

T H E S I S

on

THE IMPORTANCE OF COMBINED PATHOLOGICAL AND
CLINICAL EXAMINATION IN THE DIAGNOSIS OF MENTAL
DISEASES ESPECIALLY IN RELATION TO SYPHILIS OF
THE CENTRAL NERVOUS SYSTEM.

by

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For some time past there has been an increasing use of laboratory methods in the diagnosis of mental disorders. This Thesis aims at offering proof of the undoubted value of this method of approach in such cases. There seems however to be a growing tendency, not devoid of danger, to ascribe diagnostic specificity to one or other of the many tests in use for such examinations. Although it is undoubtedly true that an exhaustive analysis of a spinal fluid may in many cases lead to a correct diagnosis of the clinical condition of the patient from whom the specimen has been taken, still it only requires a study of the literature to show that none of the reactions or group of reactions obtained from the spinal fluid can be regarded as pathognomonic of any disease of the Central Nervous System. In this series of cases the Wassermann reaction in the serum, and most of the recognised reactions in the Cerebro-spinal Fluid have been interpreted in conjunction with an exhaustive clinical examination of the patient, in an effort to arrive at an accurate diagnosis. One must not be misled into imagining that it is possible to centrifuge, as it were, a diagnosis from a spinal fluid alone. To do so is not scientific, but is rather a misuse of valuable and scientific methods. The divorce of laboratory methods from clinical observation is therefore to be deprecated. The two are fundamentally complementary, and each will lose in value, unless they remain so.

AND

METHOD OF DEALING WITH IT.

This consisted of 150 consecutive male cases admitted to Cane Hill Mental Hospital from 26th April 1921. to 5th January 1922. These cases were numbered consecutively, and are referred^{to} throughout the Thesis by the numbers thus consigned.

The laboratory work was carried out in the Pathological Laboratory of the London County Mental Hospitals, and I would here express my indebtedness to the Director, Sir Frederick Mott, for the exceptional facilities he placed at my disposal, and for his unfailing encouragement and interest. A Wassermann Test was done on the blood serum of every patient. This was repeated in all doubtful cases, whether the doubt arose from the finding of the test itself, or because of its conflicting with the clinical evidence. Lumbar puncture with fluid examination was done in all cases in which the serum Wassermann reaction was positive, and in those in which the history or the clinical findings in any way suggested the possibility of luetic infection. This is essential, as in syphilis of the central nervous system cases are got with a negative serum, and pronounced pathological changes in the cerebro-spinal fluid. (I) The examination of the cerebro-spinal fluid included the Wassermann reaction, Pandy's Test for excess of protein, a cell count, and where considered advisable, a Lange Goldsol Test was also

performed. The rate of flow, and any after effects were noted in all cases.

Examination of the cerebro-spinal fluid was done in twelve of the thirteen cases of Dementia Praecox, and also in some cases where it was of importance, apart from any suspicion of syphilis.

Autopsies were done on all available cases which died during the period under consideration, and confirmation of ante-mortem diagnoses sought.

The results of treatment are not recorded except in a few special cases, but it may be stated that in syphilitic cases this was carried out in the patients under my charge on the lines recommended by Harrison. (2) Intramuscular injections of novarsenobillon were given, and mercury was used chiefly by inunction, but also in the form of intramuscular injections of mercury cream. Iodides were used both in short intensive courses, and over prolonged periods. The usual precautions were taken, and in all cases the preliminary dose of novarsenobillon was only .15 grms. Definite cases of general paralysis received no specific treatment.

It was by special permission of the Medical Superintendent that I was allowed access to these cases to carry out the investigations entailed in this Thesis. I wish to state that most of the patients in whom I was particularly interested were kindly transferred to my wards, so that I have seen such cases daily.

(1) S.W. Harrison. "The Diagnosis and

Treatment of Venereal Diseases". 1921.

(2) S.W. Harrison. loc. cit.

(I) Blood for Wassermann Test.

This was taken from one of the veins at the bend of the elbow. A tourniquet was tied round the upper arm over a piece of lint, the skin painted with Tincture of Iodine, and a sterilised needle inserted into the vein. The best type of needle was found to be one of fairly large bore, as the blood is very apt to clot in an ordinary hypodermic needle before sufficient has been collected. The needle must be sharp, and tapered gradually, as otherwise it fails to pierce the wall of the vein, merely pushing it aside, or wounding the coats, with resulting haemorrhage. The bevel of the needle however should not be so long as ordinarily used in serum work, as it is essential that the whole of the bevel should be in the vein. The needle is best inserted bevel upwards, and this should be ground concave, as it then picks up the vein wall better. About 5 c. cms. of blood was allowed to run into a sterilised test tube. Strict asepsis is essential throughout. If the veins are very small, it is better to use a small needle and syringe, and draw off the necessary blood. This was rarely necessary in this series. In one patient, No. 25, blood was sent on two occasions, and was so badly haemolysed that a Wassermann Test was impossible. On the third occasion the blood was kept till the serum had separated, when it was pipetted off. The reaction was negative. This

was the only case in which this procedure was necessary.

6.

The blood was sent to the Maudsley Hospital, where the WASSerman Tests were made under the supervision of Sir Frederick Mott.

in the
Cerebro-spinal Fluid and Serum.

Few laboratory methods have aroused such a volume of literature during the past few years as has this reaction. Its detractors are many, and in most instances they attempt to disprove it by the publishing of discordant results. The usual method has been to send specimens of the same serum to different laboratories, and in many cases the results obtained have certainly been extraordinarily divergent. (1)

These divergencies are probably due to fluctuations in the sensitiveness of the Wassermann reaction, as Dreyer and Ward believe, or it may be due to alterations in the amount of Wassermann substance occurring in the specimen after its withdrawal from the patient. It is possible to alter the reaction of a serum by such methods as infection, or by repeated cooling. (2) That the former is the more likely explanation is shown by the works of Simons, Jones and Goddard. (3) They found that when different workers used the same reagents, the percentage of divergencies was very much lessened. (4)

The technique followed during this investigation was that of Candler and Mann. (5) These investigators working in the Pathological Laboratory of the London County Mental Hospitals, had exceptional opportunities for the verification on large numbers of specimens, and in many instances by subsequent autopsy and microscopical examination. The test (appendix

No. II.) is on the lines of the original Wassermann reaction, and in the case of the cerebro-spinal fluid, full allowance is made regarding the warning of Plaut and others that up to one I c.c. fluid may be necessary for a positive reaction in a few cases of definite general paralysis. These workers also have endeavoured to record the intensity of the reaction by definite figures, instead of the usual collection of plus and minus signs. Taking as a unit of complement the minimum the complementary dose, the results are expressed as units of complement deviated by I c.c. of serum or cerebro-spinal fluid; all the results noted in this investigation are recorded in this manner.

Attempts to standardise the test have been made in most countries, but owing to the extreme difficulties have not materialised. Some competent observers doubt the possibility of ever doing so, in the present form of the reaction.

In doubtful cases without complete prevention of haemolysis in any tube, but with retardation of haemolysis in all, or in the upper dilutions, a provocative dose of .15 grm. of novarsenobillon was given, and the reaction again tested. (Jarisch-Herxheimer reaction) .

(I) Phelps, O.D.: " A Preliminary Report of the Result of the Wassermann Tests as Reported from Different Laboratories". Boston M. & S.J., 1915. CLXXIII., 391. .

Wolbarst: "Contradictory Findings in the Wassermann Test". N.Y. Med. Jour., 1913, XCVII., 378.

Uhle & Mackinney: "A Further Study of the Comparative Results of Wassermann Test". N.Y. Med. Times., 1916., XLIV., 301.

(2) Dreyer & Ward: "A Simple Quantitative Serum Reaction for the Diagnosis of Syphilis and the Expression of the Results in Standard Units"., The Lancet, 1921, I., 956.

(3) McDonagh. J.E.R.: "The Biology and Treatment of Venereal Diseases". London, 1915.

(4) Simons, Jones, and Goddard: "The Margin of Error in the Wassermann Test, (A Study of 1000 Cases Made Independently by Two Laboratories)"; Interstate Med. Journal, St Louis, 1916, XXIII, 654.

(5) Candler and Mann: "Archives of Neurology and Psychiatry". Vol.VI., 1914.

(3) Lumbar Puncture.

10.

(a) Technique.

A nickel lumbar puncture needle of the ordinary Barker type was used. The patient was preferably sitting astride a chair, with the back bowed, and shoulders drooped, but in feeble patients the puncture was done with the patient lying in bed on his right side. In only a few cases was a local anaesthetic considered necessary, and then 3% eucaïn⁽¹⁾ was used, and infiltrated as recommended by C.H. Mills. The needle must be sharp, as otherwise it tends to push the interlaminar ligament, ligamentum subflavum, in front of it, without piercing it. The skin was painted with Tn. Iodi., and the needle inserted between the 3rd and 4th, or 4th and 5th lumbar vertebrae in the usual way. Strict aseptic precautions are of course essential. About 5 to 10 c.cs. of fluid were collected in a sterile test tube, the fluid being allowed to run into another tube till it was quite clear of blood. If a vein is injured, the blood very soon stops, but sometimes it may prove more troublesome. Thus on one occasion I had to remove the needle, and reinsert in the next interspace.

If there is any suspicion that the case might be one of cerebral tumour, more especially if in the posterior fossa, then not more than 2 to 3 c.cs. should be drawn off, and the foot of the bed must be kept raised for some time after, the puncture being done in the recumbent position. The danger is, that sudden diminution in the high spinal pressure

may mean the forcing of the medulla into the foramen magnum, with pressure on the vital centres, which may be attended with fatal results. Also, if the tumour is very vascular haemorrhage into it might result.

The uncomplaining attitude towards even repeated lumbar puncture, and the complete absence of any after effects in the vast majority of general paralytics is almost diagnostic of this disease.

In all cases the rate of flow was noted, but this is increased in so many different conditions, and is so much affected by emotion, that it cannot be regarded as a criterion of intrathecal pressure. Different observers have got extraordinarily different results in estimating the normal cerebrospinal pressure, such widely divergent results as 50 and 450 mms. of water having been given. For one thing, no standard instrument has been used, and for another, incidental factors seem to have been rather neglected. Of the latter, gravity and venous pressure are probably the most important. Even coughing, and the movements of respiration affect it. It is for such reasons that the rough indication given in routine lumbar puncture is of very little diagnostic significance. In contradistinction to Carlile,⁽²⁾ I found that the pressure as judged by rate of flow was increased in practically all cases of general paresis. This agrees with the generally held opinion.

In no case did I get any serious after effects,

but 1³ of the 75 cases punctured complained the following day of headache, pain in back of neck, or at site of puncture. One man complained of weakness of his legs. None of these symptoms lasted more than 36 hours. One of these patients was a general paralytic, and he complained of a slight headache on waking the following morning. All patients were kept in bed for 24 hours after puncture, although in the case of paretics this scarcely seems necessary. Chauffard and Boidin report in 223 punctures only 3 cases of vomiting, and no other ill-effects apart from slight headache. (3) Boyd in 120 asylum patients recorded marked after-effects in 25 cases, and slighter sequelae in a number more, and this though he kept his patients in bed for 24 hours after puncture. The chief symptoms he observed were headache, giddiness, nausea and vomiting, and these appeared soon after patient got up. He got no after results with paretics, and suggests that the more normal the patient, the more likely he is to suffer from after-effects. (4) In over a thousand cases Fildes had no serious after-effects. (5)

(1) Harrison: loc. cit. Page 230.

(2) Carlile, H. "Hunterian Lecture on the Diagnosis and Treatment of Syphilis of the Central Nervous System".

(3) Chauffard & Boidin: "Un an de ponctions lombaires dans un service hospitalier" Gaz. de Hôp. 1904, LXXVII. Page 725. "Hospital and Field". Page 79.

(4) Boyd: "The Cerebrospinal Fluid". Page
39.

(5) Fildes, Parnell & Maitland: "Unsuspect-
ed Involvement of the Central Nervous System in
Syphilis". Med. Research Comm., Special Report
Series, No. 45. 1920.

The main chemical characteristic of pathological fluids is the presence of an excess of protein (globulin).

Many tests have been described for the detection of this excess, and the following are perhaps the best known:-

(1) Nonne-Afelt Test.

(a) Mix fluid with equal quantity of saturated Ammonium Sulphate Solution. If turbidity appears in three minutes, the reaction is positive.

(b) Ross-Jones modification. Allow cerebrospinal fluid to run gently on the surface of saturated Ammonium Sulphate in a test tube; the formation of an opaque ring at the junction of the fluids denotes the presence of globulin.

(2) Noguchi's Test.

2 parts cerebrospinal fluid mixed with 5 parts of a 10% solution of Butyric Acid in normal saline, and the mixture boiled for a few seconds; add one part Normal Sodium Hydrate solution (4%), and boil again. The rapidity with which the precipitation falls is proportional to the amount of protein present.

(3) Pandy's Test.

Place in test tube 1 c.c. of saturated solution of Phenol in distilled water, and add one drop of cerebrospinal fluid. Normal fluid gives only the faintest opalescence, but in a fluid with globulin increase

a smoke-like white cloud develops instantly.

15.

In the course of this investigation at first all three tests were employed, but later, owing to its simplicity and decisiveness, only Pandy's test was applied. In my experience, this test gave exceedingly reliable results, and possesses a sensitiveness not shared by the others. The results obtained in this series of cases are recorded elsewhere, and it will be seen that although an increased globulin content is characteristic of parasymphilitic affections, a number of definitely non-specific cases, e.g. Dementia Praecox, gave protein reactions as intense as some cases of general paralysis. These reactions were associated with an atypical Lange colour change, a negative Wassermann, and negative lymphocytosis. The significance of such reactions is not clear at present, owing to our imperfect knowledge of the pathological changes in the cerebro-spinal fluid under different conditions.

(c) Cytological Examination of the Cerebrospinal Fluid.

16.

Normal fluid is practically free from cells. In pathological conditions an estimation is made of the type and number of cells.

(1) Polynuclear leucocytosis generally indicates microbial invasion of the subarachnoid space by some organism other than the tubercle bacillus, but polynuclear cytosis may accompany lymphocytosis in a certain proportion of cases of tuberculous meningitis.

(2) Mononuclear leucocytosis, - Whereas polynuclear leucocytosis points to an acute inflammatory affection of the meninges, mononuclear leucocytosis indicates a chronic condition. It occurs almost invariably in syphilis of the central nervous system, general paralysis, tabes dorsalis, tuberculous meningitis and sleeping sickness. It has been found in other conditions, e.g. herpes zoster, acute poliomyelitis, mumps, lymphatic leukaemia, chloroma and some cases of cerebral tumour. Mononuclears may also replace the polymorphs in the later stages of microbial infection.

Quantitative Estimation.

With Fuchs-Rosenthal Counting Chamber. With Capillary pipette mix 9 parts freshly drawn cerebrospinal fluid with one part diluting fluid.

Methyl Violet	0.1 parts
Acetic Acid Glacial	2 "
Distilled Water	50 "

Transfer drop of mixture to counting chamber and count number of lymphocytes in whole field. Calculate number per cubic millimetre (Number in whole field divided by three).

More than 10 cells per c.mm means positive lymphocytosis.

Differential Centifuge cerebrospinal fluid, pour off fluid and pick up residue with capillary pipette and transfer drop to microscopic slide.

Dry and fix in incubator, stain with Leishman. Leishman. Methylene Blue Eosinate 0.15 grams.

Methyl Alcohol (Pure) 100 c.c.

Stain film for one minute, dilute with equal part distilled water, allow to remain for two minutes, rinse with distilled water and dry.

This is one of the many modifications of the French method introduced by Widal, Sicard and Ravaut in 1901. With a normal fluid at the most two or three lymphocytes are seen in the field with a magnification of 400 diametres.

The cells autolyse very quickly, so that the cell examination must be done soon after the withdrawal of the fluid.

The great advantage of the cell and protein tests is that they are so simply carried out, and can be done immediately, giving valuable information before the result of the Wassermann reaction can be obtained.

(d) The Colloidal Gold Reaction: The Lange Goldsol Test.

18.

During recent years much attention has been given to this reaction of the cerebrospinal fluid, especially in relation to its diagnostic characters in general paralysis of the insane.

