cerebral peduncles loosely with a wick of gauze dipped in iodine solution, in order that adhesions forming round the mid-brain should prevent fluid passing forwards from the posterior to the middle and anterior cranial fossæ. This he was successful in accomplishing, and as a result the animals developed hydrocephalus, although more slowly than after the iter of Sylvius had been plugged. He therefore concluded that the resorption of cerebrospinal fluid takes place chiefly from the middle and anterior cranial fossæ, and that what resorption takes place in the posterior cranial fossa and the spinal canal is insufficient to balance the amount secreted by the choroid plexuses even when the intracranial pressure is considerably raised. The work of Weed, confirming that of Key and Retzius on the arachnoidal villi, proved these structures to be the channels whereby the larger part of the fluid was returned to the circulation. He injected a solution of iron-ammonium sulphate and potassium ferrocyanide either into the subarachnoid space in the lumbar region or into the cisterna magna, and after fixation in formalin and hydrochloric acid was able to trace granules of Prussian blue into the arachnoidal villi in relation to most of the large cerebral venous sinuses.

It is true that using a similar injection fluid under higher pressure he was also able to trace the injection to the perivascular lymphatics (Virchow-Robin space) of the brain and spinal cord, and even in some cases into the nervous tissue. Both he and Mott considered that the cerebrospinal fluid passed up the perivascular channels to bathe the nerve-cells of the brain and spinal cord, but these conclusions are not universally accepted. In Weed's experiments, as above described, the injections were made under abnormally high pressures. Mott in his experiments had previously tied the carotid artery, thereby producing anæmia of the brain, and his results cannot therefore be considered as conclusive for what takes place under normal conditions.

The Virchow-Robin space normally appears completely empty in histological preparations, unless filled with cells from within the nervous tissue, as in diffuse encephalitis or poliomyelitis and in degenerative disease or destructive lesion of the brain or cord. In these diseases the cells can be traced in histological sections to the meninges in the region where the vessel enters or leaves the brain or

cord, and during life similar cells can be found in the cerebrospinal fluid. Acute syphilitic or coccal meningitis, on the other hand, does not produce infiltration of the Virchow-Robin space except in the parts nearest to the subarachnoid space. It does not therefore seem likely that there is normally a current of cerebrospinal fluid up this space from the larger to the smaller branches of the vessels. Nor can cerebrospinal fluid be absorbed by this route except by a process of diffusion in which some at least of the absorbed cerebrospinal fluid is replaced by the tissue fluid which passes into the Virchow-Robin spaces from the nervous tissue.

The other possible channel for escape of the fluid is the *perineural lymphatics*. Undoubtedly some escape of cerebrospinal fluid can take place by this route, but here again there is undoubtedly a current of lymph in the opposite direction—that is, up the nerve toward the subarachnoid space and the cord. The work of Orr and Rows, who produced toxic infection of the cord by placing celloidin capsules containing living organisms in connection with the peripheral nerves, is supported by that of Meyer and Ransome, and recently of Teale and Embleton, who have shown that tetanus toxin reaches the spinal cord along the lymphatic channels in the perineurium. Here again, therefore, any absorption of cerebrospinal fluid that occurred would merely be in exchange for the addition of a smaller or greater amount of tissue fluid to the contents of the subarachnoid space.

The spinal subarachnoid space may therefore be assumed to be a cul-de-sac from which only an extremely small bulk of fluid is drained. This does not necessarily mean that very little cerebrospinal fluid is absorbed therefrom, although on the premisses even this might be granted. But it appears that what little cerebrospinal fluid is absorbed is replaced, at least in large part, by tissue fluids from the blood-stream reaching it either by way of the Virchow-Robin space or the perineural lymphatics. It must not, however, be considered that the fluid normally stagnates in the spinal cul-de-sac. Two pumping mechanisms are at work to prevent this. The cerebral arterial pulsation constantly changes the size of the brain, and as the skull and cranial dura mater form a firm, non-expansile vessel, it follows that this pulsation must be conveyed to the fluid in the more expansile spinal theca. There is also the venous pulsation due to the varying phases of respiration, which, though probably slight under normal conditions, can become very considerable when forced respiratory efforts are made. This acts both on the cerebral veins and on the large plexus of veins which lies between the spinal canal and the dura mater surrounding the cord, and it is possible that a considerable congestion of the latter plexus might almost completely empty the subarachnoid space surrounding the cord.

