

infection of the intestinal tract, with the usually accompanying extreme diphtheroiduria. Two other cases had similar diphtheroiduria, but came under observation before the importance of anaërobic intestinal cultures was fully realised. I have been able to keep four of these cases of diphtheroidosis under observation, and they have all done well. The three with intestinal infection have shown great sensitiveness to minute doses of the diphtheroid bacillus vaccines, abdominal pain and discomfort and general malaise being the chief symptoms of focal reaction. Improvement under therapeutic immunisation in this form of infection is always slow, and treatment has generally to be continued for at least six months.

The moral of these cases is obvious. I do not deny the importance of traumatism and strain, physical and mental, as factors in the causation of neurasthenia, but after a period of rest the symptoms due to such causes should either subside, or leave residues that are distinguishable from the phenomena of true neurasthenia. If neurasthenic symptoms continue they must have a toxic basis, and the cases should be investigated and treated accordingly.

Communications from the Lunatic Asylum at Nykobing, Seeland.
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Some Experiments on Treatment of Dementia Paralytica with Subdural Injections of Neosalvarsan. By GEORGE E. SCHRØDER, Assistant Physician, Communal Hospital, Copenhagen, and HJ. HELWEG, Assistant Physician, St. Hans' Hospital.

THE demonstration by Noguchi and many other investigators after him of spirochætes in the nervous texture in tabes dorsalis and in dementia paralytica has, as is well known, quite subverted the old conception of these diseases as para- or metasyphilitic in nature. They are just as syphilitic as other diseases caused by *Spirochæta pallida* are. It is quite a different thing, however, that in certain respects they occupy a peculiar position; as a rule they do not manifest themselves till ten to fifteen years after the primary affection, and they are very little affected by antisyphilitic treatment. It is well known that it was especially this last fact which caused them to be considered as not syphilitic in the common sense.

The said proof of spirochætes has not made it less difficult to understand why the results of the ordinary antisyphilitic cure, also the salvarsan and neosalvarsan treatment, are so defective. The total outcome of the experiences so far obtained is the but little encouraging fact that in reality we have never, or very seldom, succeeded in stoppin

the progress of the disease effectively and for ever. We have quite often heard of temporary recoveries or cures, but, the said diseases in themselves showing a tendency to remissions, we have here in this country generally been most inclined to explain the achieved results as spontaneous remissions, or perhaps as results from the influence of the ordinary hospital hygiene.

However, the rational basis for the treatment—the presence of the spirochætes—having now been substantiated, we purposed, although without any great expectations, to attempt a treatment which the Norwegian-English alienist Monrad-Krohn has proposed.

Monrad-Krohn has in the *Norwegian Magazine for Physicians*, No. 5, 1914, published an article concerning “The Treatment of Syphilis of the Nervous System Spec., Tabes and Paralysis Generalis.” It contained an account of rational treatment with salvarsanised serum, and the rational point consisted in taking serum from a patient who had been under the salvarsan treatment half or one hour after the intravenous injection of salvarsan and injecting it into the spinal canal. Thereby both salvarsan and anti-substance were injected at one time, and through the perivascular lymphatic channels these make their way to the parasites. On the contrary, after a mere intravenous injection of salvarsan no salvarsan passes into the cerebrospinal fluid, and, as far as can be judged, no anti-substance either.

Monrad-Krohn has achieved good results in tabes, but no results in dementia paralytica. But he observes in a supplement to his essay that in three cases of dementia paralytica he has injected 20–30 c.cm. salvarsanised serum directly into the cranium—that is to say, through a trephine opening into the subarachnoid space. In two of the cases the result was satisfactory, and in the third one a temporary deterioration occurred, which was followed by some convalescence. In a later article in the *Journal of Mental Science*, April, 1915, “Remarks on the Intracranial Injection of Salvarsanised Serum,” Dr. Krohn touches upon his technique and on theoretical considerations which underlie the treatment. Here it has only to be observed that as a result of different experiments it was proved that a subdural injection of fluid was able to extend itself to rather a high degree over the surface of the brain, even over both hemispheres, but first to the left frontal lobe when the injection was made on the left side.