The reaction of colloidal gold solutions was investigated by Faraday in 1857, and he found that the addition of another more stable colloid increased the stability of the solution, and conferred protection against precipitation. This "protective influence" was investigated quantitatively by Zsigmondy, who determined the protecting power of various proteins and other colloidal substances. The degree of protection expressed as milligrams of protein capable of protecting 5 c.c. of colloidal gold, against 0.5 c.c. of a 10% sodium chloride solution, was specific for each protein examined, was termed the "gold number", and served for the identification of proteins.

Lange applied these results to the endeavour to distinguish between normal and syphilitic sera, but without success. The application to the cerebrospinal fluid however, showed that a fluid containing an excess of protein precipitated the gold sol instead of exerting any protective influence. The result of his researches was that normal cerebrospinal fluids diluted with 0.4% saline solution caused no alteration in suitable colloidal gold solutions, but abnormal fluids, by reason of their increased protein content, caused partial or complete precipitation of the gold

sol, and in particular the cerebrospinal fluid in general paralysis gave a characteristic precipitation. The reliability of the test, as applied to the cerebrospinal fluid, depends on the preparation of a suitable gold chloride reagent, and strict chemical cleanliness of all apparatus used. The reagent is not difficult to prepare, but extreme chemical accuracy and cleanliness is necessary. I have been fortunate in having the facilities of the Pathological Laboratory, Maudsley Hospital, placed at my disposal, and the reagent used in my series of cases was prepared there by a modification of the original Lange method, and its reliability carefully checked.

* Place 1000c.c. triply distilled water in a 2 litre flask, add 10 c.c. gold chloride solution (1%) and 10 to 20 c.c. potassium carbonate solution (1%) . Heat to boiling, remove flame, and whilst agitating vigorously add 10 c.c. pure formalin solution (1%) . The amount of alkali necessary must be determined by previous accurate titration.

The test is carried out as follows:- Place 11 chemically clean tubes in a rack, and pipette into Tube 1, 1.8 c.c. 0.4% Saline , and into the other tubes 1.0 c.c. Saline. Into tube 1 deliver 0.2 c.c. cerebrospinal fluid, mix, withdraw 1 c.c. and place in tube 2; mix and place 1 c.c. in tube 3, and so to tube 10. Each tube will contain 1 c.c. fluid of dilutions from 1-10 to 1-5120. Tube 11 contains 1 c.c. Saline only, and serves as a control.

To each tube add 5 c.c. colloidal gold reagent. Stand overnight at room temperature and note colour changes. Proper colour of control tube should be salmon red, or old rose.

The reaction results in colour changes which are noted by the following numerals:-

Change to bluish tint noted as 1.

" " lilac " " 2.

" " distinct blue " " 3.

" " pale blue " " 4.

Complete decolourization" " 5.

According to this notation characteristic reactions in pathological fluids are after the following types:-

General paralysis 555554210.

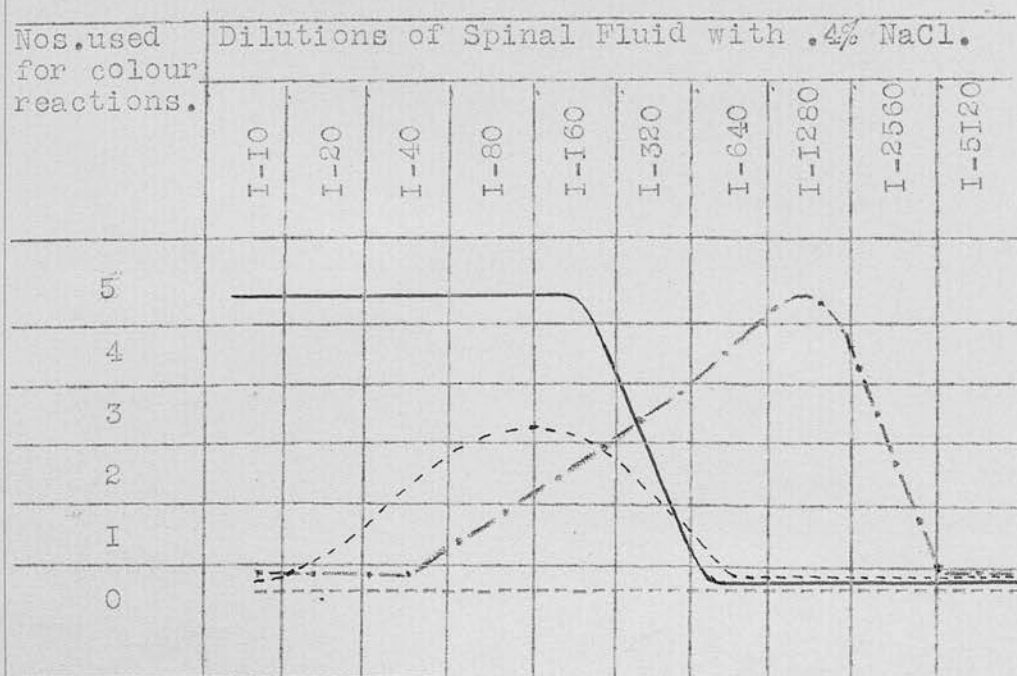
Tabes 2221110000.

Cerebrospinal syphilis I223320000.

There are now many records of observations on the use of this test, and the consensus of opinion can be summed up in the following statement:-

The colour changes in the first 5 tubes are so constant in general paralysis that the term "paretic curve", is applied to such findings. Of less diagnostic value are the so called cerebrospinal syphilitic curves, where the colour changes, though of less intensity than the parietic ones, are most marked in the 3rd to the 6th tubes. In various types of meningitis, other than syphilitic, the colour changes are at times more marked in the tubes with higher dilutions.

Diagram Showing the Four Common Reaction
Types with their Maximum Colour Changes in Different
Dilutions of the Cerebrospinal Fluid.



- 1 - - - - - 1 No reaction - Normal C.S.F.
- 2 ————— 2 Paretic Reaction Type.
- 3 - - - - - 3 Luetic " " .
- 4 - 4 Meningitic " " .

There are some observations which tend to show that the paretic curve is not specific, but may be got in any parenchymatous involvement of the brain, (5) e.g. disseminated sclerosis, cerebral syphilis with (6) marked mental symptoms, and a few other isolated cases.

The experience of some observers indicates that a positive Lange test may even be the first indication of the pathological condition noted by laboratory tests, and I have found this to be the case in my series, e.g. Case No.12. Also, confirming the observations of other workers, I have noted atypical colour changes, in non-specific mental cases. I cannot think that these are accidental, but rather that they have some significance, and with the standardization of the reagent, more refined technique, and more knowledge of the protein content of the cerebrospinal fluid, the test may have wider application than for the diagnosis of general paralysis only. I cannot agree with some investigators, e.g. F.W. Bedford, that the admixture of blood does not render the test unreliable, for in my experience an obvious trace of blood in the cerebrospinal fluid will render the result fallacious. Thus in case No.12, a trace of blood gave complete decolourisation in all tubes. The test is so very delicate that blood in one fluid seems to have quite a different effect to blood in another fluid with a different protein content. Evidence has been produced, and theories advanced, that the test in general paralysis depends on the presence of a specific protein, (Lange), or changes in the hydrogen ion concentration (McDonagh & Levinson), but beyond the fact that the reacting substance is associated with the protein fraction, or may be the property of the physical state of the protein, the explanation of the test is not yet known.

- (1) Faraday: Phil. Trans. 1857. Page 154.
- (2) Zsigmondy: Zeit. Anal. Chem. 1901. XL. Page 697.
- (3) Lange: Berlin. klin. Woch., 1912, XLIX, Page 897. Zeit. f. Chemotherap., 1913, 1, Page 44.
- (4) Whitelaw W. Jour. Mental Science LXVIII, P.66.
Bedford P.W. " " " " P.54.
Miller & Levy. Bull. J. Hopkins Hosp., 1914, XXV, P.133.
- (5) Moore: Arch. Internal Med., 1920, XXV, P.58.
- (6) Thompson: Amer. Arch. Neurol. and Psychiat, 1921, V, P.135.
- (7) McDonagh: Lancet, 1920, II, P.991.
- (8) Levinson: "The Cerebrospinal Fluid".

IV. Analysis of Results of
Examination.

- (I) The Examination of the Cerebrospinal Fluid.
(a) The Incidence of Positive Wassermann Reactions
in Serum and Fluid.

Out of the 150 cases, 44, i.e. 29.3%, proved to be syphilitic. 40 of these cases gave a definite positive reaction in the serum, 2 gave retardation of haemolysis in the top dilutions on the first examination. In one of these the blood had haemolysed, and a second specimen gave a positive 40⁺ reaction, the other case was given a provocative dose of .15 grm. N.A.B. , and the blood again tested. On this occasion the retardation was more marked, (Jarisch-Herxheimer Reaction), but the Wassermann reaction in itself could not be regarded as diagnostic. The patient however, gave a history of having contracted syphilis 20 years previously, and he had clinical evidence of the disease in the shape of aortic disease, and irregularity of his pupils. His fluid was normal. Two cases gave a negative reaction on the first examination. In view of the clinical evidence of tabo-paralysis and general paresis respectively .15 grms N.A.B. was given, and the blood again examined. Both gave weak positive reactions on this occasion, in the form of retardation of haemolysis in all dilutions, and in top dilutions respectively. Two cases not considered syphilitic gave retardation of haemolysis in the top tubes, and here again

the examination was repeated after a provocative dose of novarsenobillon. One gave a completely negative result on this occasion, and on a subsequent occasion; and the other gave retardation of haemolysis as on the first examination. He was aged 63, and suffering from arteriosclerotic dementia, and his arteriosclerosis was held to account for his clinical condition. His aortic first sound was impure, his pupils reacted sluggishly to light and accommodation, and were irregular in outline. His knee jerks were much exaggerated, and he had marked tremor of his tongue. He denied syphilis, but said he had had gonorrhoea several times. It is thus seen that syphilis cannot be entirely excluded from this case, but as said above, he has not been regarded as a case of syphilis. A course of potassium iodide and mercury had no effect on his mental or physical condition.

Of the 44 cases of syphilis, 32 were suffering from General Paresis, i.e. 21.3% of total, and 3 from cerebrospinal syphilis. The remaining 9 had no evidence of syphilitic involvement of their central nervous system, but although ^{not} the direct cause of their psychoses, owing to its devitalising influence their syphilis must be regarded as a probable important indirect causal factor.

The 32 paralytics may be grouped thus:-

- (1) 24 gave a strong positive reaction in both serum and fluid.
- (2) 6 gave a stronger reaction in the serum than in the fluid.
- (3) 1 gave a stronger reaction in the fluid than in

the serum. The latter being at first negative, and after a provocative dose of N.A.B. weakly positive.

- (4) I gave a negative result in both fluid and serum, and a weak positive in the serum after .15 grms N.A.B. This was a treated case of Taboparesis.

Mott suggests that anomalous cases like that in group 3 may be due to actively developing spirochaetes only existing in the brain in paralytics, and that not until enough complement-fixative has been formed by the reaction of the Central Nervous System to saturate the Cerebrospinal Fluid, will the blood be affected by the constant^{escape} of fluid into the general lymph and blood circulations. (1) It is extremely rare in general paralysis to get a positive Wassermann reaction in the serum, and a negative in the fluid, as happened in the case in Group 4. This patient had had intrathecal medication. No case, apart from these 31 general paretics, gave a positive Wassermann reaction in the fluid.

J.C.Wootton in 1913 examined the sera of 177 consecutive male cases admitted to Cane Hill Mental Hospital, and got positive Wassermann reactions in 31%. He did not examine the cerebrospinal fluid, nor does he give the diagnosis of these cases. (2)

As would be expected, figures obtained from mental patients show a much higher percentage of positive results than figures from the general, or hospital population. Thus Fildes got a positive Wassermann reaction in 10.3% of the males, and 5.1% of the females, of patients of 19 years and upwards, who visited the London Hospital for reasons quite

unconnected with syphilis. Bruhns in Charlottenburg (Berlin) examined 1800 cases attending a hospital for skin diseases, and found 1.5% latent syphilis in males and 11.5% latent syphilis in females. Th.E. Hess Thaysen⁽⁴⁾ of Copenhagen, in a hospital for "the poorest classes" got a positive Wassermann in 83 out of 738 unselected cases, i.e. 11%. He found latent syphilis in 4.1%.⁽⁵⁾ Faber, who has examined for latent syphilis on an extensive scale, gives the figures as 1.7% of the general population. Taking the same criteria for deciding the presence of clinical syphilis, this series contained 3 cases of latent syphilis, viz Nos. 100, 124 and 150, i.e. 2%. The other 7 cases giving a positive Wassermann in serum, and negative fluid, showed clinical signs of syphilitic infection.

- (1) Power & Murphy: "A System of Syphilis" p.513.
Vol.IV. 2nd. Ed.
- (2) J.C.Wootton: Archives of Neurology & Psychiatry, Vol. VI. 1914.
- (3) Fildes P. "The prevalence of syphilis among apparently healthy inhabitants of the East End of London." Roy. Comm. on Venereal Diseases. Final Report, 1916, App. XII, p. 139.
- (4) Bruhns: "Ueber unbewusste Spätsyphilis nebst Mitteilungen über Ausfall der Wassermannschen Reaktion an 1800 angeblich nicht mit Syphilis inficierten Menschen". Berl. Klin. Wchnschr., 1916, 53, 833.
- (5) Dr Hess Thaysen: "Latent syphilis in a Medical Department". The Lancet, Jan.29.1921, p.213.

(b) The Relation of the Protein Content of C.S.F. to the incidence of the Wassermann reaction and Pleocytosis.

28.

This was markedly increased in 28 General Paralytics. In the other 5 cases there was not the same increase, but even in these, the excess was quite appreciable. One of the latter was a Tabo-paralytic. The tabo-paretic with the negative Wassermann reaction in his fluid, had marked excess of protein.

2 of the 3 cases of cerebral syphilis showed a slight increase. These 3 cases cannot be regarded as typical of cerebral syphilis, more especially as met with outside mental hospitals. Two of them were very chronic cases, and the other had been treated with salvarsan. A positive test, even though it may be very slight, can nearly always be demonstrated in the presence of pleocytosis in untreated cases of syphilis of the C.N.S. Thus Carlile only found one man out of several hundreds in which this was not the case. He only found an excess of globulin in the absence of a lymphocytosis in 2 out of all his syphilitic cases. Like the similar case in this series, both were cases of syphilitic cerebral arteritis. Boyd describes similar cases.

Non-syphilitic cases which showed an increase were 2 cases of hebephrenic dementia praecox, 1 each of tubercular meningitis, sarcoma of brain, trypanosomiasis, G.S.W. head, and an infantile cerebropathy.

(1) H. Carlile: loc. cit.

(2) Boyd: "The Cerebrospinal Fluid".

(c) The Incidence of Pleocytosis in the Cerebro-spinal Fluid.

The normal number of cells in the cerebrospinal fluid varies from 1 to 6 per cub. mm., and up to 10 cannot be regarded as necessarily pathological. These are lymphocytes with an occasional endothelial cell. It is cases with slight increases that have to be carefully interpreted, and this can only be done in conjunction with the other changes, if any, in the cerebrospinal fluid, and the changes usually found in the diseases under consideration.

In the 2 taboparalytics the count was 14 per c.mm., whereas in the other paretics it varied from 18 to 238. Cases are quite common with over 400 per c.mm. Carlile found 12-160 lymphocytes per c.mm. in 60 paretics, and over 100 in 6 only. Boyd found that early cases of tabes and general paralysis may have 100 or more cells per cub.mm., but that this falls as the disease progresses, and that in advanced general paralysis it may only be 10-20. He reports one case with phenomenal count of 3000 cells per c. (2) mm. Purves Stewart in 40 cases found an average count of 98.7 per cub.mm., the lowest being 34.4 and the highest 462. One case of tabes gave 477.1. (3) Head and Fearnside report cases of tabes showing little or no change in the cerebrospinal fluid, and consider that such cases are in a quiescent stage, either spontaneously, or as the result of treatment. (4)

Only 1 of the 3 cerebral syphilitics had a lymphocytosis.