It is probable that in health from 400 to 800 c.c. of cerebrospinal fluid each day are secreted, circulate, and return to the general circulation. If, therefore, the communication between the various parts of the subarachnoid space is free, the normal slight addition to the cerebrospinal fluid of lymph derived from the brain, cord, and peripheral nerves is insufficient to alter greatly the chemical constitution of the whole. When, on the other hand, free communication between the ventricular and the lumbar fluids is hindered by any process which narrows the channel between the cord and dura mater, or which produces a matting of the meninges round a part of the cord, the mixing of ventricular and lumbar fluids will be reduced, or will cease completely. The fluid in the lumbar cul-de-sac will then only be able to interchange with the lymph in the Virchow-Robin space and in the perineural lymphatic channels, and it will therefore come to approximate more and more closely in composition to lymph.

On the physiological evidence just reviewed, no other factor need enter into the etiology of the syndrome than the narrowing or complete obliteration of the channel by which the cerebrospinal fluid in the cisterna magna mingles with that in the lumbar cul-de-sac. And when this factor alone is at play, the albumin content of the lumbar fluid should rise with the completeness of the block. In this connection a phenomenon described by Lantuéjoul and others is of interest. He states that in certain cases when the first puncture has given a yellow fluid coagulating spontaneously into a fairly dense jelly, a second puncture performed on the next day has given a clear colourless fluid differing little, if at all, from the normal; but after waiting for some weeks, a third puncture has given a fluid similar or approximating to the first. The explanation of this seems to be that the obstruction in the subarachnoid space, although under normal conditions complete, is of such a nature that a removal of the fluid below it will allow fresh fluid to pass it and reach the lumbar cul-de-sac. The obstruction in such cases may act as a ball-valve, allowing the passage of fluid from above downwards but not from below upwards. This would explain certain cases which present Froin's syndrome, usually in an incomplete form, and in which the fluid obtained at lumbar puncture spurts out under increased pressure. But it is clear that no valve effect is needed to produce the phenomenon described by Lantuéjoul when the obstruction in the subarachnoid space is incomplete. For the block may well be sufficient to prevent any but the slightest mixing of the fluids above and below it when the pressure on either side is approximately the same, but insufficient to prevent the passage of fluid past it when the pressure on one side is considerably reduced.

The etiology of the syndrome in cases of acute myelitis and

meningitis and of syphilitic meningomyelitis presents little difficulty. In such cases a cul-de-sac is formed by inflammatory thickening of the arachnoid, and, in most cases, by adhesions between the outer layer of arachnoid and the pia mater investing the cord. This process alone may obstruct the flow in the pial veins, and lead to capillary congestion below it; but in addition the inflammation of itself causes congestion of the vessels of the cord. Nor is the inflamed area of pia arachnoid bounded by the lower limit of the adhesions in this membrane, but extends considerably below it, and is bathed by fluid communicating with that in the lumbar cul-de-sac, which thus receives and collects the proteins coming from the inflamed vessels.

It is unfortunate that *fibrin ferment* is so often lacking in the cerebrospinal fluids which present the syndrome of Froin, and that in consequence the fluid does not clot spontaneously. It is, in fact, doubtful if fibrin ferment occurs naturally in any of the cases where the syndrome is produced by the pressure of a tumour, and this is probably the reason why the earliest cases, e.g., those described by Froin and Babinski, were of an inflammatory origin. In these fibrin ferment is constantly present, at any rate while inflammation is active. It is lucky for the history of the subject that in the operation of lumbar puncture the fluid is not always drawn off without blood contamination, for, when this occurs, fibrin ferment is provided and clotting takes place. This occurred in *Case 3*. Mestrezat has suggested that in order to demonstrate the presence of fibrinogen a drop of fresh blood or serum should be added to the fluid.

I have several times seen highly albuminous yellow fluids coagulate during the Wassermann test after the addition of complement. This completely nullifies the result of the test, and ought to be guarded against. This may be done by coagulating the fluid previously with a drop of human blood (from a non-syphilitic) or by heating the cerebrospinal fluid for half an hour to 56° C. It is stated by Starling that fibrinogen is precipitated by heating to 56° C. to 60° C., but I have never found clotting occur in the Wassermann test after the fluid had been heated at the lower temperature.

2. The earlier French writers on the subject have insisted that for the production of the syndrome, in addition to stagnation of fluid in the lumbar cul-de-sac, there should be venous congestion below the level of the block. Surgeons with great experience in the operation of laminectomy have told me that in cases of spinal compression the veins on the dorsal surface of the cord below the compression are always congested, owing to the current in these veins being chiefly upwards.

