

rigidity, are sometimes seen in the rigid muscles of Parkinsonism. Here the resemblance breaks down, for while mental changes are common in Parkinsonism, the stolidity and inaccessibility of the katatonic are never seen; indeed, it may be said that if a Parkinsonian were to become inaccessible, *ipso facto* he would become a katatonic.

(For discussion, *vide* p. 738.)

Spirochætes in the Brain in General Paralysis. By A. R. GRANT, M.D.Aberd., Deputy Medical Superintendent, and H. T. KIRKLAND, M.A., M.B., Ch.B.Glasg., Senior Assistant Medical Officer at the County Mental Hospital, Whittingham, Preston, Lancashire.

FOLLOWING on the momentous discovery of the causative organism of syphilis by Schaudinn and Hoffmann, some eight years later Noguchi, working under the great difficulties of his own method, demonstrated the presence of spirochætes in the brain of a general paralytic.

Since that time, with improved technique in staining, numerous observers, including Jahnel (1), Hauptmann (2), Sioli (11), Hans Hermel (8) in Germany, Lelio Grimaldi (10) in Italy, and Dunlap (3) in America, have made detailed and, in most cases, confirmatory and additional observations on the morphological, biological and pathological characteristics of the *Spirochæta pallida*, as demonstrated in the central nervous system of general paralytics.

However, of recent years little has appeared in the literature on the demonstration of the organism in the central nervous system of general paralytics who have undergone the various forms of treatment, *e.g.*, (1) specific anti-syphilitic therapy by the various arsenical preparations, tryparsamide and salvarsanized serum; (2) non-specific treatment by (a) chemical substances as phlogetan and sodium nucleinate, (b) derivatives of infectious agents, as tuberculin; and (3) artificial inoculation of intercurrent infectious diseases, *e.g.*, malaria.

Such an investigation would seem to us essential, having a material bearing on the various hypotheses advanced to explain the *rationale* of the treatment by the various therapeutic agents above, in particular (a) Hauptmann's view that the favourable action lies in the formation of immune bodies, and the production of phagocytes, which prevent the general toxic process by the absorption of the *Spirochæta pallida*, and (b) on the destructive influence of high temperature as such on the organism as outlined

in Jahnel's and Weichbrodt's (15) experiments. In addition, we are of opinion that it would throw some light on the subject and assist us to distinguish the symptoms due to the presence of spirochætes and those assignable to the toxins generated by them.

In this series of some 50 cases are included cases which have been treated with malaria, with tryparsamide and phlogetan, of whom some showed at one period so remarkable an improvement, mentally and physically, as to warrant their discharge to their former life for a considerable period.

In each case a complete clinical record was available to correlate with the *post-mortem* findings, and no case has been included which did not show on admission the physical signs, the mental picture and the serological findings of a general paralytic. In all cases the Wassermann reaction of the blood and cerebro-spinal fluid was positive. In no case was the *Spirochaeta pallida* demonstrated in the cerebro-spinal fluid during life, although constant search was made in each case by the various methods, namely, (a) dark-ground illumination, (b) Alzheimer method, using Jahnel stains, (c) Wharton Starry method. The *post-mortem* was conducted as soon as practicable after death, and fresh specimens obtained, macerated and stained immediately by the method of Tribondeau, and examined for the presence of the organism. Thereafter sections were cut and stained by Jahnel's (13) method.

This was observed: In 3 cases a negative result was obtained when Tribondeau's (14) stain was used in macerated specimens, while the Jahnel stain revealed the spirochætes scattered throughout the sections of brain-tissue. The reverse, a negative section by Jahnel's method and a positive by that of Tribondeau, was never found to hold true.

From time to time we have given the various methods for the staining of spirochætes in the central nervous system a trial, including Levaditi's, Fontana's and their modifications, and the Noguchi and Wharton Starry methods, by using tissue which was known to be positive with Jahnel's method. The results, however, have been disappointing for the most part, and Jahnel's method has, in our hands, proved the most reliable. We have found that it brings out the organism vividly and unequivocally on a yellowish-brown background; and on well-stained specimens no difficulty is experienced in differentiating the organism from the nerve-fibres, etc., which appear to have given some other observers trouble.

The organism has been demonstrated in the brain in 62.5% of the cases examined. This figure is somewhat higher than other observers have obtained—a fact which we consider may be due to the minute and systematic search of sections of all parts of the brain by various trained observers at different times. We can therefore say with confidence that the 37% of cases in which spirochætes cannot be demonstrated are negative. We believe that there is a close analogy between these cases and those of old

gummata or tubercular granulomata, where also the organism can not be demonstrated, and that the presence of the spirochætes in the central nervous system is not essential for the paralytic process to progress and terminate in the usual fatal result.