As there is no inflammation of the meninges in Dementia Praecox, cell increase would not be expected, nor is it usually present. The largest number found in this series was 8 in NO.10, a hebephrenic. This case was unusual in showing a slight protein increase, a mid-zone Lange reaction, and in coming out under considerable pressure. His excitable state may have accounted for the latter phenomenon. Boyd found no changes in the cerebrospinal fluid of catatonic or paranoid dementia praecox patients, but in 10 hebephrenics he found a marked lymphocytosis together with some globulin increase. (5)

The 9 alcoholic cases, including cases of Korsakow's Psychosis, showed no pathological changes in the cerebrospinal fluid. An alcoholic meningitis with changes in the fluid is described. (6)

(1) Carlile: loc. cit.

(2) Boyd: loc. cit. p. 117.

(3) Purves Stewart: "The Diagnosis of Nervous Diseases". 3rd Ed., p. 425.

(4) Head & Fearnside: Brain, 1914, Vol. 37, p. 101.

(5) Boyd: loc. cit. p. 146.

(6) Alcoholic Meningitis. The Lancet, Feb. 14th. 1920. P. 393.

ANALYSIS OF RESULTS OF SERUM AND FLUID EXAMINATION.

	No. of Cases	Serum W +	Serum W -	% of re-sults	C.S.F. W +	C.S.F. W -	% of Cases +	Pleocytosis	%	Protein +	%	No. Cases confirmed by autopsy.
GENERAL PARESIS	30	30	0	100	30	0	100	30	100	30	100	8
TABO-PARESIS	2	2	0	100	1	1	50	2	100	2	100	0
C.S.SYPHILIS	3	3	0	100	0	3	0	1	33	2	67	1
OTHER PSYCHOSES*	115	9	106	8	0	40	0	3	3	7	6	12

* The percentages in this line presume that cerebrospinal fluids unexamined were normal.

This test was performed in 53 cases. The exact results are recorded in the tables in Appendix I. 29 of the 32 paretics gave the typical paretic curve. The other three all tended to the paretic curve. They did not show complete decolourisation in any tube, but the colour changes were most marked in the first 5 or 6 tubes. One of these only gave a positive 8 Wassermann reaction in his fluid, and the other 2 were taboparalytics. One of these gave a negative ^{Wassermann} in his fluid, a mild pleocytosis, and marked glob.increase; the other gave a positive 8 Wassermann reaction, and slight cell and protein increase.

The test was done in 2 of the cases of cerebral syphilis, and in these, changes were got in the middle tubes, but no complete decolourisation was obtained. Similar results are recorded by most observers. In one of the cases treatment cleared up this reaction, as it also did the protein and cell increase originally present.

The reaction was carried out on the fluid of 7 schizophrenics; 5 were quite normal, while 2 showed slight atypical changes in the mid-zone. One was a hebephrenic, the other a catatonic. The latter's fluid was otherwise quite normal, whereas the former showed a slight protein excess, and 8 cells per cub. mm.

The case of Trypanosomiasis showed rap-

id complete decolourisation of all tubes. I have not seen a case of this previously reported.

33.

The only other case which showed any change at all, was the case of infantile cerebro-pathy previously mentioned as having a slight excess of protein. Here, slight changes were obtained in the mid-zone.

The other 14 cases showed no changes in any tube. They were, in addition to the 5 schizophrenics already mentioned, 3 cases of Alcoholic Insanity, 2 of Mania, and one each of Paraphrenia, Insane Amentia, Confusional Insanity and Head Injury.

(a) In General Paresis.

Of the 32 cases of General Paresis only 2 had normal knee jerks on admission, in 16 they were exaggerated, usually on both sides, in 4 diminished, and in 10 absent. The reflexes in this disease vary throughout the course of the illness, and it is probable that no case reaches a termination without the knee jerks being abnormal at some period or other. In tabetic cases they are usually absent, on one or both sides. In taboparalytics Mott found them absent on both sides in 77%, and present on both in 6%. Both the taboparalytics in this series had absent knee jerks on admission, but in one this reflex has returned slightly on one side, since he has had seizures. The "floppy" knee jerks described by Stoddart were present in several cases, These are most characteristic.

In no case was an extensor plantar reflex elicited on admission. As often happens, however, several showed extensor responses, during, and for short periods after, seizures. Mott says that a Babinski reflex is only present in 2% - 3% of general paretics, and when found is strongly suggestive of pseudo-paresis.

The same variation is met with in the pupillary conditions. Thus 12 general paretics (37.5%) had Argyl-Robertson pupils; 14 (43.7%) showed sluggish reaction to light, rigidity to both light and

convergence, irregularity or inequality of the pupils; 6 (18.7%) were normal, including consensual and sympathetic reflexes. Bevan Lewis says latter is often one of the earliest signs of general paresis. (4) The majority of cases with Argyll-Robertson phenomena had in addition, irregularities and inequalities of the pupils. Paradoxical reaction was observed in one case. Pilcz says he found it in 40% of his tabetics. Siemerling gives the pupil rigidity as 68%, whereas the Berlin statistics give 34%, and sluggish reaction in 35.5%. (5)

(6) Nonne has described a few cases of chronic alcoholism with A.R. pupils in the absence of syphilis, and it is said to be occasionally present in disseminated sclerosis. (7) Whether the causal lesion is in the ciliary ganglion, or in the corpora quadregemina is not yet settled. (8) Purves Stewart agrees with Marina in thinking it is due to degeneration of the ciliary ganglion.

All cases of general paresis except 2 showed tremor of the tongue, with defect of articulation, more or less marked. The lesion is cortico-bulbar, and is accompanied by a corresponding defect in the handwriting. Sir Frederick Mott describes it as " hesitant, tremulous, slurred speech, with elision of syllables." It is, of course, not an aphasic disorder, but one of articulation. This tremor of the tongue, with or without closely allied articulatory defects, is so common in the diseases with which G.P. is apt to be confused, that its diagnostic im-

importance is much reduced. In many cases however, it is almost pathognomonic. The tremor of the tongue was often of the "trombone" character described by Stoddart, and this with the characteristic fibrillary tremor of all the muscles around the lips and nose is very typical. It is in early stages of the disease, when correct diagnosis is so important, that these physical signs are absent or slight, and in many cases, even in conjunction with the mental state, they are quite insufficient to justify a diagnosis of General Paralysis. In the prodromal stages of the disease, this is even more so. Thus, NO.77 only showed a slight inequality in the size of his pupils, his knee jerks were normal, he had no tremor of his tongue, and no articulatory defect. No.99 had an exaggerated right knee jerk, slight irregularity and dilatation of his pupils, but no speech defect. He had a remission which was so complete, that a competent authority was only convinced of the accuracy of the diagnosis by repetition of his fluid examination. The paranoid delusions, and the depression present on admission quite disappeared in 6 to 8 weeks. In No 199, the only physical sign was increased knee jerks, but his mental state was very typical.

(b) In Cerebral Syphilis.

Nothing characteristic was found in the physical signs of the 3 cases of Cerebral Syphilis, but they alone were not sufficient to exclude a diagnosis of General Paralysis.

The same applies to the cases of systemic Syphilis. Over 50% had exaggerated knee jerks, and 4 out of the 9 showed pupillary changes. None showed the A.R. phenomena, but some were very myotic, and then it was very difficult to exclude this. 6 showed tremor of the tongue, and 3 of these had an articulation resembling the slurring of a general paralytic.

(d) In Alcoholic Insanity.

In the 10 cases of different forms of Alcoholic Psychoses the knee jerks were exaggerated in 9, and normal in 1; the pupils were normal in 4, sluggish, irregular or unequal in 6; there was tremor of the tongue in all, and an articulatory defect in 5.

(1) Power & Murphy: loc. cit. p.362.

(2) Stoddart: "Mind and its Disorders". 3rd Ed.
p.427.

(3) Power & Murphy: loc. cit. p.270.

(4) Bevan Lewis: "A Text Book of Mental Diseases".
London, 1889.

(5) Power & Murphy: loc. cit. p. 265.

(6) Nonne: Neurologisches Centralblatt, 1912, p.5.

(7) Sicard & Galezowski: Revue Neurologique, 1914.
p. 300.

(8) Ferrier: Lumleian Lectures: Tabes.

When this is examined, the same difficulties in differential diagnosis are encountered. The most straightforward cases are those with the classical euphoria and exalted delusions, but even here there are many pitfalls, as in cases Nos. 61 and 115, fully described later. Of the 32 cases 14, (44%) were of the classical exalted type. It is said that these cases are becoming less frequent, but it is possible that the decrease is only a relative one, due to the more frequent recognition of the other types. In several of these 14 patients delusions of grandeur were not prominent, an unwarranted euphoria, very similar to that met with in other mental diseases, being the prominent symptom. In 9 patients dementia was the only marked mental feature, in 6 acute depression was present, 1 was of the confusional type, and the other 2 were tabo-paralytiks. Many showed tabetic signs, but only those cases in which these were more marked than the mental symptoms have been classed as tabo-paralytiks. (I) Kraepelin found signs of tabes in 6 - 8% of his paretics, and Mott gives the figure as 10%.

Dementia is the most constant psych-ic phenomenon in general paresis, and could be detected in all cases of this series. It has many points in which it differs from the dementia of cerebral syphilis. In the latter the dementia is usually partial, whereas

in G.P. there is a slow insidious diminution of the whole intellectual life, with a profound alteration of the personality, usually with disorientation for time and place, if at all advanced. The General Paralytic loses his autocritical sense, and unlike the other, cannot give a good account of the course of his illness. In the remission of G.P. one can usually detect intellectual and affective deficiencies, whereas in those of Cerebral Syphilis the patient may appear quite normal. The latter disease proceeds by fits and starts, whereas the evolution of General Paresis is more or less continuous.

The cases met with in asylums are usually past the prodromal stage, the stage in which clinical diagnosis is difficult and most important. Mott gives an extremely good description of this stage in *Abnormal System of Syphilis*. Ballet insists on the importance of recognising a neurasthenic form of the prodromal stage.

It must not be forgotten that these patients may exhibit psychical automatism, otherwise one may be misled by it into thinking that the patient cannot be demented. Lumbar puncture in such cases is all-important.

(1) Kraepelin: General Paresis, 1914.

(2) Power & Murphy: loc.cit. p.260.

(3) Ballet & Paul Blocq: Traite de Medecine.

(40) The Results bearing on the Theory that there are Dermatotropic and Neurotropic Forms of the Spirochaeta Pallida.

40.

(I)

Sir Frederick Mott and other authorities suggest that there may be two different biological forms of the spirochaete pallida, one dermatotropic, the other neurotropic. The latter is supposed to cause General Paresis and Tabes, whereas other syphilitic diseases of the central nervous system and visceral syphilis are supposed to be due to the dermatotropic form acting through the general lymphatic system. One type of evidence deduced in favour of this theory takes the form of histories of several men contracting Tabes or General Paresis from the same source, and of their absence in certain communities where syphilis is rife. More convincing evidence that the organism is modified in these two diseases is provided by the animal experiments of Noguchi, Förster, Tomaszewski, and other workers. What is probably the strongest evidence against the theory is the prevalence of syphilitic aortitis in General Paralysis and Tabes. When Fournier's parasyphilis was excepted, this lesion was regarded as being of this nature, but as the organism can usually be isolated from the lesions post-mortem, the aortitis must be excepted as definitely due to the living spirochaete. This lesion differs from arteriosclerosis of the aorta, which is also very common in all syphilitic affections, both in distribution and in the coat affected. Syphilitic aortitis forms

puckered, often fleshy, patches bearing no relation to emergent vessels, usually transverse, and as with the cerebral vessels the disease first attacks the middle and outer coats, and the intimal changes are compensatory. In arteriosclerosis, on the other hand, the patches usually form around the orifices of the branches of the aorta, and the change begins in the inner coat, and calcareous deposits are common. The two conditions are sometimes combined. Heubner held that syphilitic endarteritis never ended in atheroma, but Mott and other authorities consider this statement too sweeping. (4)

This atheroma and nodular fibrosis of the aorta was present in several of the General Paralytics, including 6 of the 8 on whom autopsies were performed; apart from this, this series of cases showed typical skin lesions in 5 of the 12 Syphilitics not General Paralytics, while in 32 cases of that disease no skin lesions were present, but 2 showed evidence of systemic affection. Thus, No. 79 had mitral disease, and was blind in right eye from very advanced retino-choroiditis, and had the same condition, though less marked, in the left eye. No. 123 had leukoplakia.

It may be stated here that none of the 8 autopsies on General Paralytics showed any prominent lesions of the viscera, e.g. liver, spleen, etc.

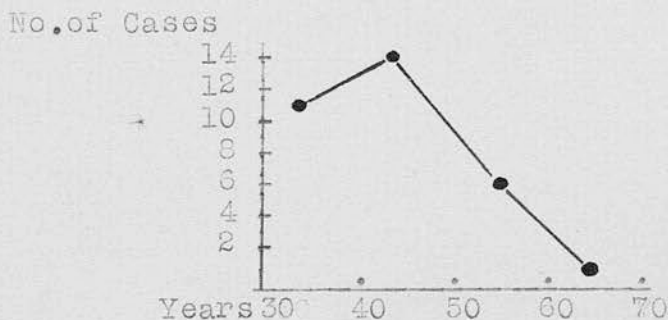
(1) F.W.Mott: "Neurotoxic Variety of Spirochaeta Pallida". B.M.J. 4th Jan. 1908.

(2) Förster & Tomaszewski: "Untersuchungen des Paralytikergerhirns". Deutsche med. Wochenschr., April 2nd. 1914.

- (3) Warthin, A.S: Amer. Journ. Med. Science, 1916,
CLII.
- (4) Power & Murphy: loc.cit. p. 49.

(5) The Results of the Examination of the Age and Civil State in Syphilitics.

In General Paresis the ages varied from 31 to 65, the most usual age being from 30 to 50, as shown in the accompanying chart. These ages agree with those usually met with in this disease. (1) Dr. Herschmann of Vienna has recently made an interesting study of 84 cases of General Paresis which developed after the age of 60. In these old people he found the disease usually ran a slower course than in younger patients, and that the time since infection was usually above the average. (2)



25 General Paralytics were married, and 7 single. 8 of the other Syphilitics were married, and 4 single.

In the 3 cases of Cerebral Syphilis, the ages were 26, 50, and 67, and the disease developed 1, 26, and 40 years after infection respectively.

(1) Power & Murphy: loc. cit. p. 236.

(2) Dr. Heinrich Herschmann: Medizinische Klinik,

(6) The Results of Examination into the Duration of Illness, and Time since Infection, in Syphilitic Cases.

44.

The length of time since infection could not be accurately ascertained in the majority of cases. In no less than 11 of the cases of General Paralysis was venereal disease denied, showing how utterly unreliable is the history of infection in such cases. As none of these men could be considered to be denying infection from ulterior motives, this suggests that the original symptoms were mild. In 1 case the patient was too demented to give any reliable history. In those General Paretics who gave a history of infection, the time varied from 8 to 33 years, the majority being from 10 to 20 years. This late development of General Paresis and Tabes is of diagnostic importance, as the majority of other syphilitic diseases of the Central Nervous System appear in less than 6 years after affection, usually in 2 to 3 years. (1) Cases are not even infrequent during the primary and early secondary stages, and fluid examination shows that it is frequently affected at this stage in the absence of symptoms. That the spirochaete itself is present in the fluid in these cases has been shown by inoculation experiments with rabbits. This is in accord with view that syphilis is a general organismal infection, with migration of the parasites to the perivascular lymphatics of the skin, mucous membranes, viscera, and meninges. (2)

In the Non-nervous Syphilitics the time varied from 5 to 24 years, but in No.124, age 75, who denied infection, the time was probably much longer.

The duration of the disease before admission in General Paresis is a very difficult point to decide with any accuracy. The only evidence is that given by the patients' friends, and this is often most unsatisfactory. Thus, it is not uncommon for a wife to say that she sees no change in her husband, even when he is showing quite a marked degree of dementia. The times given vary from 1 month to 5 years, the latter being a Taboparalytic.