As to the technique, it shall also be only briefly mentioned. A trephine opening with a trephine of $1\frac{1}{2}$ –2 cm. diameter was made 10–12 cm. above the temporal end of arcus zygomaticus under the usual anti- and aseptic measures. The dura, which was not opened, was then pierced aslope from behind forwards with a fine cannula, and 25–30 c.cm. salvarsanised serum was slowly injected. The operation was undertaken under local anæsthesia.

Unfortunately the essay was not accompanied by accounts of the illness, and a direct written application to Dr. Monrad-Krohn only elicited that the method had been tried a few times with good results, but that the war had to such a degree increased the work at that English hospital to which he was appointed that further experiments had to be suspended.

Others, and especially English authors, have occupied themselves with the subject. However, we shall not enter into details, but only refer to articles by Swift and Ellis, Mapother and Beaton (*Journal of Mental Science*, October, 1914), and in this country Carl With (*Hospital Magazine*, Nos. 40 and 41, 1917, and *Medical Weekly Paper*, No. 39, 1917). They are expecting more or less from these methods, which, however, have not got beyond the stage of experiment.

Although absolutely convincing communications were not forthcoming, we yet resolved to attempt this treatment, partly on account of the principle being supposed to be rational, and partly and not least on account of dementia paralytica being in itself such a hopeless disease that it is simply a duty to attempt any new and "rational" therapy. It ought here to be observed that previous experiments with subcutaneous injections of natr. nuclein and other fever-producing means have now and then proved to be of some effect, yet not in such a way that real power over the disease was obtained (Hallager, *Medical Weekly Paper*). Of course we did not expect the new method to be able to cure the disease, but we had the hope of possibly stopping its progress—that is, of making it effectively stationary, and that at so early a period in its course that the working ability of the patient would be in part retained. We seize this opportunity to thank Mr. Krarup, the chief physician, for permission to make these experiments, and the then assistant physician, Mr. v. Thun, for his aid at the first trephine operation.

The technique of the treatment used by us was at the beginning quite like that indicated by Monrad-Krohn, for which reason we refer to this. We gave intravenous injections of salvarsan, took some blood from the patient one hour after, had it coagulated under aseptic measures, and took 20 c.cm. of the exuded serum for the injection. However, through different difficulties presenting themselves, we were obliged to alter our technique somewhat. I shall shortly give an account of it for the use of eventual later experiments. For, in spite of our experiments not being specially encouraging, we still think that they ought to be carried on.

The operation itself presents no difficulty. It may be undertaken by any physician in a lunatic asylum, provided a small operating-room can be adapted for the purpose. It is always done under general narcosis.

The situation of the trephine opening in the temporal region at the

line of the hair was such that there was no danger of injuring the sinus sagittalis or the temporal artery. In some cases, however, a small branch of A. mening. passed across the visible part of the dura. In such cases the opening was prolonged to one of the sides with a small curvature, so as to have a place where you could make sure of not injuring the vessel when injections through the skin were to be undertaken later on. This little alteration was most easily executed by biting off the edge of the bone with an ordinary gouge-tong. The injection through the dura caused no difficulty either; on the other hand the later injections through the healed-up flap of the skin and dura were sometimes difficult. They were always made in such a way that the skin was first congealed with ethyl-chloride; then the cannula was pierced through the skin so deeply that the dura was supposed to have been pierced also. The last part of this penetration was quite free from pain, neither the dura nor the brain reacting painfully to the introduction of a fine cannula. It was no doubt unavoidable that now and then you happened to thrust the cannula a little way into the cortex, but when nothing was injected it did not cause the patient any inconvenience. In the case of brain-punctures, which were formerly used, small pieces of tissue were even removed without inconvenience to the patient. When making these injections it is, however, for other reasons absolutely necessary to make sure that you are within the subdural space, and this is done by letting the cerebrospinal fluid run out or be sucked through the cannula.