It is true that although the main effluent of the spinal veins is

into the vertebral veins at the lower border of the foramen magnum, there are also emissary veins leaving the dural sheath along with all the nerve-roots. These veins, however, especially in the lumbar region of the cord, are relatively much smaller than the accompanying arteries; and while it is possible that long-continued congestion, such as might occur below the level of a spinal tumour, might increase their lumen, the firmness of the dural sheath would form a considerable barrier to any such process. It would therefore seem to be a necessary corollary to any form of spinal compression that there should be an increase of blood-pressure in the intrathecal veins and capillaries below it.

It is probable that, apart from the effect of bacterial and other toxins on the walls of capillaries, the obstacle which these present to the escape of fibrinogen varies inversely as the pressure within them. It would follow therefore that the venous congestion resulting from the pressure of a tumour would lead to the escape of a relatively higher proportion of fibrinogen than would otherwise occur. It is stated that there are no capillary vessels in the arachnoid, and therefore the transudation of lymph into the spinal subarachnoid space must come from within the cord.

3. Froin's Syndrome in Polyneuritis and Landry's Paralysis.—While the theory of 'cavité close' is justified by the findings at autopsy or operation in a number of cases, it does not seem to explain the pathogenesis of the syndrome of Froin in the cases of polyneuritis and Landry's paralysis recorded in the literature. No such case, so far as I am aware, has come to autopsy while showing the syndrome in a typical manner, and it is therefore impossible to dogmatize on the subject. But the rapidity with which the cerebrospinal fluid regains its normal characters, as the patient is restored to health, militates against any theory which postulates inflammatory adhesions in the meninges. Nor are such adhesions found at autopsy in cases of acute polyneuritis. On the other hand, it is possible that there may be in such cases considerable swelling of the lumbar enlargement of the cord, and that this may form a slight barrier to the mixing of the fluid in the lumbar cul-de-sac with that at a higher level in the subarachnoid space.

Another factor influencing the amount of albumin in the fluid obtained at lumbar puncture in such cases is found in the inflammation of the nerves. It has been seen that there is a lymph-current up the sheaths of the nerves towards the subarachnoid space and the cord. And although the quantity of lymph which travels along this path is probably very small in conditions of health, it may be very considerable when the nerves are acutely inflamed. And when

the large size of the sciatic nerves is remembered, it is easy to understand how lymph travelling up them and reaching the subarachnoid space among the roots of the cauda equina would influence the character of the fluid drawn off from this situation.

It is, however, only a small proportion of cases of polyneuritis which shows more than a slight excess of albumin in the cerebrospinal fluid. Mestrezat considers that this increase is only shown by those cases in which the ventral horns of the cord participate in the inflammation. Eskuchen thinks that the changes in the fluid in polyneuritis are due to involvement of the meninges. But as in the cases which I have examined no definite increase in cells has accompanied the increase in albumin, I find it difficult to accept the latter hypothesis.

Landry's paralysis does not always produce changes in the cerebrospinal fluid, and Eskuchen states that the cases which he has followed to autopsy have not shown any such changes. In the present state of our knowledge, therefore, it seems impossible satisfactorily to explain why the syndrome of Froin should be present in some cases of polyneuritis and absent in others.

4. The composition of the fluids presenting the syndrome of Froin is thus accounted for in a general way by stagnation and vascular congestion. But there are some other points in connection with the syndrome into which it may be worth while briefly to inquire.

Situation of the Block.—It has been shown by Raven that the syndrome usually occurs with greatest intensity when the block is low down in the thoracic or lumbar region. This may be explained on several grounds. In the first place, the segmental vascular supply (i.e., excluding that derived from the vertebral artery) is much greater in the lumbar than in the thoracic region. Therefore a block which obstructed the longitudinal vascular supply in the upper thoracic region would produce more vascular congestion in the lumbar than in the thoracic regions of the cord. That is to say that, whatever the level of the block, the greatest lymph transudation would take place from the lumbar region of the cord.

Secondly, the amount of cerebrospinal fluid to which this lymph is added varies with the level of the block, being much larger when the block is high up than when it is in the lumbar region.

Thirdly, the pulsations transmitted to the fluid in the spinal theca from the vessels of the brain diminish in force from above downwards, and are probably very weak when they reach the lumbar cul-de-sac.

Nature of the Lesion Producing the Block.—This has been shown to influence the changes in the fluid only to a limited extent and only

in certain directions. As regards the cellular picture, while acute inflammatory processes may lead to comparatively little increase of cells in the loculated fluid, meningitis of syphilitic origin usually shows its presence by a definite lymphocytosis.

It has been seen that usually, as the albumin in the fluid rises, the glucose also rises in percentage, although to a much less degree; but when the block is caused by acute meningitis, glucose may be diminished or absent.