8 cases have already died, and including this period before admission, the disease had lasted 3, 5, 6, 8, 13, 13, 13, and 15 months. Apart from seizures, and intercurrent diseases, the duration of General Paralysis is usually from 1 to 5 years, depending to a large extent on the type of the disease, the demented cases tending to be more prolonged than the others. Some cases last very much longer, especially if remissions are got, and Prof. G.W. Robertson records the case of a patient who lived for 30 years after the first appearance of the disease. These 8 fatal cases were acute, and as is usual in such cases, the cerebrospinal fluid changes were marked. 5 died in seizures, including 1 from rupture of aneurism on the Circle of Willis, 2 from hypostatic pneumonia, and 1 from gangrene of the lung. 6 of them had had seizures, before or after admission, or both. These seizures were of the severe form. It is in the earlier

stages of the disease that incomplete seizures are usually met with. Different authorities give the incidence of seizures at figures varying from 30% to 90%. Kraepelin found 30% to 40% of his cases had one or more seizures during their illness, and he points out that these are rarely due to haemorrhage or thrombosis, and that usually only microscopical changes are produced in the cortex to account for them, this being the reason of the usual rapid recovery. In the above cases, the patient whose death is recorded as from haemorrhage was the only one in which any naked-eye changes could be found to account for the fatal seizures. None of them showed Pachymeningitis Haemorrhagica. Mott points out that this is an infrequent condition to find at these autopsies. ⁽³⁾ Personally, I have only encountered it once in the course of over 50 post-mortem examinations on General Paralytics.

(1) Power & Murphy: loc. cit. p.13.

(2) " " " " " p.36.

(3) " " " " " p.277.

It is suggested by some authorities that Dementia Praecox is due to Syphilis in the parents, and in support of this contention statistics are produced to show how frequently the stigmata of Congenital Syphilis is present in Schizophrenic patients. Thus, Klutscheff found 41.6% of 60 cases of Dementia Praecox had signs of hereditary Syphilis. Pilez reports Tabes in 5% of the parents of 416 Praecox cases, as against .6% in Manic-Depressive Insanity. Further figures of his, quoted by Kraepelin, are that 44 Hebephrenics had General Paresis in parents 23 times, and 27 Catatonics 5 times. He also states that the brothers and sisters of these Schizophrenics are often Juvenile Paralytics. (1)

Koenig thought that Dementia Praecox was commoner in the offspring of Syphilitics. (2)

Stinnes and Poltzl think acquired syphilis may bring disease to an outbreak. This was not so in any of the 13 cases in this series. (3)

Kraepelin disagrees with above theories. He only found Syphilis in 4% - 5% of the parents of his Praecox cases. This, of course, is not above what one would get in a similar investigation of unselected members of the community. He also failed to find that General Paralytics beget Schizophrenics. He suggest that if Syphilis has any influence at all,

it must be by injury to the germ cells, as with chronic alcoholism .

48.

In none of the 13 cases under consideration was a history of Syphilis in the parents obtained, but this cannot be regarded as reliable.

Teeth, tibiae, face, eyes including ophthalmoscopic examination, ears, and testicles were examined in all cases, and no evidence of Congenital Syphilis found. In all 13 the serum Wassermann reaction was negative, and in the 12 fluids examined it was also negative. Slight changes were found in 2 of these fluids, but nothing to suggest that these changes might be in any way due to Syphilis.

Twenty successive cases of Dementia Praecox were similarly examined by Drs Harper, Smith, and Rae Gibson at Claybury Laboratory, and in every instance the result was negative.

McDonagh states that in Congenital Syphilis, if the Wassermann in the serum is positive during the first three months of life, even if the child is left untreated, the reaction tends to become negative about the age of puberty. A negative reaction in the serum of these cases could not therefore be taken as proof that Congenital Syphilis was absent, but as Dementia Praecox is a disease with active changes in the brain, it is difficult to imagine, that even in a small series like the present, both clinical examination, and examination of serum and fluid should give absolutely negative results if the disease were due to Congenital Syphilis.

- (1) Kraepelin: Dementia Praecox, English Trans., by R.M.Barclay, 1919, p.235.
- (2) Koenig: "The Problem of Heredity from the Psychiatrical Aspect". B.M.J. 1904, Vol.11, p.966.
- (3) Kraepelin: loc. cit. p.241.
- (4) Power & Murphy: loc. cit. p.308.
- (5) McDonagh: "The Wassermann Reaction in Congenital Syphilis". The Lancet, 8th Oct.1921, p.768.

Kraepelin found Syphilis in 8% of his male patients with Manic-Depressive Insanity. Zeiken has described cases of periodic or circular psychoses which he traces back to acquired or Congenital Syphilis, but Kraepelin holds that these are either Manic-Depressives with concomitant syphilis, or syphilitic psychoses with circular forms, and not cases of Manic-Depressive Insanity due to Syphilis. (I)

In 2 of the 36 cases on M.D. Insanity in this series a positive Wassermann reaction was got in serum, i.e. 5.6%. In neither case could the Syphilis be regarded as a psychic trauma, for neither was aware that he had it. Enough however does not seem to be known of the causes of Manic-Depressive Insanity to say that Syphilis cannot be an exciting cause.. Thus, No. 80 contracted the disease 5 years ago, and his first attack of mania took place 2 years later. That he recovered from this without treatment for his Syphilis is against Syphilis being the cause of his mania. As his Cerebrospinal Fluid is quite normal Cerebral Syphilis is eliminated. Both cases presented mental pictures much resembling General Paralysis, and their serum reactions tended to support this suspicion. They show the importance of fluid examination in such cases. Only 2 other Manic-Depressives had their fluids examined, and these were quite normal. Both these had many points of similarity to General Paresis.

No22 was a case of Chronic Mania, with expansive egocentric delusions, marked tremors of hands and tongue, increased knee jerks, and pigmented scars on shins. His pupils were normal, and his serum negative. No.142 was euphoric, with delusions of grandeur, and no autocritical sense, irregular pupils which reacted normally, tremor of his tongue with normal articulation, knee jerks much diminished, and systolic aortic bruit. His serum was twice negative, and his fluid was normal. Both denied Syphilis.

(I) Kraepelin: Manic-Depressive Insanity and Paranoia. Eng. Trans. by R.M. Barclay, 1921.



(I) Cerebral Syphilis - 3 Cases.

Syphilitic Meningitis in Secondary Syphilis.

Case No.1. J.B. Age 26 years. Single. Admitted 26-4-21. He had contracted Syphilis twelve months previously, and stated that he had had six intravenous injections of Salvarsan, and three intramuscular injections of Mercury, after which his serum was tested and found to be negative. He was advised to take mercury pills for two years, ~~but years~~, but did not do so. These statements were verified later. The treatment was given at the Venereal Clinic, Soho Square, London. On admission six months later his serum was positive 8, and his Cerebrospinal Fluid showed 45 cells per c.mm., and the Lange Gold Test showed changes in tubes 2 to 8, none showing complete decolourisation. There was only slight excess of protein, and his Wassermann was negative. His general health was fair, heart, kidneys, and lungs showing nothing abnormal. His knee jerks were exaggerated; Pupils slightly dilated, but otherwise normal. No tremor of his tongue, and his articulation was normal. Fundi normal, and sight unaffected. He was depressed, and gave voice to suicidal tendencies, though he made no effort to carry these out. There was no evidence or history of vertigo, fainting, vomiting, fever, or convulsive attacks. He was lethargic, and there was

considerable psychomotor retardation apart from his outbursts. He complained of more or less constant headache, and had impulsive outbursts of violence, when he would strike anyone in his neighbourhood, and shout at the pitch of his voice. Afterwards he only had a very vague idea of what had happened, and could recall no details of his conduct. These attacks bore a strong resemblance to attacks of petit mal. He had delusions of sin, and thought he heard God tell him how displeased He was with him. Hallucinations and delusions are uncommon in these cases, and insight is usually better than it was in this case. This latter fact made him object very strongly to treatment. His orientation was somewhat deficient. He was difficult with his food, and had to be hand fed at first.

He was given twelve bi-weekly intramuscular injections of .3 grms N.A.B. in glucose and guaiacol, as suggested by T. Anwyl-Davies, and made up by May & Baker. He also had daily inunctions with Ung. Hydrarg. Mit: He had three such courses with short intensive courses of Potassium Iodide for a fortnight after each course, as advised by Col. Harrison. His serum and C.S.F. were normal after the first course and have remained so since.

He gradually improved mentally, his headache and depression being the first things to go. He continued to have occasional impulsive outbursts for a month, though at less frequent intervals. He still was rather childish in his talk, and lacking in judgment and reasoning power, but these were doubtless

due to mental deficiency, as his previous history suggested that he was distinctly backward mentally, and his relatives considered that he had returned to his normal self. His impulsive outbursts and his depression have quite disappeared.

As the work of C.H.Mills at Rochester Row,
(3)
and of Dreyfus show, meningeal mischief is very common in secondary Syphilis of from six months to five years standing, and in the majority of cases no clinical symptoms are present, if headache is excepted. Fildes found involvement of Central Nervous System in
(4)
11% of late primary cases. Mills got changes in Cerebrospinal Fluid in 47% of his secondary, and 32% of his tertiary, Dreyfus figure for secondary Syphilis is 80%, and Gernnerich's for relapse cases is 90%. The changes are usually most marked at the base of the brain around the interpeduncular space, and focal symptoms though absent in this case, are the rule rather than the exception in cases with symptoms. These may be due to local pressure on brain, deprivation of blood supply, or affection of the neighbouring cranial nerves.

Regarding the Wassermann reaction in Cerebrospinal Syphilis different workers in the past have recorded very different results. With the original Wassermann technique a positive result was rare, and it was considered very doubtful if this could ever be got rid of if once present. Thus Plaut only got a
(5)
positive result in 6% of his cases. More delicate technique, and larger quantities of fluid have given

a much higher percentage. McIntosh and Fildes condemn the use of more than .2 c.m. of fluid, and say that non-specific results are got with the larger quantities. Too little is yet known of the rationale of the Wassermann test to decide this point. At present it is always the last pathological sign to disappear, the order of going being endothelial cells, lymphocytes, protein, and lastly, if ever, the Wassermann.

- (1) E.W.Harrison: "The Diagnosis & Treatment of Venereal Diseases in General Practice".
- (2) T.Anwyl Davies: The Lancet, Nov.23rd, 1918.
- (3) K.Altmann & G.Dreyfus: "Salvarsan und Liquor Cerebrospinalis bei Frùshyphilis, nebst ergänzenden Liquoruntersuchungen in der Latenzzeit," München. Med.Wohnschr., 1913, 60, 464, 531.
- (4) P. Fildes, R.J.S. Parnell, & H.B.Maitland; "Unsuspected Involvement of the Central Nervous System in Syphilis". Med. Res.Council, Spec. Rept. Series, No.45. 1920.
- (5) Felix Plaut; Die Wassermannsche Serodiagnostik der Syphilis in ihrer Anwendung auf die Psychiatrie. 1909.
- (6) I.C.Walker & D.A.Halles; "Treatment of Syphilis of Central Nervous System". Arch. Int. Med. 1916. XVIII. p.376.

Case No. 52. A. L. Age 67. Widower. Admitted 4 - 7 - 21. On admittance his mental state was one of depression, with somatopsychic delusions. He had little or no insight. He showed subjective certainty, with only slight anxiety, being a case of Melancholia Vera (Farrar). He complained of headache which was not definitely localised, and which he said was worse at night, but this information he did not give voluntarily. He had mild attacks of giddiness on assuming the erect posture. He slept fairly well, but gave a history of insomnia for six months prior to admission. There was marked psychomotor retardation. He was completely oriented, and his memory was fair, especially for past events. No history of seizures. He gave a history of Syphilis contracted 40 years previously. He had clinical and physical signs of aortitis with marked accentuation of the 2nd sound in the vessels of the neck. His knee jerks were exaggerated; his pupils reacted to light and accommodation, and the sympathetic reflex was present; the right was dilated. There were Syphilitic scars on both legs. He had tremor of the tongue, and his articulation was indistinct. No speech defects. His serum gave a positive Wassermann reaction of 40 plus. His Cerebrospinal Fluid showed 6 cells per cub.mm., a negative Wassermann, and a slight increase of protein. The Lange Test gave a mid-zone reaction in the 4th to 8th tubes inclusive.

This case showed the importance of multiple

The case was diagnosed as one of Syphilitic Endarteritis of the cerebralvessels, but this may only be one of several causal factors of his Psychosis.

Salvarsan medication was not considered advisable, and the patient was put on iodides and mercury.

On 24-1-22 his serum and fluid were reexamined and found to be unchanged from condition on admission. There was very little change in his mental condition.

This case, like case No.14, supports the theory that endarteritis can be got without meningeal change existing as shown by Cerebrospinal Fluid changes.
(I)

The disease most probably originates in the vaso-vasorum, and the subsequent thickening of the coats of the artery may be looked upon as compensatory.
(2)
Heubner thought the condition originated by an overgrowth of the endothelium due to irritation from the syphilitic virus, and that this extended to the vaso-vasorum in the media.
(3)

So far this patient has shown no focal symptoms, but these are often very late developments in these cases, though they may appear quite early.
(4)
As Mott points out, there may be very extensive endarteritis obliterans without focal symptoms as long as thrombosis does not occur. In these cases general symptoms due to cerebral anaemia may be got owing to narrowing of lumen of vessels, and interference with

normal vasomotor control, whether by effect on muscular coat, or vasomotor nerves. This may account for this patient's mental enfeeblement. 58.

According to Gowers, about a quarter of the cases of endarteritis with clinical symptoms occur within the first two years following infection. It is much commoner however for Cerebral Syphilis to occur a long time after infection than for Tabes or General Paresis to occur early. (5)

(1) Boyd: "The Cerebrospinal Fluid". p.113.

Harrison: loc. cit. p.159.

(2) Power & Murphy: loc. cit. p.46.

(3) Heubner: Die leutische Erkrankung der Hirnarterien.
1874.

(4) Harrison: loc. cit. p.159.

(5) Gowers: "Syphilis of the Nervous System". Letts-
omian Lectures, 1890.

(6) Power & Murphy: loc. cit. p.296.

Syphilitic Cerebral Arteritis.

Case No.14. W.K. Age 50. Married. Admitted

59.

23-5-21. On admission he presented a picture of Confusional Insanity. He gave a history of Syphilis 26 years previously. He had a double aortic murmur, his apex beat was outside the nipple line in the 6th interspace. There was slight albuminuria, and some tube casts were found. His knee jerks were normal, as were also his pupils. He had tremor of the tongue, with an indistinct, rather thick, articulation. He had scars on his legs below the knee. He had always been extremely moderate in the use of alcohol. His serum gave a positive 40⁺ Wassermann reaction, but his Cerebrospinal Fluid was normal, with 3 cells per c.mm., and no excess of protein detected by Pandy's Test. A Lange Test was not done.

Salvarsan therapy was considered to be contraindicated on account of the condition of his heart and kidneys, and only Potassium Iodide and Mercury were given. His confusional attack cleared up in 10 to 12 weeks, leaving a slight amount of dementia. He suddenly became unconscious of 4-11-21, and died an hour later. At the autopsy, death was found to be due to haemorrhage from a ruptured aneurism on the Circle of Willis. There were several aneurismal dilatations of the Basilar Artery, and of the vessels of the Circle of Willis. The Cerebral arteries showed advanced disease, with greyish yellow nodules on the larger vessels, and a uniform thickening of the smaller vessels. The condition is an obliterating endarteritis, the thickening of the arterial wall being due to a

cell hyperplasia in the non-vascular layer, between the lining endothelium of the vessel and the fenestrated membrane. The walls of the veins are also infiltrated with lymphocytes. Microscopical confirmation was obtained that arterial changes were of above nature, and not due to arteriosclerosis, of which Syphilis is such an important causal agent. The tissues were hardened in 5% formol in saline for 48 hours, sections cut, and stained with Van Geison's Stain. No areas of softening, recent or otherwise, were found. The brain showed none of the changes characteristic of General Paralysis, the most constant of which is probably "frosting" of the ependyma of the 4th ventricle. Mott states that he has very seldom found it absent. He had a *Cor Bovinum* weighing 680 ounces, with diseased incompetent aortic valves. The Ascending Aorta was fleshy, much dilated, with several calcareous patches on it and on the arch of the aorta. The kidneys showed the changes of chronic interstitial nephritis. The serum taken p.m. gave a positive 40+ reaction. This of course was to be expected, as these long standing positive reactions are notoriously difficult to get rid of.