If you are not on your guard in this way you may happen to inject fluid into the cortex itself, which is thereby destroyed to a greater or less extent—a lesion which may possibly result in a paresis of the arm or the leg on the opposite side of the opening for the place of introduction. It sometimes occurred that we injected a solution of fluid without the cerebrospinal fluid being evacuated, trusting that the needle had really only been subdurally placed, and the consequence was as described.

Later on sections from some of these cases were examined, and there appeared to be an extensive leptomeningitis, which had probably hindered the outflow of the cerebrospinal fluid. Therefore you may certainly take it for granted that in all cases where you are unable to drain out the fluid through the cannula it is owing to such a chronic leptomeningitis, and this negative result of the puncture, and this disease ought then to be considered a counter-indication for continuing the treatment.

Moreover, it is most likely that a needle formed at the point like a catheter could more easily be passed subdurally, and an injection could be made without thereby injuring the cerebrum, but we did not get so far as to use such a one. However, we modified somewhat the injection-fluid, which was of more vital importance. There appeared, namely, to be

various inconveniences in using neosalvarsanised serum. Firstly, it was rather difficult to obtain sufficient sterilised serum for the injection without making the venesection comparatively large. Of course this difficulty could be overcome. But secondly—and this was of greater importance—you could not prove that the neosalvarsanised serum contained arsenic, or at best traces thereof, and that only when very large doses of neosalvarsan had been given intravenously, and of course it is arsenic which is the effective substance. After injections of 45–60 cgrm. neosalvarsan we submitted various samples of blood of 20 c.cm. to Stein's laboratory. These could not be proved to contain the least arsenic. Traces were only found in a sample of blood after an injection of 75 cgrm. neosalvarsan. The blood sample was supplied by Dr. C. E. Jensen, who treated a syphilitic patient with these large doses.

After that we resolved to inject neosalvarsan subdurally dissolved in fresh, distilled, sterilised water. The doses varied from $2\frac{1}{2}$ to 15 mgrm. neosalvarsan in the following solution: neosalvarsan 0.45–0.60 cgrm. in 20 c.cm. distilled water—a somewhat weaker solution than Ravault has used for his intraspinal injections. The injections were repeated after an interval of two to four weeks. The largest number of injections given to any patient were five subdural injections, and in no case whatever has infection occurred from these injections.

In the following we shall state the achieved results. They are, as may be noticed by the shortly quoted accounts of the cases, not especially excellent.

But before coming to any conclusion from these attempts it will be fair to examine whether the results are a consequence of a wrong treatment, or whether the problem must be considered as altogether insoluble.

CASE 1.—M. S—, æt. 34, workman. Syphilis treated with fifty salving-cures when æt. 24. Taken to the lunatic asylum at Nykøbing, S., January 10th, 1916. The disease commenced at the age of 32 with an initial phase of depression. When taken to the hospital there was pupil diff. Left pupil insensitive. Slight paralytic disorder of speech. Spinal fluid, cells, 7; Nonne-Appelt, 0–35; Wm. in the cerebrospinal fluid, 0.3–20. 0.2–100; in blood, 0.2–50, 0.1–100.

Trephining was done on April 17th, 1916. Neosalvarsan was injected intravenously, and 10 c.cm. neosalvarsanised serum subdurally.

May 13th, 1916: Injection of neosalvarsan, 0.003 grm. subdur. through the skin; 0.3 grm. intravenous.

May 24th: Injection of neosalvarsan, 0.006 grm. subdur.; 0.6 grm. intravenous.

June 16th: Injection of neosalvarsan, 0.12 grm. subdur.; 0.6 grm. intravenous.

July 7th: The patient is much better; able to work part of the day.
November 29th; 0.006 grm. subdur.; 0.6 grm. intravenous.

November 21st: The patient is dull and without interests.

December 21st: The patient does not want to work. Feels unwell.