FACTORS DETERMINING THE SUCCESSFUL DEMONSTRATION OF
SPIROCHÆTES IN GENERAL PARALYSIS.

(a) The time which elapsed between the death and *post-mortem* has been carefully noted. In only 3 cases, which proved negative, has it exceeded 50 hours. In 6 others in which the time exceeded 50 hours, spirochætes have been demonstrated by Tribondeau's and Jahné's methods. The average time in the positive cases is 27 hours, and in the negative 28 hours. It would appear that the time elapsing, within due bounds, has little influence on the successful demonstration of the organism of Hauptmann (9) who has demonstrated them alive in the brain-cortex 48 hours after death, and dead one month after death. Seldom did we observe any sign of their having changed their position *post-mortem*—*e.g.*, penetrating and invading the blood-vessels or the white matter of the brain.

(b) It has been the experience of Jahné and other observers that spirochætes are found, almost without exception, in those cases which died in seizures. But in our observations the rather significant fact has been brought to light that only 21% of those cases in which we have successfully demonstrated spirochætes have the patients died in or ever have had seizures, whereas 50% of the negative cases actually have so died. The onset of the paralytic attacks evidently is not due to an invasion of spirochætes, but rather, as Hauptmann postulates, to an anaphylactic reaction, entirely independent of the presence of spirochætes in the central nervous system.

(c) In complete agreement with other observers it has been found that the cases which have run a long course before death usually proved negative in the examination for spirochætes; whereas the acute, fulminating type have been, without exception, the happy hunting-ground for the successful demonstration of the organism. The average residence in this hospital, has been in the former case 17 months and in the latter 6 months.

(d) The often-changing mental symptoms presented in the various stages of the disease in individual cases seem to have no bearing on the presence and final demonstration of the organism, for it has come to light, from a search through the clinical records, that the confused, elated, euphoric, excited, depressed and grossly demented types occur in almost equal

numbers throughout both series of cases. But in marked contrast to these, it appears more than a coincidence that we have never failed to demonstrate the organism in the 4 cases of juvenile general paralysis which are included, whose age at death varied from 19 to 26 years. It would appear that the organism present in the nervous tissue of hereditary syphilis, as part of the general invasion, has still survived to this, the later stage, although absent in meninges, etc. In addition, the only case of senile general paralysis, æt. 73, proved to be a fertile ground for the demonstration of the spirochæte in all parts of the central nervous system, as did other cases enumerated in the succeeding paragraph.

(e) In all, 11 cases have, at some period, undergone treatment with malaria, and in 8 of these no spirochætes could be demonstrated. Freeman (7) reports similar findings in his series of cases; but he is a bold person who would ascribe their absence to the results of the fever therapy, as in the remaining 3 cases we have, like Gurewitsch (4), found the organism scattered throughout the tissue in fair numbers, and in one case appearing almost in a swarm. This case, it is interesting to learn, had been discharged recovered, had followed his work outside for some time, only to be readmitted again. Five cases had been treated with the new arsenical preparation, tryparsamide, 3 proving negative in the search for spirochætes. In the cerebro-spinal fluid the colloidal gold curve showed marked alteration from the paretic type—in one case being quite negative and in the other having changed to the luetic type, the Wassermann reaction altering from + to —, and the cell-counts becoming normal in all 3 cases. In the other 2 cases the spirochæte has been demonstrated after laborious search, but the serological findings had not been altered to any extent, except in the case of the cell-count. Of the cases which have been treated with phlogetan, one showed spirochætes, but neither showed any alteration in the serology.

THE DISTRIBUTION OF THE SPIROCHÆTES.

(a) *General.*—The organism has, as a general rule, been located in one of the layers of the cortex, and up to the present time we have never been able to demonstrate it in the white matter. In untreated cases it is most easily seen in areas in which the infiltrative processes are most marked. Despite prolonged search we have not been able to confirm Manouilien's (5) finding the spirochæte in the cortical nerve-cells. In our series they appear to have no definite relation to the cells, or to have any elective site, but are scattered, apparently indiscriminately, throughout the tissues. The swarm or nest type, as described by Jahnel, is

infrequently met with, and occurred only in 5 of the cases under review, and in the frontal area. However, spirochætes are often seen, especially in the case of juvenile paralysis, clumped together, but not so thickly as to warrant the descriptive term of "swarm" or "nest." Generally they are scattered in units of one or two throughout the positive cases. The vascular type, an offshoot of the swarm type, we have observed but infrequently, and we have never been able to find any relation between the gummatous vascular transformations, or the miliary gummas which are occasionally met with in general paralysis, and the situation of the spirochæte.

In those cases treated with malaria, or with arsenical compounds, the organism has been found in few numbers, and is generally demonstrated in areas showing marked vascularity of the cortex. It is seldom observed in those parts where the degenerative process is most marked.