Aneurismal formation in these cases, Mott says, is due to an intense inflammation weakening the middle coat rapidly, with formation of aneurism before proliferation of intimal connective tissue cells can fill up the bulge.

Unfortunately, a Lange Test was not done in this case. It would probably have given a mid-zone

reaction as in case No. 52. The absence of any discoverable change in the Cerebrospinal Fluid shows how advanced Syphilitic Cerebral Arteritis may be present without being detected by fluid examination.

It is possible that his confusional attack was due to thrombosis of one of the branches of his cerebral arteries, though evidence of this was not discovered at the autopsy. The vessel may have become patent again, or anastomosis may have prevented softening.

- (1) Power & Murphy: loc. cit. p.45.
- (2) Idem. p.281.

Case No. 12. H. M. Age 53. Married.

Admitted 22-5-21.

On January 8th 1919 he had what he describes as a fainting attack, while boarding a tramcar. He was taken to St George's Hospital where he was admitted under the care of Dr Golla. He states that he had been quite well up to this time. Tabes Dorsalis was diagnosed on the clinical symptoms, though his serum and fluid gave negative Wassermann reactions. He was given three intrathecal injections of mercurialised serum, and two intravenous injections of Salvarsan, .45 grm. and .75 grm. respectively. He was discharged on 28th January, with his clinical symptoms still present.

On admission, his ankle and knee jerks were absent, his pupils reacted sluggishly to light, he had well marked rhombergism and tabetic gait, tremors of tongue, and of muscles around mouth. His leg muscles were hypotonic. His articulation was slurring, and typical of a General Paralytic. He said his sight had been failing for about two years, but not to any serious degree, and he put it down to his glasses not being strong enough. Examination of his fundi revealed slight optic atrophy. Mott has pointed out how frequently the onset of optic atrophy in a tabetic is the precursor of general paresis. He states that no less than 50% of Tabo-paralytics have optic atrophy. He often^{found} a history of mental stress in these cases,

which he thought might account for the disease passing to the cerebral tissues. (I) This patient had been much upset by the loss of his son, aged 18, who had been killed while flying in France in 1918. He was euphoric, and indignant at being sent to a hospital, saying he was quite fit, and should be home looking after his wife and children. He had no definite hallucinations or delusions at first, but there was some dementia, and his autocritical faculty was much enfeebled. He denied Syphilis, but he had been a sailor before he married 20 years previously, and no doubt contracted the disease during that period of his life. There was no history of lightning pains, ocular paralysis, or any visceral disturbances. No sensory abnormalities could be elicited, apart from loss of pain sense in his hypotonic calf muscles. This part of the examination was unsatisfactory however, as is so frequent in mental cases. His serum and fluid Wassermann reactions were negative. On this, and on future occasions, his fluid came out under greatly reduced pressure. He was given a provocative dose of .15 grms. Novarsenobillon, and his serum and fluid again examined. His serum now showed retardation of haemolysis in all dilutions, a weak positive reaction. His fluid Wassermann was again negative; it contained 14 cells per cub. mm., and the protein was much increased. His Lange gave a modified paretic curve.

On 15-11-21 he had four seizures with temporary paresis of his left arm, which lasted 24 hours. He recovered from this with only a slight

increase in his fatuousness, but he was more tottery on his feet. Mott got seizures in 64% of 60 Tabo-paralyt⁽²⁾ics. He also noted that patients with optic atrophy often had visual hallucinations. This patient used to see his dead son come down from heaven at night, and he used to claim various patients as this son.

On 1-2-21 his Cerebrospinal Fluid was again examined, but no changes were found corresponding with his increasing dementia. By this time his dementia and fatuous euphoria were much increased. His left knee jerk could now be faintly elicited by Jendrassik's method of reinforcement, and his ataxic gait was becoming shuffling, and his rhombergism less. He had become much fatter. His optic atrophy had increased, and his field of peripheral vision, as far as one could ascertain, was much diminished.

The absence of irritative phenomena in this Tabetic may be correlated with the mild pleocytosis in his Cerebrospinal Fluid, in suggesting that any meningeal changes present are slight. These are much less constant in Tabes than in General Paresis. While latter is a chronic meningo-encephalitis, there may be no meningitis in Tabes, the infection passing up perivascular lymph spaces and lymph spaces of nerves to the posterior spinal protoneurons. It is doubtful if the spirochaetes themselves need be present in the nervous tissue in Tabes as in General Paresis. The experiments of Orr and Rows show, that toxins generated outside

the vertebral canal can pass up the nerves, and cause 65.
degeneration of the posterior columns only. These
(3)
differences between Tabes and General Paresis may
account for the different results of treatment by
Salvarsan etc. in the two diseases.

Different workers place the percentage
of positive Wassermann reactions in the serum at 60
to 76 for Tabes, and 96 to 99.5 for General Paralysis.
Tabo-parastics are intermediate. Untreated Tabes gives
a much higher percentage, Boas even putting it as
high as 100%.
(4)
More delicate technique is raising
the percentage of positive results.

The incidence of positive Wassermann re-
actions in the Cerebrospinal Fluid in Tabes is usu-
ally put at 50 to 70%, but McIntosh and Fildes in a
small series, and using only .2 cc., got positive re-
sults in 92%. With larger quantities Boyd got a pos-
itive reaction in 90% on untreated cases. It is in
(5)
very chronic cases that most negative results are got.
In General Paresis Wassermann and Plaut got 95% posi-
tive reactions in the fluid, while Browning found it
in 96%.

(1) Power & Murphy: loc. cit. p.326.

(2) Idem. p.377. and 278.

(3) Orr & Rows: "Lesions of Spinal Cord, the Result
of Absorption from Localised Septic
Foci". Review of Neurology & Psych-
iatry, Jan. 1906.

- (4) Boas: Die Wassermann'sche Reaktion. Berlin, 1911.
- (5) Boyd: "The Cerebrospinal Fluid". New York, 1920,
p.77.

Harrison: loc. cit. p.266.

McIntosh & Fildes: Brain, 1914, 37, 141.

H. Carlill: loc. cit.

Case No. 127. C. C. Aged 41. Married. Admitted 4-11-21.

He was admitted in a state of acute confusion, and the question arose as to whether he was a case of Tabes with concurrent psychosis, or of Taboparesis. His serum Wassermann was positive 40 + , his fluid Wassermann positive 8, and it contained 14 cells per cub. mm., slight protein increase, and gave modified paretic gold curve. His mild euphoria, poor autocritical sense, and distinct dementia left little doubt that it was a case of Taboparesis.

His tabetic symptoms also improved with his mental condition; his ataxia, which had been most extreme, became much less, so that from being unable to stand alone, he could walk about the ward with a fair degree of comfort. His rhombergism was still very marked, and his base very wide. The anaesthesia of his body, which had been almost complete, excluding face, (4th Cervical downwards) up to a month after admission, gradually improved, but remained complete in right leg below knee, (4th Lumbar to 1st Sacral) and on ulnar aspects of both arms (8th Cervical to 1st Dorsal) . His knee jerks were quite absent, and he had no sense of position in knees, ankles, or toes. His pupils were sluggish to light, but otherwise quite normal. He had tremors of hands, facial muscles, specially round mouth, and tongue; and his articulation showed slight, but distinct, slurring. These physical signs are not changed.

He had no optic atrophy.

68.

Confusional attacks with return to more or less normal intelligence are not uncommon in Syphilitic Meningitis. (I) That his attack was not due to this is suggested by the low cell count in his cerebro-spinal fluid.

(I) Power & Murphy: loc. cit. p.63.

Case No. 72. E. P. W. Aged 54. Married.
Admitted 10-8-21.

This case shows the result of failing to treat Cerebral Syphilis in its early stages. The patient contracted Syphilis 11 years ago, and 2 years later had a Syphilitic right hemiplegia with aphasia, which cleared up after a month in bed. He was unconscious for a few hours. No specific treatment appears to have been given. Seven years later, i.e. two years ago, he had a similar attack which did not clear up. Again no specific treatment was given, and on admission the case had passed from an eminently curable form of disease into General Paresis. His right arm and leg were very spastic; his left side less so. He was quite unable to walk owing to his marked spasticity, and his general tremulousness. His knee jerks were very exaggerated, especially the right, but no Babinski could be elicited. His eyesight was poor, and he had optic atrophy. He had typical trombone tremor of the tongue, and his articulation was so slurring as to render him almost incoherent. His articulatory defect had to be diagnosed from the pseudo-bulbar paralysis and dysarthria of bulbar softening due to arteritis. He was very demented, and his wife said that he had had delusions of grandeur; these could not now be elicited. She had noticed the mental change three months prior to admission. "He had been violent two or three times a

week, and had threatened to kill her and the children. He seemed to be wandering for half an hour, then would come to himself, and say he had been dreaming." He was wet and dirty in his habits, restless and noisy, especially at night.

His serum Wassermann was positive 40+ ; his fluid gave Wassermann reaction positive 40+ , cells 62 per c.mm., protein much increased, and parietic curve with Lange Test. Branches of both his Mid-cerebral Arteries are presumably thrombosed , especially the left. He has no valvular disease, nor nephritis.

Treatment with Novarsenobillon, Iodides, and Mercury had very little effect on his physical condition, and none on his mental. Mott states that in his experience it is rare for Cerebral Syphilis to be followed by General Paresis. Here however, not only the clinical, but also the serological findings point to the diagnosis. Microscopic examination of his brain will clear up this point. In either case the prognosis is equally grave, for even if the case is one of pseudo-General Paresis, there is a generalised syphilitic infection of his cerebral vessels, and the substance of his brain, as well as his membranes, so that he is permanently affected in body and mind. It means a widespread destruction of nervous matter, with secondary degeneration, and liability to further destruction by thrombotic softening or encephalitis, conditions which cause irreparable damage. If the post-mortem shows this case

to be one of pseudo-paresis it would be of interest in connection with his paretic Lange reaction.

Prior to the discovery by Noguchi in 1913 of spirochaetes in the brains of those dying of General Paralysis,⁽²⁾ Mott held that this disease was a primary parenchymatous encephalitis, and that the vascular and glia changes were secondary to the nerve-cell degeneration. In the same way Tabes was supposed to be a primary degeneration of the sensory spinal protoneurons, and the vascular and meningitic conditions described merely concomitant and quite inconstant. These views were shared by most authorities, but many notable names were associated with the view that the changes in the nervous elements in the two diseases were secondary to interstitial changes. The lymphocytosis got in Tabes was held by some to be proof that a meningitis was always present as the causal factor.

Since the above-mentioned discovery however, the parasymphilitic theory of Fournier has been rendered untenable, and Mott describes them as parenchymatous syphilitic affections, the acute manifestations being due to the active development of the spirochaetes which had been lying latent, probably in a granular form,⁽³⁾ while the paralytic and demential phenomena are due to the destruction of nerve cells and fibres following the meningo-encephalitis and meningo-myelitis induced by the spirochaetal toxins.

It was formerly held that only 3 to 4% of people infected with Syphilis developed General Paralysis or Tabes, but the investigation by Mattauschek and

Pilcz into the cases of over 4000 Austrian officers, who contracted Syphilis between 1880 and 1900, and were well treated for same, showed that 7.5% of these men were dead by 1913 of General Paralysis or Tabes, while over 2% had died of Cerebrospinal Syphilis.

- (1) Power & Murphy: loc. cit. p.299.
- (2) Noguchi & Moore: "A Demonstration of Spirochaete Pallida in the Brain in cases of General Paralysis." Journs. of Exper. Medicine. Feb.1913.
- (3) O'Farrel & Balfour: "Granule Shedding in Treponema Pallidum and associated Spirochaeta". Journal of the R.A.M.C. Sept.1911.
- (4) Mattauschek & Pilcz: "Ueber die weiteren Schicksale 4134 Katamnestisch verfolgter Fälle luetischer Infektion". Med. Klinik, Sept.21, 1913.

Case No. 99. D. G. Aged 49. Single.
Admitted 15-8121.

In this case there were comparatively mild changes in the Cerebrospinal Fluid. The Wassermann reaction was only positive 8, there were 24 cells per c.mm., and only a slight increase of protein. The Lange, however, gave a typical paretic curve. His physical signs also were not very marked. His left knee jerk was normal, and his right slightly exaggerated, his pupils were dilated and of irregular outline, but reacted well to light and accommodation. There was no tremor of his tongue, and his articulation was normal. He had aortitis. He gave a history of Syphilis contracted 20 years ago, and on examination his serum was positive 40⁺. He was depressed on admission, and had paranoid delusions of persecution. He gradually improved, and two months after admission appeared normal mentally, apart from a certain lack of judgment and reasoning power. That his remission was not connected with any parallel change in his Cerebrospinal Fluid was shown by a further examination on 24-1-22., when it showed exactly the same changes as on admission except that his cells were now 32 per c.mm. instead 24.

Marie and Levaditi state that there is a parallelism between the rapidity of progress of General Paresis and the degree of intensity of the Wassermann reaction, suggesting connection between the

breaking down of nervous substances and the amount of the complex colloidal substance which determines the reaction. (1) The length of time since infection, and the mild nature of the disease agree with above in suggesting that apart from intercurrent disease this case will run a comparatively protracted course. The majority of workers however, do not agree with this theory of Levaditi's.

In General Paralysis the psychic phenomena and convulsive seizures would appear to be due to the pullulation of the spirochaetes. This causes a reaction on the part of the whole cortex with the formation of antibodies antagonistic to the spirochaetes. If nature succeeds in this attempt at cure, the symptoms subside, and a remission is the result. As in this case however, some dementia is usually left, and not only that, but some of the spirochaetes are not killed, and being immune to the formed antibodies, proceed to multiply and form toxins, and when this has reached a certain intensity a relapse occurs. (2) This is in accordance with view of Ehrlich that each relapse is due to the multiplication of spirochaetes resistant to the antibodies already formed, and that these continue to multiply and form toxins until the tissues have formed an efficient antibody.

(1) Levaditi et Yamanouchi; "Seroneaction de la Syphilis et de la Paralysis General"; Societe de Biol. Comptes Rendus. IXIV No.8.p.349.

(2) Power & Murphy: loc. cit. p.502.

Case No. 149. E. G. P. Aged 42.
Married. Admitted 5.1.22.

This case shows the importance of not depending on the Wassermann reaction in the serum alone. He was a typical General Paralytic of the exalted type. He was duke of over a hundred different places, and his children were too numerous to be counted. His autocritical sense was nil.

Pupils irregular and unequal, but reacted to light and accommodation; knee jerks exaggerated and "floppy"; pharyngeal reflex absent; "trombone" tremor of tongue and slurring articulation with elision of syllables; handwriting showed parallel defects.

He denied Syphilis, and his serum reaction was negative. A provocative dose of Novarsenobillon was given, and his serum again examined. On this occasion there was a weak positive reaction shown by retardation of haemolysis in the top dilutions. (Herxheimers's Reaction). Lumbar puncture was done. His fluid came out under pressure, showed a Wassermann reaction of positive 8, marked protein increase, and 23 cells per c.mm. His Lange gave a typical parietic curve. There were no after-effects.

As already mentioned, Mott considers that in such cases any reaction got in the serum is due to escape of Wassermann bodies from the fluid into the general circulation. (c.f. Page 25.).

Case No. 115. G.F.J.S. Age 42.

Married. Admitted 5-10-21.

This case is of particular interest, for not only was he regarded as a General Paralytic by several alienists of wide experience, but he was boarded by the Ministry of Pensions, and gets a pension on the grounds that he is suffering from General Paralysis of the Insane, aggravated by military service. A preliminary examination of his Cerebrospinal Fluid would have prevented this injustice.

On admission he was very euphoric, and insisted on the fact that he had never felt better in his life, and that it was all a mistake putting him in a mental hospital. He was very talkative; very full of his own prowess, and in speech closely resembled the euphoric General Paralytic. He had no delusions however, unless his exaggerated opinions of his abilities could be regarded as such. He had marked slurring of his articulation, with tremor of the tongue. On protrusion, his tongue goes over to left side, though there is some wasting of right side, and he can put it over to right side when he tries. His right pupil is larger than the left, but they are regular, and react to light and accommodation. Knee jerks much exaggerated especially right, and he has patellar and ankle-clonus, and slight Babinski on right side, with fanning of toes. He has fine tremor of hands, and deep reflexes are exaggerated in both arms, though more marked on

right. There is slight paresis of right arm and leg, but no inco-ordination. Abdominal cremasteric reflexes could not be elicited. His facial paralysis is in lower part of face. Fundi normal. Eyesight good. No history of fits. Had very severe headache for six months after demobilisation, but never since.