February 14th, 1917: 0.0025 grm. subdur.; 0.45 grm. intravenous.

February 17th: In spinal fluid, Nonne-Appelt 2-35; in cerebral fluid, Nonne-Appelt 3-35 after a respite of twenty-four hours.

February 20th: The patient lost his comb yesterday which he had in his left hand. He explains that his left hand and arm a few times have been as if they were dead, but quite temporarily. No paresis of muscles, but a somewhat reduced sensibility of the left hand.

February 25th: In the course of the last twenty-four hours has had seven times some contortions of the face. Had injection of sulph. mag. 5 c.cm. of a 10 per cent. solution.

February 26th: Some slight attacks of contortions.

March 5th: Irritable and discontented.

May 25th: Works a little.

July 1st: Working better.

August 8th: Discharged, after having paid a visit to his home.

CASE 2.—C. L. J—, æt. 36, unmarried, assistant. Taken to the lunatic asylum at Nykøbing, S., on November 17th, 1915.

The patient contracted syphilis when 22, and when 35 he became nervous, tired and restless.

In the Frederiksberg Hospital, where the patient was first quartered, pleocytosis and positive Nonne-Appelt reaction and positive Wassermann reaction in blood and spinal fluid had been demonstrated.

When the patient was taken to the lunatic asylum at Nykøbing, S., and for a long time after, he was over-excited, but quite brisk and comparatively little demented. However, after a period of six months he began to pilfer, which he had never done before; he also evidently became more dull and had to cease working at the hospital.

In the spinal fluid there were then—cells, 40, and Nonne-Appelt reaction 5-20.

Wm. in the spinal fluid, 0.15-20, 0.075-80; Wm. in blood, 0.2-40, 0.1-100.

Trephining was performed on May 23rd, 1916, followed by injection of neosalvarsan, 0.006 grm. subdurally; 0.45 grm. intravenous.

June 10th: Is again more brisk. Goes to work. Yet he is somewhat low-spirited. Complains of a feeling of strain in the masticatory muscles on both sides.

June 15th: Neosalvarsan was injected, 0.012 grm. subdur.; 0.60 grm. intravenous.

Six hours after the injection there was difficulty of speech and paresis of the left arm and leg. Slight facial paresis and Babinski's reflex in the left foot.

However, in the course of a fortnight the patient was again able to walk about and was relatively well, but could not at all times move the left arm. The difficulty has later on improved somewhat, but there is still a slight paresis left.

The dementia of the patient has become rather stationary. Bodily the patient is getting on well.

November 7th, 1917: Spinal fluid, cells, 7; Nonne-Appelt, 2-10; Wm. in spinal fluid, 0.20-20, 0.1-100; Wm. in blood, 0.01-0.

CASE 3.—C. A. W. J—, policeman, æt. 42. The patient was infected with syphilis when æt. 20, and was treated with many salving-cures and injections.

The disease commenced when the patient was æt. 40 with depression and irritability.

There was then strong pleocytosis in the spinal fluid. Nonne-Appelt, 1-50. Wm. in spinal fluid, 0.05-0.

November 23rd: Was taken to the Frederiksberg Hospital, treated with strong antiluetic cure and had tuberculin treatment. The patient was discharged with — Wm. in blood.

May 3rd-May 22nd, 1915: Renewed treatment.

August 4th: Again at the Frederiksberg Hospital, with disorder of speech, facial paresis, and strong depressive unrest. Wm. + in blood.

March 25th, 1916: Taken to the lunatic asylum at Nykøbing, S.: far advanced dulness.

April 25th: In spinal fluid, cells, 112, and of these many extraordinary polymorphonuclear-formed lymphocytes. Nonne-Appelt, 7-25. Wm. in spinal fluid, 0.07-60; 0.003-100; in blood, 0.1-60; 0.05-100.

May 9th: Trephined. Injection of neosalvarsan, 0.015 grm. subdurally; 0.309 grm. intravenous; 0.009 grm. subdur.; 0.45 grm. intravenous.