The proportion of the various albumin fractions is a question to which little attention has been paid, probably owing to the difficulty of the chemical analysis involved. It is not difficult to make a rough estimate of the proportions of the various globulin fractions present in a fluid by fractional salting out with ammonium sulphate after the method of Kafka. According to him, 28 per cent saturation causes precipitation of fibrinogen; 33 per cent saturation, precipitation of euglobulin; and 40 per cent saturation, of pseudoglobulin. The method is not delicate enough to show one part in 10,000 of a particular type of globulin, but will probably give a positive result with two or three parts in 10,000. I have recently applied this method to the examination of highly albuminous fluids, but it has not so far yielded any definite results in my hands.

The exact quantity of fibrin present in fluids presenting the syndrome of Froin has been estimated by several observers. Blanchetière and Lejonne found 0.17 per cent and 0.16 per cent of fibrin in their case, with 2.55 per cent and 2.75 per cent albumin. Lantuéjoul and Souques found 0.275 per cent fibrin with 4.285 per cent albumin and 0.155 fibrin with 4.2 per cent albumin. Derrien, Mestrezat, and Roger found 0.03 per cent fibrin with 0.6 per cent albumin, and no fibrinogen with 0.4 per cent albumin.

In several of my cases I have found albumin in the region of 0.2 per cent or 0.3 per cent without a trace of fibrinogen being discoverable. On the other hand, I have never examined a meningitic fluid in which the albumin had reached these levels and which did not give a copious fibrin coagulum. It would therefore appear that the proportion of fibrinogen to albumin in cerebrospinal fluids presenting the syndrome of Froin is small by comparison with that found in acute inflammatory conditions.

The proportion of globulin to albumin, on the other hand, is much higher than in meningitis. Mestrezat found in one case globulin 0.13 per cent to albumin 0.49 per cent; in another, globulin 0.22 per cent to albumin 0.65 per cent, in both cases a proportion of about 1 to 3. Blanchetière and Lejonne found globulin 0.808 per cent to albumin 1.742 per cent, a proportion nearer 1 to 2. In meningitis the proportion of globulin to albumin is much lower, 1 to 8 (Mestrezat)

or 1 to 12 (Eskuchen). In fact, the proportion of globulin to albumin found in the syndrome of Froin is only equalled by that found in progressive general paralysis, in which disease Eskuchen computes it at 3 to 7.

Albumoses.—Sicard drew attention to the presence of albumoses in certain spinal fluids which presented the characteristics of the syndrome of Froin, especially in cases of Pott's disease of the vertebræ. He attributed it to the disease in the spinal bones, and considered that it had the same significance as the Bence-Jones protein in the urine of cases of sarcoma of the spine. Mestrezat, on the other hand, considered that the albumoses and peptones arose from the disintegration of the stagnating albumins. It is to be noted that both writers agree that albumoses are never found except at the first puncture, and then only in exceptional cases, in which the syndrome is present in its most complete form. Only one of my own cases showed the presence of albumoses by the biuret reaction after the albumin had been removed by boiling and filtering. This was a case of tuberculous meningitis following on Pott's disease, and the albumoses may therefore have been produced either as a result of the disease in the bone, as in Sicard's hypothesis, or as a product of digestion of the pre-existing albumin in the fluid by toxins derived from the adjacent area of meningitis.

This is one of the many questions presented by the syndrome of Froin which still require elucidation, and to which a satisfactory answer can only be given after fresh work on general tissue metabolism and the interchange of tissue fluids has cleared away the haze in which these subjects are wrapped.

SUMMARY OF CONCLUSIONS.

1. The syndrome of Froin consists essentially in the approximation of the character of the fluid obtained by lumbar puncture to that of blood-plasma. This approximation is never so complete as to render it identical.

2. This change takes place characteristically when the fluid in the lumbar cul-de-sac is completely cut off from communication with the fluid in the ventricles and cisterna magna. This may be produced by tumours or other disease in the bones of the spine, by tumours of the meninges or cord, or by inflammatory adhesions in the pia-arachnoid membranes.

3. The degree of change in the fluid depends more on the completeness of this block than on the nature of the blocking process. But certain constituents of the fluid may vary in relation to the nature of the obstruction.

4. The production of the syndrome is aided by venous congestion below the level of a compression, or by inflammation in the meninges and cord below an area of meningeal adhesion.

5. It is not necessary to postulate any obstruction of the perineural or perivascular lymphatics. The lymph which reaches the subarachnoid space along them aids in the production of the syndrome. Acute peripheral neuritis may in fact itself produce an analogous condition in the cerebrospinal fluid.

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