His wife had three children, all healthy, aged 8 years, 2 years, and 8 months respectively. No miscarriages.

He denied Syphilis, but he had been a regular soldier, and his serum gave a Wassermann reaction of positive 40. It was on these facts and the history supplied by the wife that the aforesaid diagnosis of General Paralysis was made. His history however, was most significant. He had received a Gun Shot Wound of the head at the Hohenzollern Redoubt in July 1917. He has a horizontal operation scar 4 inches long on his left parietal, 2 inches above attachment of ear to skull, and a small scar over his left eyebrow. Indentation and rough ledge on left parietal, but no bone missing. After being wounded he was paralysed down right side, including face, and had complete loss of speech. He was sent to hospital at Havre, where a skiagram showed shrapnel, but he refused operation. After 3 months he was discharged to duty, though still mute, and paralysed down right side. He had no power in his right arm, and his right leg was spastic. Six months later he was persuaded to go into hospital at Marseilles, and have the shrapnel removed. This was done, and next day his speech returned, but he states

it was slurring, and rather difficult, as at present. There was probably a functional element in his mutism. His paralysis gradually improved till there was only slight weakness of arm and leg, but his face and tongue did not improve so much. He was in hospital six months, and was then sent to England and demobilised in July 1918. A year later the paralysis returned, and he was sent to Orpington Hospital, Kent. He was there five months, when he left of his own accord. His condition was then as at present. He then went back to his work as a fish hawker, but on information received from his wife he was taken to Greenwich Infirmary by the Relieving Officer, and there certified, his certificate saying he was suffering from General Paralysis of the Insane! His wife states that he had been drinking a good deal since he came home from France, and that he was excitable, and of violent temper towards her, that his talk and actions towards her were often immoral, even in front of the children. She could not keep him clean and tidy, and for the past three months he had got into the habit of following her about the house and streets, and she was frightened of him. He often said he would be better dead, and would go out for hours day and night. It might be said that the patient strenuously denied these accusations, and says his wife has made them to get rid of him, and keep his pension. A fact which makes it necessary to treat the wife's statements against the patient with caution, is that she committed bigamy during the war, and only came out of

Holloway last year, where she had served a three months sentence, the offence having been reported to the authorities by the patient. He took her back, the reason he gives being that he wanted her to look after his children. It may be stated that so far he has shown no signs of irritability, violence, or deficiency of moral sense.

Examination of his Cerebrospinal Fluid negatived the diagnosis of General Paralysis. The Wassermann was negative, cells 4 per c.mm., slight protein increase, and a completely negative Lange. His fluid came out under considerable pressure; there were no other signs of increased intracranial pressure, no headache or vomiting, and his fundi were normal, and his eyesight unaffected. There can be little doubt that this man's mental condition is entirely due to his Gun-shot Wound, which must have affected his left motor area, chiefly at its lower end in the region of the tongue fibres. His handwriting is tremulous, but it is not that of a General Paralytic. The mental picture of instability which he presents is not uncommon in such head injuries. Syphilitic endarteritis may be present attacking the ~~power~~ locus minoris resistentiae afforded by his wound. The severe headaches of 1918, and the apparent spread of organic disease to his left arm and leg points to Syphilitic disease, nor can the result of his Cerebrospinal Fluid examination altogether negative it. Carlill remarks on how frequently he found signs on the opposite side in syphilitic hemiplegia. On the

(1)

other hand a double lesion may have been present from the beginning, as was not uncommon in such head injuries during the late war. His military papers bearing on the subject have unfortunately been lost.

It may be stated that re-examination of his Cerebrospinal Fluid, with similar results to first examination was necessary to convince the aforesaid alienists.

(1) H. Carlill: loc. cit.

Korsakow's Psychosis with Syphilis.

Case No. 107. W. F. S. Aged 46.

Single. Admitted 28-9-21.

I have not seen Syphilis suggested as a cause of Korsakow's Psychosis, nor was it necessary to do so in this case as he gave a history of prolonged alcoholism. Dupré reports that he has known the disease caused by intensive mercurialisation of Syphilis. This patient could not be put in this category. He had been under treatment for Syphilis for three months, fifteen years previously at the Seaman's Hospital, Greenwich, and had taken no mercury since. His serum gave a positive 40⁺ Wassermann reaction.

Cestan described cases of polyneuritis in which Syphilis is the only assignable cause. These however, are cases which come on only a short time after the appearance of the chancre. (2)

His pupils were irregular, but reacted to light and accommodation. His knee jerks were exaggerated instead of being diminished as is more usual. He had tremor of the hands and tongue, and his articulation was thick. His calf muscles were tender, and the skin of the leg below the knee showed impaired sensation, not amounting to anaesthesia. He had lateral nystagmus of both eyes, but no scotomata. He had physical and clinical signs of aortitis and myocardial degeneration. His fundi were normal. On

admission he was completely disoriented for time, place, and identity of persons, and even after his confusion cleared up his orientation was poor. He had pseudo-reminiscences, and showed the typical fabrication of this disease. He was most suggestible. He retained his autocritical sense. On being asked he would tell of how many times he had been to London that week, with full details of how he had passed the time, though he had been in the Hospital for some months. His Cerebrospinal Fluid was normal, Wassermann negative, cells 3 per c.mm., no increase of protein, and no decoloration in any tube in the Lange Test.

- (1) Stoddart: "Mind and its Disorders". p.365.
- (2) Cestan: "La Polyneurite Syphilitique" Nouvelle Iconographie de la Salpêtrière. au XIII: Revue Neurologique 1900.p.810.

Alcoholic Dementia.

Case No. 61. W. T. Aged 56. Single.
Admitted 25-7-21. Coachman.

On admission this man presented a mental picture indistinguishable from that of the classical type of General Paralysis of the Insane. He was euphoric with delusions of grandeur, and wished to be discharged to marry his last employer, who was in love with him. His knee jerks were exaggerated, his pharyngeal reflex absent, his pupils contracted and sluggish, there was marked tremor of his tongue, and his articulation was defective. He had a chronic ulcer on his right shin, and gave a history of shooting pains in the thigh, and of difficulty of micturition, due as a matter of fact to urethral stricture. He stated that he had had venereal disease thirty years previously, and thought it was Syphilis. So typical did the disease appear that in spite of his age he was certified as a General Paralytic without waiting for blood and Cerebrospinal Fluid examination. These were examined twice, and on each occasion found to be quite normal, including Lange Test on the Cerebrospinal Fluid. He was an alcoholic, and his condition was no doubt due to this. Up to the present it shows no signs of clearing up, and the patient remains as childishly euphoric as on admission.

Case No. 109. J. L. Aged 45.
Married. Admitted 29-9-21.

This case presented the same difficulties as Case No. 14. He differed in being an alcoholic, and when his confusional attack cleared up he was found to have a considerable degree of dementia, chiefly affecting the cognitive aspect of his consciousness. He had a history of Syphilis twenty four years before admission. His serum Wassermann was positive 40⁺. His physical signs were not inconsistent with a diagnosis of General Paralysis. Thus, his knee jerks were much exaggerated, his pupils contracted, unequal and irregular, and reacted sluggishly to light and accommodation. He had pigmented scars below both knees, which he said were due to ulcers, dating from 1917. Heart sounds normal.

He had had a similar confusional attack in the army in 1917.

His Cerebrospinal Fluid was normal, giving a negative Wassermann reaction, and having 2 cells per c.mm., and no excess of protein. A Lange Test was not done in this case.

There seems little doubt, that next to Syphilis, alcohol is the most dangerous, as it is the most prevalent, poison of the nervous system, though it does not multiply in the body like Syphilis. It has a direct action on the nervous tissue, and an indirect action, by devitalising the

tissues and making them more susceptible to the attacks 85.
of other poisons, such as Syphilis and Tubercle.

(6) Manic-Depressive Insanity with Syphilis.

Case No. 100. E. J. Aged 42. Single.
Admitted 16-8-21.

It required examination of the Cerebro-spinal Fluid in this case to prove that his Central Nervous System was not affected by his Syphilis, and that he was a case of Manic-Depressive Insanity with Syphilis.

On admission he was euphoric, and showed the flight of ideas, increased psychomotor activity, and mental excitement, associated with manic states. He had a history of a previous attack of depression lasting two years. On the other hand, his serum Wassermann reaction was positive 40⁺, and he stated that he had had pains around his chest, and shooting pains in his legs. He had had gastric trouble, with severe vomiting, and difficulty with micturition. Examination of sensation suggested impairment of sensibility to light touch over abdomen. As in most mental cases subjective symptoms proved unreliable, for he had no objective signs of Tabes. Thus, his knee and ankle jerks were normal, and there was no hypotonus or incoordination; no marked tremor of his tongue, and no articulatory defects. The condition certainly pointed to mania, but one could not feel absolutely sure, till examination of his Cerebrospinal Fluid, showed it was quite normal, with negative Wassermann reaction, 3 cells per c.mm., protein not increased, and no decolorisation in any tube with Lange Goldsol Test. After

12 bi-weekly injections of .3 grms Novarsenobillon with Mercury inunctions, and a course of Potassium Iodide, his serum was again tested, It gave a positive 40†. It would appear doubtful if it is on any use treating cases of long standing, where the only sign of Syphilis is a positive Wassermann reaction.

Harrison thinks it is, but Mott suggests that if the Wassermann does not respond to three injections of a Salvarsan preparation, and there is no evidence of active mischief, then further treatment is useless.

(personal communication.) The weight of evidence seems to be against the view that a positive Wassermann reaction in the serum necessarily means living spirochaetes in the body. McDonagh is certain that
(I)
it does not.

(I) McDonagh: "The Rationale of the Wassermann Reaction". The Lancet, 24th Dec., 21.
p,1319.

Case No.10. D. F. Aged 37.

Single. Admitted 19-5-21.

This was the only case of Schizophrenia which suggested General Paresis. His pupils were unequal and sluggish to light; moderately dilated. He had tremor of his hands and tongue, and his articulation was slurring. He denied Syphilis. His mental state was certainly more suggestive of Schizophrenia than General Paresis, but his negativism might have been mistaken for the self-will of a Paretic, and his impulsive actions and stereotypies were not inconsistent with that disease. He however exhibited the fundamental disorders, described by Bleuler as characteristic of this disease.
(I)

His serum Wasserman was negative. His Cerebrospinal Fluid showed Wassermann reaction negative, 8 cells per c.mm., slight increase of protein, mid-zone Lange reaction, and increased rate of flow. He had no after-effects following lumbar puncture.

Meyer found the pupils dilated in 10% of Dementia Praecox cases, and suggests inhibition from cortex as a cause. Inequality and sluggish reaction to light were also noted fairly frequently. Irregular pupils with obliquely oval positions are very suggestive of Dementia Praecox.

Kraepelin found knee jerks exaggerated in 45% to 60%. He also found seizures in 16% of his cases, though these were rarely of the typical

paretic type, more commonly taking the form of fainting attacks, and attacks of vertigo. Fits, spasms in groups of muscles, and apoplectiform attacks with paralysis were also got. He also mentions that slurring articulation similar to that of General (2) Paralysis may be present.

(1) Bleuler: "The Theory of Schizophrenic Negativism"
Nervous and Mental Disease Monograph
Series. No.11.

(2) Kraepelin: Dementia Praecox , 1921.

Case No. 34. R. H. Aged 26.

Single. Admitted 14-6-21.

He spent fifteen months at Mabang in Sierra Leone, where he had several attacks of malaria. There are several rivers and small streams in this neighborhood. Three months after leaving Mabang he had an attack of fever with urticaria of legs and trunk, and went into hospital in Freetown on the coast, and here he says Trypanosomes were found in his blood, but no treatment was given. This was in 1918. They told him that he was the first white man in 12 years to get the disease in that neighborhood. On arrival in this country in Feb. 1919, he went to the West India Dock Hospital for two months, where the parasite was again found in his blood. He was given intramuscular injections of Soamin (Sodium para-aminophenyl arsenoxide) 1 grain every second day, and this treatment he continued for two years, except for the time he spent in hospital. He injected himself. He was in New York in 1919, and was admitted to hospital, where he was found to be suffering from Syphilis. He was given 5 intravenous injections of Salvarsan, and 1 intramuscular injection of Mercury. His serum then gave a negative Wassermann reaction, and continued to do so at subsequent four monthly periods up to time of his admission, when the only evidence of the disease was a scar on the dorsum of the glans penis. Some observers have reported positive Wassermann reactions in

the serum in Trypanosomiasis, but patient says he had a chancre at this time. Considering that he was taking Soamin regularly this is rather remarkable. In this same hospital in New York, Trypanosomes were recovered from his cervical glands. He first noticed his glands swollen in his neck and groins whilst in England at the beginning of 1919.

He returned to England in 1920, made another voyage, and on his return in Jan. 1921, he went to the Hospital for Tropical Diseases, Euston Road, London. The parasites were again found in his blood, and he was given antimony. While attending here, the organism was found in his Cerebrospinal Fluid, and shortly afterwards he was certified, and sent to Cane Hill Mental Hospital.

On admission he was anaemic, but fairly well nourished; heart, kidneys, and lungs appeared healthy, spleen was palpable, no doubt largely due to previous malaria. His liver was not enlarged, no glands were palpable, in neck, and only a few small shotty glands in groin. The clinical signs of involvement of his Central Nervous System were not very marked. He complained of more or less severe continual diffuse headache. He was rather childishly petulant, and if annoyed, had outbursts of obscenity. This latter habit ceased after six to eight weeks. His emotional reaction was increased, but his affective state on the whole was one of mild depression. He had very good insight, and was quite aware of the hopelessness of his condition. His lethargy was very

mild for first two or three months, but later became very marked. Even then he could always be roused from his drowsy stupor to answer questions intelligently, and to do any simple act that was requested of him. Even on admission however, he had a strong disinclination to exertion, and would not occupy himself apart from occasional light reading. His father had noticed his tendency to drowsiness four months prior to his admission, but of course this may have been due to his anaemia.

His serum and fluid Wassermann reactions were negative. There was excess of protein in his fluid, and the cells numbered 125 per c.mm. These cells were most characteristic; they were chiefly vacuolated endothelial cells, and there were several pathognomonic small cells with abundant deeply staining granules. These cells are described by Sir Frederick (1) Mott, and were demonstrated by him in this case. His Lange Goldsol reaction was most interesting, causing complete decolourisation in all 10 tubes.

No Trypanosomes were found in his blood or fluid, in spite of repeated examinations. His blood films showed the remarkable clumping of the red blood corpuscles described by Manson-Bahr. (2)

His face was nearly expressionless, and became more so as the disease advanced, with his emotional facility suggesting lenticular involvement.

He gradually developed a cerebellar gait, and shuffled about like an old man. The tremor of his tongue became worse, and his hands also became

tremulous. He became very emaciated, with a dry harsh skin.

His fundi were examined on 17th Jan. 1922, and "choked disc" found. His eyesight had been failing for a month, but he had not mentioned it to anyone, and as optic neuritis and atrophy are not usual in this disease, his fundi had not been previously examined. The condition may have been due to a plug of Trypanosomes. On this date his knee jerks were still slightly exaggerated, fine tremor of tongue was very marked, and comparatively slight in hands; on pointing to an object he pointed below and to left of it, but had no vertigo. His face was flushed, but not as wasted as rest of body; no enlarged glands. He was fairly reasonable and could be made to smile at a joke; he complained of occasional pains in his legs. He had had no local or general convulsions, and had retained control of his sphincters. It was now seven months since the organisms had been found in his Cerebrospinal Fluid. According to Low and Castellani the average duration of this stage is four to eight months, often less, and cases lasting over a year are rare. Cases lasting as long as three years have been reported, these sometimes showing remissions.

Ehrlich has pointed out that certain strains of Trypanosomes are "arsenic-fast". This would seem to apply to this case, considering the uselessness of his extensive Soamin medication, and it is most unfortunate that antimony was not administered.

along with it, as these "arsenic-fast" organisms may respond to antimony.