June 16th: Attempt at injection in vain.

August 29th: 0.01 grm. subdur.; 0.60 grm. intravenous.

February 10th, 1917: Attempt at injection in vain. Lumbar puncture. In the spinal fluid there are now 450 cells, about $\frac{1}{4}$ - $\frac{1}{5}$ of them, polymorphonuclear formed.

February 18th: Incision above the place of trephining, then injection of neosalvarsan, 0.0025 grm. subdur.; 0.60 grm. intravenous.

March 1st and March 3rd: Spasms in the right arm.

November 3rd: His psychical condition is unaltered.

Spinal fluid, cells, 7. Nonne-Appelt 2-10. Wm. in spinal fluid, 0.1-20, 0.05-100; in blood, 0.025-60, 0.05-100.

In the following three cases a temporary recovery in response to the treatment occurred, but after the lapse of some time the disease progressed and the patients died.

CASE 4.—M. P. P—, blacksmith, æt. 45.

When the patient was 22 years of age he contracted syphilis, which was treated at the Communal Hospital, fourth ward; later on a fresh outbreak occurred, which was treated ambulant. At forty-three years of age he became irritable, capricious, and got megalomania.

June 19th, 1914-February 13th, 1915, at the Frederiksberg Hospital. Wm. in the spinal fluid was weakly positive. He was treated at the Frederiksberg Hospital with tuberculin, salvarsan, and hydrargyrum.

Discharged recovered with negative Wm. in blood.

November 14th, 1915-April 5th, 1916, again at the Frederiksberg Hospital, treated with injections of sublimate and salving-cures. When taken to the hospital he was a typical dementia paralytica, and was discharged unchanged. There was a considerable increase of the quantity of albumen and positive Wm. in the spinal fluid.

June 14th, 1916: Taken to the lunatic asylum at Nykøbing, S., with rather advanced dementia. In the spinal fluid, cells, 13; Nonne-Appelt, 5-30. Wm. in spinal fluid, 1-20; in blood negative, 0.6-100.

July 11th: Treated, with injection of neosalvarsan, 0.006 gm. subdurally; 0.45 gm. intravenous.

August 29th: 0.006 gm. subdurally; 0.45 gm. intravenous.

October 6th: The patient is getting better; is working in the workshop and the garden. Has had an attack of unconsciousness.

February 14th, 1917: Injection of neosalvarsan, 0.0025 subdur.; intravenous failed.

In the spinal fluid 24 lymphocytes, and in the cerebral fluid 21 lymphocytes.

February 20th: Has attacks of convulsion in arms and legs, mostly in the left side.

February 22nd: Numerous attacks of convulsion, mostly in the left side.

February 26th: Increasing attacks of convulsion. Mors.

Section: Under the trephine opening on the left side a small, yellowish-grey softening is to be seen quite superficial in cortex; ependymitis granularis; myocardial degeneration; broncho-pneumonia.

On the right side on inner surface of dura flat fibrinous deposits and slight bleedings; pachymeningitis hæmorrhag. interna.

CASE 5.—G. V. P—, dairy manager, æt. 24.

Nothing known about syphilis. Patient was taken ill during his military service, and was at once treated with potassic iodide and salving cure. Wm. positive in the blood. He was taken to the lunatic asylum at Nykøbing, S., on November 15th, 1915. He presented a typical paralysis with megalomania and disorder of speech.

February 6th, 1916: The spinal fluid showed cells, 23. Nonne-Appelt, 3-20. Wm. in spinal fluid, 0.1-60; 0.05-100; in blood, 0.025-60; 0.01-100.

March 22nd: Treated. Injection of neosalvarsanised serum, 10.00 gm. subdur.; neosalvarsan, 0.60 gm. intravenous.

April 11th: 10.00 gm. subdur.; neosalvarsan, 0.60 gm. intravenous.

May 8th: Injection of neosalvarsan, 0.003 gm. subdur.; neosalvarsan, 0.60 gm. intravenous.