(b) *Local*.—In common with other observers, we have found that the organism may be demonstrated in any part of the cortex, especially the anterior of the frontal lobes—when absent there it has never been found in any other region of the brain. The gyrus rectus has proved the commonest resting-place for the organism; the motor area and the superior frontal gyrus have not proved suitable places for the demonstration of it. In 4% of the cases we have been able to demonstrate it in the superior and inferior parietal lobes, supra-marginal and angular gyri, the island of Reil and the temporal and the occipital lobes, but we have never seen it in the pia mater or in the choroid plexus, although it has been found in the thalamus, the corpora quadrigemina, pons, cerebellum, and the grey matter of the cerebral aqueduct.

FORM OF SPIROCHÆTE.

The spirochætes are of three varying types, as in ordinary somatic syphilis, long, medium, and short, with the spirals well preserved, though the organism, as a whole, appears much thicker under the silver stain.

THE DEMONSTRATION OF THE SPIROCHÆTES IN OTHER ORGANS.

In two of the cases the organism has been demonstrated in the aorta. An observation worthy of note, in view of the postulation of the theory of a neurotrophic strain of spirochætes, is that in one of these two cases we have been unable to demonstrate the organism in any part of the central nervous system. In the other

a senile general paralytic (73 years of age) in which the spirochæte found was widely disseminated throughout the brain areas already mentioned, we have been able to show its presence, not only in the cortex of the suprarenals, which is embryologically developed from the genital ridge, *i.e.*, mesodermic cells, but also in the medulla, which is recognized to be developed from tissue common to it and the sympathetic nervous system. This observation, we are of opinion, in correlation with the work that has been done on the organs of internal secretion, should give added significance to the endocrinal factor in general paralysis, and Kraepelin's (12) view on its pathogenesis—that it is a partial phenomenon of a general trophic disorder, and not primarily a disease of the central nervous system.

Summary and Conclusions.

(1) In a series of 50 cases of general paralysis spirochætes were found in 62.5% of the brains.

(2) Spirochætes are more likely to be found in the brain of recent acute cases than those which have run a long course, but—

(3) In 4 cases of juvenile general paresis whose ages ranged from 19 to 26 years at death, spirochætes were found in the brain.

(4) In cases which had been treated by malaria or tryparsamide, spirochætes were found in a much smaller percentage than in those untreated, and when present were not in such large numbers. As the number of treated cases was small, the statement requires further confirmation.

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Clinical Notes and Cases.

An Interesting Case of Meningitis. By NEIL McDIARMID, M.B.,
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THE following case is of interest because of the mode of onset and the causal organism:

Patient, A. B—, a woman, æt. 53, was admitted to Whittingham Mental Hospital on October 7, 1918. With the exception of several attacks of bronchial asthma she had enjoyed fairly good physical health since admission. She was also afflicted with slight deafness on both sides, but had no other evidence of aural disease.

On getting up on the morning of May 9, 1927, she was affected with headache and vertigo, with slight vomiting. On examination she was found to have a Bell's paralysis on the left side. It had all the characteristics of an infra-nuclear lesion. Spasmodic bilateral nystagmus was present and could be elicited in all directions, but was most marked towards the left side. Pulse, temperature and respirations were normal, and examination of the nervous system revealed no other abnormality.

Lumbar puncture on the following day showed the cerebro-spinal fluid to be turbid but not under pressure. The Ross-Jones and Pandy's tests were positive. The sugar content was 0.05% and the cell-count was 1,253 per c.mm., consisting of polymorphonuclear leucocytes and lymphocytes. The differential count was 87.5% of the former and 12.5% of the latter. No red blood-corpuscles and no organisms were demonstrated on this occasion. The Lange gold sol test gave a reading of 0011221000 and the colloidal gamboge a reading of 121000.

In spite of the cerebro-spinal fluid findings it was not until May 14 that she showed other signs and symptoms of meningitis.

The cerebro-spinal fluid was withdrawn on three other occasions, and on the last occasion (May 19) the cell-count was 7,732 and the cells were of the same type and percentage. The sugar content was 0.18%. The Ross-Jones and Pandy's tests were positive. The Lange gold sol reading was 0000012332 and the colloidal gamboge 001220. It was not until this withdrawal of fluid that any organisms were isolated. On this occasion a Gram-negative organism, microscopically resembling the typhoid bacillus, was demonstrated, but no growth was obtained on culture.

Death took place on the following day, and the *post-mortem* findings were those of a basal meningitis. The fourth ventricle and the cerebellar tissue immediately surrounding it was the area most affected. The ventricle was greatly distended with a thick, greenish exudate and the tissues in that area were softened and disintegrated. Microscopically the exudate was found to consist of pus-cells in various stages of disintegration, and the same type of organism as