This disease presents many resemblances to General Paralysis. In both, the nervous lesions may be preceded for a long time by a systemic infection. In both, one of the chief features is a lymphocytic infiltration of the meninges, and the perivascular lymphatic sheaths. In both the Cerebrospinal Fluid shows a lymphocytosis. Mott points out that there is not the same neural degeneration in this disease, but rather a neural exhaustion, and I was much struck in this case with the preservation of memory and autocritical sense even in the advanced stages of the disease. This was quite unlike any advanced Paralytic. Polyadenitis is got in both. Unlike Syphilitic meningo-encephalitis there is no tendency to endarteritis, or to the formation of definite tumours.

The base of the brain is chiefly affected, especially around the perforating arteries, i.e. where the perivascular spaces are largest. This is like gummatous meningitis. A possible explanation in both cases for this apparent predilection may be a spread along the lymphatics of the large arteries and nerves entering the base of the skull. Mott suggests that the difference in results is due to fact that the Trypanosome is surrounded by cells in perivascular space and killed, whereas, the spirochaete under such conditions multiplies and spreads, with increased hyperplasia, in which arteries participate with consequent gummata and endarteritis. In both cases the

sleepy drowsy condition, and absence of spontaneous initiative are due to cerebral anaemia.

The causal organism is a protozoon, and the similarity between the lesions produced by it and the Spirochaete Pallida led many authorities to regard the latter also as a protozoon. The work of Mr Clifford Dobell, of the Imperial College of Science, makes it fairly certain that the Spirochaete is neither protozoon nor bacterium, but belongs to the Spirochaetoidea.

- (1) F.W. Mott: "Histological Observations on the Changes in the Nervous System in Trypanosome Infections". Arch. of Neur. & Psych., Vol.3.
- (2) Manson-Bahr: Tropical Diseases, 7th Ed., 1921. p.128.
- (3) Power & Murphy: loc cit. p.32.
- (4) Idem. p.31.
- (5) F.W. Mott: Loc. cit.

Case No. 146. J. A. N. Aged 34.
Married. Admitted 4-1-22.

He had suffered from fits of depression for past two and a half years. Nine months ago he had paresis with pain and swelling of both lower extremities from which he recovered in a week. Two weeks prior to admission twitchings of arms and legs started, his gait became very unsteady, and he had a constant severe headache. This was his condition on admission. He also had outbursts of singing, and he was rambling and incoherent, and quite disoriented. He had a coated, dirty tongue and mouth, his lips were dry and cracked, gums spongy. No albumen or sugar in urine. His lungs were normal. Temperature was sub-normal. Apical systolic bruit present, and heart's action irregular. Knee jerks exaggerated. Plantars flexor. Pupils normal. Fundi could not be examined. No ocular paralysis detected. He died on 12-1-22, having been maniacal throughout, with great restlessness of the large movement type, and hallucinated, aurally and visually.

His serum Wasserman was negative. His Cerebrospinal Fluid gave a negative Wassermann reaction, but there was excess of protein, and his cells numbered 52 per c.mm., and were small lymphocytes. This lymphocytosis is one of the most constant signs of Tubercular Meningitis, and is often between 100-200 cells per c.mm., but Boyd states it may often be

so low as to cause grave doubt as to the diagnosis. His fluid came out under considerable pressure, and was quite clear.

Post-Mortem. Pia was congested, and there were numerous tubercles the size of a pin-head scattered along the vessels passing up the Sylvian Fissure, and over the frontal area on both sides. There were also a few tubercles and thrombosis, of the vessels in the choroid plexus. No tubercles were seen at the base of the brain, nor on the arteries withdrawn from the anterior and posterior perforated spots. There was no matting of the meninges. The naked eye changes were really slight. There was great excess of Cerebrospinal Fluid, and the gyri were somewhat flattened. The lateral ventricles were dilated, and the ependyma somewhat softened. The fornix and septum lucidum were intact. The spinal cord and its meninges did not show any naked eye changes. No cedema of cerebral substance contiguous to meninges was apparent, but, as condition is really a meningo-encephalitis, the usual lymphocytic infiltration in the perivascular spaces would doubtless have been apparent under the microscope. The tubercles were examined microscopically, and showed the epithelioid and giant cells of tubercle. No organisms were found in a specimen of Cerebrospinal Fluid taken at autopsy.

Lungs showed some congestion at bases, but no evidence of tubercular infection. The bronchial glands were enlarged, and some caseous, and doubt-

less this was the primary infection.

98.

The other organs showed cloudy swelling,
but no other changes of importance.

(I) Boyd: loc. cit. p.102.

Case No. 133. D. S. Aged 47.

Widower. Admitted 15-11-21.

He was admitted on a stretcher, and was obviously in a dying condition. He had a history of pleurisy (?), of five months duration, and had been sent to Camberwell Infirmary a month previously. He had been sent from there certified on account of his great restlessness, and rambling, incoherent talk. He had a history of fits for two months. Right base showed complete dullness, no air entry, and no adventitious sounds. Harsh breathing, with some rhonchi at both apices. Heart rapid and feeble. Tongue clean. Urine normal. Articulation normal. Knee jerks exaggerated. Plantar reflexes flexor. Sight fair, fundi could not be examined. Pupils dilated, but otherwise normal. Temperature 101° F. Severe cough with dirty green sputum, containing small blood clots. Serum gave negative Wassermann reaction. Cerebrospinal Fluid came out under considerable pressure, and it had a distinct red colouration. Wassermann was negative.

Centrifuging had no appreciable effect on the fluid, showing that haemolysis had taken place, and that the blood present was not accidental. Cell count gave 50 cells per c.mm., but these were difficult to count accurately, owing to the considerable amount of debris present. They were lymphocytes. No red blood corpuscles were seen. There was marked

It was only after the P.M. examination that these changes in the fluid were understood; ante-mortem, the diagnosis lay between Tubercular Meningitis secondary to phthisis, and Cerebral Tumor secondary to growth in mediastinum. The Cerebrospinal Fluid findings tended to support the former diagnosis. The condition differed from Xanthochromia, which it somewhat resembled, in having a cellular increase, nor was there spontaneous coagulation.

Boyd reports a case of pituitary tumor with marked protein, but no cellular increase, and another with marked pleocytosis. Another of his cases had acute meningitis, with marked yellow coloration of Cerebrospinal Fluid.
(1)

In erythrochromia red blood corpuscles can usually be found, but they were not seen in this case. In Xanthochromia they are absent.

In Cerebral Tumor the cell count is usually normal, but may be increased, especially if meninges are involved. The protein content varies
(2)
much as the cell count.

The patient showed much clouding of consciousness, and was completely disoriented. He was quite irrational, and unable to answer any questions. There was some delirium, and he was very restless for the first twenty four hours, after which he became moribund. He died on 18-11-21, three days after admission.

Post Mortem. Heart healthy.

Kidneys showed chronic interstitial nephritis. Large tumor in posterior mediastinum involving all mediastinal glands, with direct spread into middle and lower lobes of right lung and pericardium. No lung tissue could be recognised in these lobes, and tumor was broken down in parts and very vascular. Meninges were somewhat oedematous, and underneath them numerous areas of softening and depression could be seen over convexity. There was considerable excess of Cerebrospinal Fluid. Innumerable growths, varying in diameter from half to one inch were scattered throughout the brain. There were at least fifty, the smaller ones being solid and very vascular, while the larger ones had broken down and formed cysts containing either blood or a straw coloured fluid. There was no attempt at capsule formation. The largest growths were in the basal ganglia of both sides, and in the dentate nuclei of the cerebellum. One large one in the right optic thalamus had ruptured into the lateral ventricle, and no doubt accounted for many of the changes in the Cerebrospinal Fluid. Sections of the primary and secondary growths were examined, and proved to be lymphosarcomas.

(1) Boyd: loc. cit. p.45.

(2) Idem. p.125.

1. Owing to the high incidence of Syphilis in patients admitted to mental hospitals, in this series 29.3%, serum Wassermann reactions should be tested as an invariable routine measure.
2. For diagnosis of Syphilis of the Central Nervous System serum results alone are insufficient, and in all Syphilitics, certain or suspected, fluid examination is essential.
3. In suspected General Paralysis neglect to examine the Cerebrospinal Fluid is unpardonable. The mental and physical factors can be very deceptive, and serum examination alone may be more misleading than helpful. Thus, two cases in this series were actually certified as suffering from General Paralysis of the Insane, diagnoses proved to be wrong on subsequent fluid examination.
4. Early diagnosis and treatment of Syphilis of the supporting and nutritional tissues of the Central Nervous System will often prevent the case passing into disease of the parenchymatous tissue, and thus changing from curable into an incurable disease. One very marked instance of this was found in present series.
5. Fluid examination must consist of several tests if accurate diagnosis is to be arrived at, as no single reaction is pathognomonic of any particular disease of the Central Nervous System, syphilitic or otherwise. Several examples of this finding were present in this series of

fluid examinations. Thus, in no Syphilitic disease, not even General Paresis, is the percentage of positive Wassermann reactions, or typical parietic gold curves in fluid, 100%. Proof of this was not wanting in present investigation.

6. In all cases where the clinical findings suggest Syphilis one negative Wassermann reaction in the serum or cerebrospinal fluid must not be regarded as final, but the examination must be repeated, after a provocative dose of a Salvarsan preparation if possible. In this series, two Paretics gave negative serum Wassermann reactions on first examination.

7. More frequent examination of the Cerebrospinal Fluid in mental cases will lead to the detection of causal factors which would otherwise be missed, e.g. Meningitis of various origins, Cerebral Tumours, Trypanosomiasis, etc.

8. The diagnosis of Syphilis of the Central Nervous System cannot be left to the pathologist alone. The clinical findings must also be taken into account. This is especially the case in Tabetics, and for differential diagnosis between the various forms of Syphilitic disease of the Central Nervous System. Although not emphasized in this Thesis, in which treatment has not been recorded, the last word often rests with the therapeutic test.

Tables showing Results of Examination of
Central Nervous System.

(I) Table showing Results of Serum and Fluid Examination of 3 Cases of Cerebral Syphilis.

No.	Serum W	C.S.F.					Lange
		Rate of Flow	After effects	Pro- tein	Cells per cm.	W	
1	+ 8	+	-	+ -	45	-	0111232100
	*	+	-	-	3	-	0000000000
14	+40 ⁺	+	+	-	3	-	
52	+40 ⁺	N	+	+ -	6	-	0001122100

* Reexamined after treatment.

Under C.S.F. + = increase.

+ - = slight increase.

- = negative.

N = normal.

(2) Table showing some Clinical Facts in connection with 3 Cases of Cerebral Syphilis.

No.	Age	Civil State	Duration	Time since Infection	Pupils	K.Js.	Tremor & Slurring
1	26	S.	2 mths.	12 mths.	Dilat ^α	+	Absent
14	50	M.	6 mths.	26 yrs.	Normal	N.	Present
52	67	W.	18 "	40 yrs.	unequal	+	Present

+ = Increased.

N = Normal.

S. = Single. M. = Married. W. = Widower.

(3) Table showing Results of Serum and Fluid Examination of 32 Cases of General Paralysis.

No.	Serum W.	C.S.F.					Lange.
		Rate of Flow	After- effects	Pro- tein	Cells per cent	W.	
11	+ 40 ⁺	+	H.I.	++	62	+ 40 ⁺	5555442100
12	-*	-	-	++	14	-	3222111000
17	+ 40 ⁺	+	-	++	37	+ 40 ⁺	5555554210
20	+ 40 ⁺	+	-	++	34	+ 40 ⁺	5555543310
24	+ 40 ⁺	+	-	++	59	+ 40 ⁺	5555432000
26	+ 40 ⁺	+	-	++	44	+ 40	5555543210
28	+ 40 ⁺	N.	-	++	98	+ 40 ⁺	5555432100
41	+ 40 ⁺	+	-	++	42	+ 40 ⁺	5555542100
43	+ 40 ⁺	+	-	++	32	+ 40 ⁺	5544443210
46	+ 40 ⁺	+ -	-	++	18	+ 40 ⁺	5555543320
47	+ 40 ⁺	+	-	++	60	+ 40 ⁺	5555554210
48	+ 40 ⁺	N.	-	+ -	40	+ 40	5555543210
50	+ 40 ⁺	+	-	++	38	+ 40 ⁺	5555553310
53	+ 40 ⁺	N.	-	++	120	+ 40 ⁺	5555544200
72	+ 40 ⁺	+	-	++	62	+ 40 ⁺	5555554210
73	+ 40 ⁺	+	-	+ -	32	+ 40	5555443210
74	+ 40 ⁺	+ -	-	++	22	+ 20 ⁺	5554432100
77	+ 40 ⁺	+	headache	++	45	+ 40 ⁺	5555544310
79	+ 40 ⁺	+	-	+ -	108	+ 20	5444332210
86	+ 40 ⁺	+	-	++	46	+ 40 ⁺	5555554310
99	+ 40 ⁺	N.	-	+ -	24	+ 8	3332211000
108	+ 40 ⁺	+	-	++	100	+ 40 ⁺	5555544310
113	+ 40	N.	-	++	82	+ 40 ⁺	5555421000
119	+ 40 ⁺	+	-	++	69	+ 40 ⁺	5555432000
122	+ 40 ⁺	-	-	++	46	+ 40 ⁺	5555532200
123	+ 40 ⁺	+	-	++	86	+ 40 ⁺	5555321100
127	+ 40 ⁺	+	-	+ -	14	+ 8	3222211000
131	+ 40 ⁺	+	-	++	26	+ 40 ⁺	5555443100
140	+ 40 ⁺	+	-	++	105	+ 20	5555442210
143	+ 40 ⁺	+	-	++	238	+ 40 ⁺	5555554210
148	+ 40 ⁺	+	-	++	74	+ 40 ⁺	5555542100
149	-*	+	-	++	22	+ 8	5555432110

* After .15 gm. NAB. retardation of haemolysis in top tubes got.

Under C.S.F. + = increase.
 ++ = marked increase.
 + - = slight increase.
 - = diminished.
 N = normal.

(4) Table showing some Clinical Facts in connection with 32 Cases of General Paralysis.

No.	Age	C.S.	Dur.	Time since Infection	Pupils	K.Js.	T & S	Type.
11	51	M.	6mos	30 yrs.	A.R.	++	Pres.	Confusional
12	53	M.	2yrs	Denied.	Slugg.	Abs.	"	Tabo-
					Irreg.		"	Paresis
					Unequ.			
17	46	M.	3mos	Denied	Normal	+	"	Demented
20	42	M.	2yrs	Denied	A.R.	+	"	Exalted
24	46	M.	6mos	33 yrs.	A.R.	Abs.	"	Exalted
26	34	S.	3yrs	8 yrs.	Unequ.	Abs.	"	Depressed
28	33	M.	4mos	12 yrs.	Rigid	+	"	Depressed
41	40	M.	6mos	20 yrs.	A.R.	Abs.	"	Exalted
43	58	w.	1 yr.	30 yrs.	A.R.	-	"	Exalted
46	40	S.	2mos	15 yrs.	A.R.	Abs.	"	Depressed
47	37	M.	4yrs	19 yrs.	Normal	Abs.	"	Exalted
48	65	w.	6mos	20yrs.	A.R.	+	"	Depressed
50	50	M.	1mos	30 yrs.	Slugg.	-	"	Exalted
53	46	M.	1yr.	10 yrs.	A.R.	+	"	Depressed
72	54	M.	3mos*	11 yrs.	Normal	+	"	Demented
73	32	M.	3 $\frac{1}{2}$ yr	Denied	A.R.	+	"	Demented
74	47	S.	7mos	Denied	A.R.	+	"	Demented
77	34	M.	1mo.	Denied	Irreg.	N.	Abs.	Exalted
79	42	M.	1yr.	?	Irreg.	N.	Pres.	Exalted
86	35	M.	2yrs	10 yrs.	Normal	-	"	Demented
99	49	S.	1mo.	20 yrs.	Irreg.	+	Abs.	Depressed
108	31	M.	?	12 yrs.	Irreg.	-	Pres	Demented
113	58	M.	1mo.	30 yrs.	Normal	Abs.	Pres.	Exalted
119	38	M.	2yrs	18 yrs.	Normal	+	Abs.	Exalted
122	41	M.	1yr.	8 yrs.	Slugg.	Abs.	Pres	Exalted
123	50	S.	2yrs	Denied	Slugg.	+	"	Demented
127	41	M.	5yrs	Denied	Slugg.	Abs.	"	Taboparesis
131	54	M.	1yr.	Denied	Slugg.	+	"	Exalted
140	39	S.	?	15 yrs.	A.R.	+	"	Demented
143	46	M.	?	Denied	Slugg.	+	"	Demented
148	42	S.	2mos	16 yrs.	A.R.	Abs.	"	Exalted
149	42	M.	1mo.	Denied	Irreg.	+	"	Exalted
					Unequ.			