May 18th: The patient has written a letter, which, compared with previous letters, was excellent.

May 25th: Injection of neosalvarsan, 0.009 gm. subdur.; 0.60 gm. intravenous.

June 8th: More clever at assisting in the garden and in the ward.

June 17th: Neosalvarsan, 0.012 gm. subdur.; 0.60 gm. intravenous.

July 14th: In the spinal fluid, cells, 0. Nonne-Appelt, 3-75. Wm. in spinal fluid, 0.2-60, 0.0025-100; in blood, 0.05-60, 0.1-100.

August 20th: The patient is getting more restless and dirty, evil-tempered and obscene, then steady psychical and somatical descent to Mors. On November 16th, 1916, sections examined: Leptomeningitis, ependymitis, aortitis luica. Dura a little adherent at the trephine opening, but no local alterations in front of this.

CASE 6.—V. C. C—, butcher's journeyman, æt. 37. The date of infection is unknown. When 32 years of age he received antiluetic

treatment, because Wm. was positive. He was able to work after the treatment.

He was taken to the lunatic asylum at Nykøbing, S., on November 29th, 1916. Dementia paralytica with far advanced dementia. Spinal fluid, cells, 12·0; Nonne-Appelt, 5-40. Wm. in spinal fluid, 0·3-40, 0·2-100; in blood, 0·1-20, 0·005-100.

He was trephined, and was then altogether twice injected with neosalvarsan 0·006 grm. subdurally, and at the same time 0·45 grm. intravenous. There was a quite transitory convalescence after the last injection, but from that on his paralysis advanced steadily. At a later spinal puncture his spinal fluid was found not to contain more cells.

Section-diagnosis: Diffuse inspissation of the soft membranes. Ependymitis granularis. No softenings. Aortitis luica; bronchitis chr.

In the following four cases the patients died without the injections having influenced them at all. Sections showed nothing but the usual and characteristic appearances seen in cases of dementia paralytica. We had no impression of these injections having influenced the paralysis in any way. In any case, three of these patients, when taken to the lunatic asylum, had reached such an advanced condition of dementia that it would have been a doubtful advantage even if we had really been able to retard their disease.

The disease was in all four cases quite typical and well substantiated, also as to the cerebrospinal fluid. We shall only give a short account of them.

CASE 7.—G. K—, æt. 55. Far advanced paralysis. The patient had previously had paralytic attacks with temporary paresis of the left arm.

The spinal fluid showed—cells, 6; Wm. in spinal fluid, 0·3-80; in blood, 0·2-30.

August 20th, 1916: Trephining, with injection of neosalvarsan, 0·006 and 0·045 grm.

August 30th: Spasms in the left arm with continuing paresis, which in the following months partly improved.

February 15th, 1917: Thirteen cells in the spinal fluid. June 1st: Mors.

Section: A small superficial softening in front of the trephine opening. Extensive paralytic alterations in the brain. Aneurysma aortæ.

CASE 8.—O. S—, æt. 41. Taken to the hospital on December 28th, 1915.

On October 13th, 1914, there was found in the spinal fluid a considerable increase of cells and albumen reaction and positive Wm. reaction.

When taken to the hospital the patient presented the picture of far-advanced paralysis with typical attacks, after which there was for a time some paresis of the left arm.

February 9th, 1916: Spinal fluid, cells, 16; Nonne-Appelt, 2-60; Wm. in spinal fluid, 0·1-60, 0·05-100; in blood, 0·2-30, 0·1-100.

April 10th: Trephined. After that there was injected subdurally 0·003, 0·012 and 0·015 and 0·006 grm., and intravenous, 0·60 grm., four times. A few days after the third subdural injection there was a temporary

paresis of the left hand, and later on attacks of convulsion in the left side.

Section: Strong diffuse pia-inspissations. No softening.

CASE 9.—C. P. C.—, æt. 36. Taken to the hospital on July 13th, 1916. The patient contracted syphilis when 23 years of age. After he had been taken to the hospital a lumbar puncture was performed. The spinal fluid showed—cells, 97; Nonne-Appelt, 5-40; Wm. in spinal fluid, 0.3-20, 0.2-100; in blood, 0.1-60, 00.5-100.

Trephined with subdur. injection of neosalvarsan 0.01 and 0.45 grm. intravenous was given. The injection was made without succeeding in evacuating fluid first. The day after there was a slight paresis of the left arm and the left side of the face.

Section: Leptomeningitis chr. Cortical softening of cerebrum. Aortit. luica.

CASE 10.—N. M.—, æt. 37. Taken to the lunatic asylum at Nykøbing, S., on July 7th, 1916. The patient presented a typical paralysis.

August 20th, 1916: Trephining with injection of neosalvarsan, 0.006 and 0.45 grm. respectively subdur. and intraven.

September 2nd: Slight paresis of the left arm.

September 4th: Evident paresis of the arm, which, however, got somewhat better in the course of a month. In the course of six months the patient began to fall away, and then died.

Section: Dura was adherent to the cranium and to pia in front of the trephine opening. No softenings.

All these very concise extracts from records do not, as already mentioned, present any very encouraging results from the treatment, yet, before denouncing such an apparently rational treatment as the one in question, you ought, as also observed, first to examine whether "primary mistakes" should impair this issue, as is generally the case as regards recently evolved methods of treatment, and to ascertain whether these mistakes were avoidable, so that in time the treatment might become of advantage.

Therefore it will be necessary to consider the groups previously mentioned a little more closely—first of all the one where the treatment was ineffective. It presents two features which may partly explain the bad result. One of them is that at any rate three of the cases mentioned showed far-advanced paralysis; the fourth case was also rather advanced, but the dementia was somewhat less than in the other cases. Consequently these were cases where it was conceivable that the disease was too far advanced for the treatment to be of effect. To this must be added the other not less important point that the complication which frightened us from further treatment occurred so quickly, namely after the first or the second injection, that, in fact, a systematic treatment of three of the cases, including the one less advanced, was out of the question. The only one which got a series of four injections was already, when taken to the hospital, so far

advanced that, as indicated, it would be beyond all expectation that the treatment would be effectual.

Therefore these bad results can hardly be chargeable against the method. There are hardly any other methods, which, under similar circumstances, would have given a better result.

The next group, in which the patients died, but where, however, there was a temporary improvement in response to the treatment, also proves, but certainly less obviously, that similar circumstances have influenced the result. At any rate in two of the cases the dementia was far advanced before the treatment, and the treatment was not resumed because of the improvement having subsided, and the dementia again being in advance. Here the remissions occurred after the second injection.

The two cases had also previously had remissions after antiluetic treatment, but in the third no such treatment had been attempted, and this is therefore the most interesting. The remission was here quite beyond doubt: the patient did not quite recover before he got a relapse; he consequently presented a somewhat childish behaviour, which, however, was possibly constitutional with him.

Here five injections were given, but two of them being of neosalvarsanised serum, which, as proved, did not contain arsenic, only three injections may be reckoned with.

Finally, there is the last group, the three cases in which for the present the paralysis seemed to have become stationary or improved. In one there were given four double injections, in the other two, and finally in the third were given five double injections.

All three cases have been amongst the less seriously attacked; in one of them—the slightest—the patient has been discharged.

However, before regarding these results as being in favour of the treatment, there is no doubt a circumstance which must be taken into consideration—the very essential one that paralyses also present remissions spontaneously. If we examine how our ten patients have got on, it appears, including the previous quarterings at the hospital, that four of the patients have previously had antiluetic treatment—that is, with Hg. and neosalvarsan—and all four had undoubted remissions, and in this hospital the seven have, as mentioned, had remissions of shorter or longer duration—altogether a number which surely is somewhat more than the number of spontaneous remissions would be in the case of ten other paralytics which had not been treated. Consequently it really appears as if a more energetic antiluetic treatment than a mere salving-cure is able to exercise a temporary effect on the paralysis. And other investigators, who have greater material at their disposal, have come to the same conclusion. Here I shall only refer to the statements of Leredde.

Leredde insists that the reason of failure to cure the paralysis is, that the treatment is not sufficiently energetic. And Nonne (¹), surely the investigator who has the best knowledge of lues cerebrospinalis in all its shades, has also commenced to esteem the energetic salvarsan treatment more highly than before. Formerly he warned against it, and was of opinion that the treatment consisting of increasing the leucocytes was the best one—the tuberculin and natrium nucleicum treatment—but now, having become acquainted with the remedy along with Gennerich in Kiel, he thinks that you may expect something from intraspinal injections of neosalvarsan.

Here it would be of importance if you could prove that the treatment had any influence on the pathological processes discovered in the cerebrospinal fluid and the blood, as it has now and then been proved by other investigators both as regards the ordinary antiluetic and the fever treatment. But in this domain the material is doubtless very deficient. There ought to have been many more re-punctures than has been the case. Only in six cases have cells been repeatedly counted, and in four of them the number of these has, after the treatment, become nought, and in two it has increased. As known beforehand, you are to a certain degree able to influence the pathological process in the spinal fluid.

Finally, just a few words on the complication which prevented us from carrying through so energetic a treatment as we should otherwise have considered ourselves bound to do. As seen from the records, in several of the cases—altogether four—an unfortunate consequence of the injections appeared. There was a continuing paresis of the arm—sometimes, but more seldom, of the leg also—on the opposite side to where the injections had been made. At first we supposed that it was owing to a local cortical softening produced by the needle, and through injection of the concentrated fluid. The first sections, namely, showed such a small softening, but the section in Case 10 showed that also without softening a paresis might come—probably a consequence of the local irritation of leptomeninges. Such an acute partial leptomeningitis also explains the paresis in the other cases better than the said small softenings, it seeming strange that so superficial and limited a softening could cause so great disturbances. Therefore in all cases it is to be supposed that the acute local leptomeningitis has been the cause, and this you will be able to avoid in the future if neosalvarsan in more dilute solutions is used—for instance, an injection made with 10 or 20 c.cm. sterilised salt water.

In the preceding remarks we have tried as objectively as possible to weigh what is in favour of and what is against the treatment described. We have not reached convincingly good results, but perhaps useful ones; and that this has not been done to a greater extent by the proceeding

used by us cannot, as we have proved, be unjustly charged as altogether against the method. On comparing it with so many others we must recollect that not seldom has it occurred that methods, which at the beginning have had difficulties to encounter, have proved useful in the long run. Before passing a final sentence there is still an important question to be settled.

For the present the question may be stated thus: Is it altogether worth the trouble to treat paralytics, and especially in the way indicated, which consequently should be given preference over the mere intravenous injection in that it affects the spirochætes in the cortex directly? However, this must be answered in the affirmative. We know that the paralysis in itself is such a hopeless disease that any chance, be it ever so inconsiderable, of being able to make the disease stationary would be an advantage. If we succeed in this, it will surely also be possible to do it at so early a stage of the disease that the working ability of the individual may be wholly or partly retained.

As therefore the method, with suitable alterations and limits as indicated by us, seems to give a faint hope, the experiments ought to be carried on. For instance, it is possible that a continued series of examinations of the spinal fluid in the case of the same patients will prove that there are certain forms of paralysis which can be more influenced than others.

(¹) Nonne, "Ueber die Frage der Heilbarh. der Dem. paralyt.," *D. s. f. Nhlk.* Bd. 58, H. 1 and 2.

*Medico-Psychological Association of Great Britain and Ireland:
Report of English Lunacy Legislation Sub-Committee.*

A Sub-Committee of the Parliamentary Committee of the Association was appointed in January, 1918, the terms of the reference being "to consider the amendment of the existing Lunacy Laws."

The Committee was composed as follows:

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