* Hemiplegia nine years ago.

C.S. = Civil State.

T & S = Tremor of tongue and slurring of articulation.

N. = Normal.

+ = Increased.

- = Diminished.

(5) Table showing Result of Serum and Fluid Examination in 9 Cases of Systemic Syphilis.

No.	Serum W.	C.S.F.						
		Rate Flow	After effects	Pro- tein	Cells per cm.	W	Lange	Type of Psychosis.
69	* Weak	+	Nil.	N.	5	—		Senile De- mentia.
80	40**	+	"	N.	3	—	N.	Mania.
82	40	+	"	N.	7	—	N.	Paraphrenia.
100	40**	+—	"	N.	3	—		Mania.
107	40	+	+ #	N.	1	—		Korsakow's Psychosis.
109	40	+	Nil.	N.	2	—		Alcoholic Insanity.
115	40	+	"	+—	4	—	N.	G.S.W. Head.
124	40	+	"	N.	3	—		Senile De- mentia.
150	40	+	"	N.	0	—	N.	Confusional Insanity.

* Retardation of haemolysis in top dilutions. Repeated twice after provocative dose of NAB.

** Same after twelve intramuscular injections of .3gm. NAB, and course of Hg and KI.

Pain in back of neck for 24 hours.

+ = Increase. +— = Slight increase. N. = Normal.

(6) Table showing some Clinical Facts in connection with 9 Cases of Systemic Syphilis.

No.	Age	Civil State	Time since Infection	Pupils	K.Js.	Tremor & Slurring
69	58	M.	20 yrs.	Slugg.	+	Tremor of tongue.
80	23	M.	5 yrs.	Normal	+	Nil.
82	41	W.	20 yrs.	Normal	N.	Tremor & Slurring
100	42	S.	20 yrs.	Normal	N.	Nil.
107	46	S.	15 yrs.	Irreg. Unequ.	+	Tremor & Slurring
109	45	M.	24 yrs.	Slugg. Irreg.	+	Tremor of tongue.
115	42	M.	Denied	Irreg.	+	Tremor & Slurring
124	75	W.	Denied	Normal	N.	Nil.
150	48	S.	20 yrs.	Normal	N.	Tremor of tongue.

N. = Normal.

+ = Slight Increase.

(7) Table showing Results of Serum and Fluid Examination in 12 Cases of Dementia Praecox.

No	Serum W.	C.S.F.						Type.
		Rate Flow	After effects	Pro- tein	Cells per cm.	W	Lange	
5	-	+	Nil.	N.	1	-		Heb.
7	-	N.	Head- ache	N.	2	-	0000121100	Cat.
10	-	+	Nil.	+ -	8	-	0001122100	Heb.
13	-	N.	"	N.	0	-	0000000000	Cat.
16	-	N.	Head- ache	N.	2	-		Par.
23	-	N.	Nil.	N.	3	-		Cat.
49	-	N.	"	N.	1	-	0000000000	Heb.
68	-	N.	"	N.	1	-	0000000000	Par.
96	-	N.	Head- ache	N.	2	-	0000000000	Heb.
106	-	N.	Nil.	+	2	-		Cat.
120	-	N.	"	N.	8	-		Cat.
136	-	N.	"	N.	4	-	0000000000	Cat.

N. = Normal.

+ = Increase.

+ - = Slight Increase.

- = Negative.

Cat. = Catatonic.

Heb. = Hebephrenic.

Par. = Paranoid.

(8) Table showing Result of Serum and Fluid Examination in 19 Miscellaneous Cases of Mental Disease.

No	Serum W.	C.S.F.					Type of Psychosis.
		Rate Flow	After effects	Pro- tein	Cells per cm.	W Lange	
22	-	N.	Nil.	N.	3	-	Chronic Mania
25	-	N.	"	"	4	-	Insane Amentia
29	-	N.	"	"	1	-	Insane Amentia
30	-	+	"	"	2	- 0000000000	Insane Amentia
33	-*	+	Slight	+ -	8	- 0000112210	Infantile Cerebropathy
34	-	N.	Nil.	+	125	- 5555555555	Trympan- osomiasis
35	-	N.	Slight	N.	9	-	Alcoholic Dementia
37	-	N.	Slight	"	2	-	Epileptic Insanity
45	-	+	Nil.	"	4	- 0000000000	Alcoholic Insanity
56	-	N.	"	"	2	-	Alcoholic Dementia
59	-	N.	Slight	"	1	-	Alco. Pseudo- Paranoia
61	-	+	Nil.	"	5	- 0000000000	Alcoholic Insanity
81	-	+	Slight	"	1	-	Confusional Insanity
88	-	N.	Nil.	"	1	-	Korsakow's Psychosis
89	-	N.	"	"	4	-	Fracture of Skull
132	-	N.	Slight	"	3	-	Confusional Insanity
133	-	+	Nil.	+	50	-	Sarcoma of Brain
142	-	N.	"	N.	4	-	Mania.
146	-	+	"	+	52	-	Tubercular Meningitis

* Retardation of haemolysis got on first examination.

N. = Normal. - = Negative. + = Increase.
+ - = Slight Increase. W. = Wassermann Reaction.

Technique of Wassermann Reactions as employed ~~at~~ ~~the~~ ~~Pathological~~ ~~Laboratory~~ ~~of~~ ~~the~~ ~~London~~ ~~County~~ ~~Mental~~ ~~Hospitals~~.

Estimation of the Minimum Haemolytic Dose.

A series of tubes is prepared containing .5c.c. of a 5% suspension of washed blood corpuscles and .2 c.c. of a 1 in 5 saline dilution of fresh guinea-pig serum and falling doses of the appropriate haemolysin (generally 1 c.c. to 0.1. c.c. of a 1 in 1000 saline dilution). The tubes are heated in the 37°C water-bath for one hour, when the minimum amount of haemolysin giving complete haemolysis is noted; this quantity is the minimum haemolytic dose. A suspension of sensitized cells is now prepared, each cubic centimetre containing .5 c.c. of the 5% suspension of washed blood corpuscles, an amount of haemolysin equivalent to four times the minimum haemolytic dose, and saline to 1 c.c.

Tubes	(A) Saline Dilution Complement 1 in 5 (2)	(B) Haemolysin 1-1000 Saline Dilution* (3)	(C) R.B.Cs. (4)	(D) Saline to 3 c.c. (1)
No.1	.2 c.c.	1.0 c.c.	.5 c.c.	1.3 c.c.
2	.2 c.c.	0.9 c.c.	.5 c.c.	1.4 c.c.
3	.2 c.c.	0.8 c.c.	.5 c.c.	1.5 c.c.
4	.2 c.c.	0.7 c.c.	.5 c.c.	1.6 c.c.
5	.2 c.c.	0.6 c.c.	.5 c.c.	1.7 c.c.
6	.2 c.c.	0.5 c.c.	.5 c.c.	1.8 c.c.
7	.2 c.c.	0.4 c.c.	.5 c.c.	1.9 c.c.
8	.2 c.c.	0.3 c.c.	.5 c.c.	2.0 c.c.
9	.2 c.c.	0.2 c.c.	.5 c.c.	2.1 c.c.
10	.2 c.c.	0.1 c.c.	.5 c.c.	2.2 c.c.

* Further dilution must be made (viz. 1-10,000) if prevention of haemolysis does not occur with this series. It is not advisable to use a haemolysin that reacts weaker than in 1-1000 dilution.

(A) Complement. - Guinea-pig serum collected from the blood of an animal killed the previous evening. The animal is stunned and its throat cut, and no narcotic is used. The blood is collected in a porcelain basin, placed in ice-chest over night, and the separated serum collected with a capillary pipette.

(B) Haemolysin. - Inactivated serum of animal injected with foreign corpuscles. A suitable reagent, sheep corpuscles into horse, is supplied by Messrs Burroughs, Wellcome.

(C) Corpuscles. - Sheep's blood is collected into a bottle containing half its volume of sterile citrated saline (.8% Sodium Citrate in Saline Solution) and the bottle at once briskly shaken. The corpuscles are separated from the citrated blood by centrifugalisation and washed with Saline Solution (.9%) three times, the last washing is pipetted off, and 5 c.c. of the residual corpuscles made up to 100 c.c. with Saline Solution.

(D) Saline Solution. - .9% Sodium Chloride (Chem. Pure) in distilled water.

Into a number of tubes are introduced 1 c.c. sensitized cells and falling doses of guinea-pig serum diluted 1 in 50 with saline (1.0. c.c. to .1 c.c.), Each tube is then filled with saline to a total volume of 3 c.c. They are now heated in 37° C water-bath for one hour, when the minimum amount of guinea-pig serum (complement) giving complete haemolysis is noted; this quantity is the minimum complementary dose.

	Complement. Saline Di- lution 1-50 (2)	(A) Sensitized Cells. (3)	Saline to 3 c.c. (1)
Tube No.1	1.0 c.c.	1.0. c.c.	1.0. c.c. ,
" " 2	0.9 "	1.0. "	1.1. "
" " 3	0.8. "	1.0. "	1.2. "
" " 4	0.7. "	1.0. "	1.3. "
" " 5	0.6. "	1.0. "	1.4. "
" " 6	0.5. "	1.0. "	1.5. "
" " 7	0.4. "	1.0. "	1.6. "
" " 8	0.3. "	1.0. "	1.7. "
" " 9	0.2. "	1.0. "	1.8. "
" " 10	0.1. "	1.0. "	1.9. "

The figures (1), (2), and (3), indicate the order in which the reagents should be placed in the tubes.

(A) Sensitized Cells.- 0.5 c.c. 5% corpuscle suspension to which has been added a quantity of haemolysin equivalent to four times the minimum haemolytic dose, made up to 1 c.c. with saline solution. Thus, if

the minimum haemolytic dose is .5 c.c. of 1-1000
haemolysin, each cubic centimetre of sensitized cells
will contain :-

.5 c.c. 5% corpuscles + .2 c.c. 1-100 haemolysin
+ .3 c.c. Saline.

A series of five tubes is used for each test; into each tube is placed a quantity of guinea-pig serum equivalent to four times the minimum complementary dose, (this is generally represented by .2 c.c. of a 1 in 5 saline dilution of guinea-pig serum), .2 c.c. of a 1 in 10 saline dilution of antigen, a quantity of the cerebrospinal fluid or inactivated serum to be tested and saline to the total volume of 2 c.c.

In the case of cerebrospinal fluid the quantities range from 1 c.c. to .1 c.c. and in the case of the serum from .5 c.c. to .1 c.c. When it is required to estimate exactly the intensity of the reaction a wide range of tests is made containing doses falling to .01 c.c. by means of saline dilutions of serum or cerebrospinal fluid.

The tubes are now heated in 37° C water-bath for one hour when 1 c.c. of sensitized cells is added to each tube. After shaking, the tubes are returned to the water-bath for another hour, when haemolytic reaction will have taken place and the results can be read off.

S E R U M T E S T.

Tube No.	Complement	Antigen. (A)	(B)	Saline to 2 c.c. (1)
	1-5 Saline Dilution (2)	1-10. Saline Dilut. (3)	Serum (4)	
1	.2 c.c.	.2 c.c.	.5 cc.	1.1 c.c.
2	.2 c.c.	.2 c.c.	.4 cc.	1.2 c.c.
3	.2 c.c.	.2 c.c.	.3 c.c.	1.3 c.c.
4	.2 c.c.	.2 c.c.	.2 cc.	1.4 c.c.
5	.2 c.c.	.2 c.c.	.1 cc.	1.5 c.c.

Incubate for one hour. Then add 1 c.c. sensitized cells to each tube. The numbers (1), (2), (3), and (4), indicate the order in which the reagents should be placed in the tubes.

Tube No.	Complement 1-5 Saline Dilution (2)	Antigen.(A) 1-10 Saline Dilution. (3)	(C) C.S.F. (4)	Saline to 2 c.c. (I)
1	.2 c.c.	.2 c.c.	1.0 cc.	.6 c.c.
2	.2 c.c.	.2 c.c.	.8 cc.	.8 c.c.
3	.2 c.c.	.2 c.c.	.5 cc.	1.1 c.c.
4	.2 c.c.	.2 c.c.	.2 cc.	1.4 c.c.
5	.2 c.c.	.2 c.c.	.1 cc.	1.5 c.c.

Incubate for one hour. Then add 1 c.c. sensitized cells to each tube.

The numbers (1), (2), (3), and (4), indicate the order in which the reagents should be placed in the tubes.

(A) ANTIGEN.- Heart muscle extract and Cholesterol.

Heart Muscle Extract.- Heart muscle obtained from any necropsy and freed from fat is minced and weighed. It is then ground up with Silver Sand, transferred to a bottle, and absolute alcohol added in the proportion of 9 c.c. for every gram of heart muscle. The mixture is then shaken on a shaking machine for two hours, filtered and stored in a cool place.

Cholesterol can be bought but can be easily prepared from any formalin-hardened nervous tissue. The tissue is allowed to dry, the mass is then broken up and cold acetone poured on. After standing overnight the acetone solution is decanted and more acetone added. The acetone is distilled off the combined extracts, and the residual crude Cholesterol purified by recrystallization from absolute alcohol.

The Antigen consists of :-

- 2 parts of alcoholic human heart extract (leathin).
- 1 part of a 1% solution of Cholesterol in absolute alcohol.

The two constituents are kept separately and mixed before using, and made up to a 1 in 10 dilution with saline. This answers all the requirements of a standard Antigen. The Cholesterol solution keeps indefinitely but the heart extract should be prepared every four weeks. This Antigen was first described by Bordet and Roulens. (1) It has many advantages over syphilitic liver extracts. (2)

(B) SERUM. - At least 5 c.c. of blood should be collected. After coagulation the clear serum is pipetted off, centrifuged if necessary, transferred to a tube and inactivated by heating in 56°C water-bath for 30 minutes.

(C) C.S.F. - Cerebrospinal Fluids are examined for lymphocytes and globulin excess by usual methods; inactivation is not essential, but all error is obviated by the routine inactivation of all cerebrospinal fluids for 10 minutes in 56 C water-bath.

INTERPRETATION OF RESULTS.

Prevention of Haemolysis represents a positive, and Haemolysis a negative Wassermann reaction. In the majority of positive cases there is complete prevention of haemolysis in all tubes, but chronic syphilitic subjects, cases under treatment, and parasyphilitics may give less marked but, nevertheless, important positive reactions. The above technique enables a quantitative expression of the results to be made which, in nervous cases especially, is of much greater value than the usual mixture of plus and minus signs. Taking the mini-

imum complementary dose (which is generally represented by 0.01 c.c. of pure guinea-pig serum) as a unit of complement, in each tube there are four units of complement and when any quantity of serum or cerebrospinal fluid gives total prevention of haemolysis we know that four units of complement have been absorbed or fixed, and the results can be expressed as units of complement absorbed per 1 c.c. of cerebrospinal fluid or serum. For example, if a tube containing .1 c.c. cerebrospinal fluid or serum shows complete prevention of haemolysis, the reaction is recorded as plus 40 and similarly for tubes containing other fractions of a cubic centimetre of cerebrospinal fluid or serum. By taking a wide range of dilutions of serum or cerebrospinal fluid the exact degree of absorption of complement can be determined, but in the figures given .1 c.c. is the smallest amount of fluid noted and if total prevention of haemolysis occurs the result may be noted as + 40+; which indicates a further absorption of complement if the range of dilution of serum or cerebrospinal fluid were extended.

In definitely positive cases in complete prevention of haemolysis is shown in at least one of the tubes; but in very chronic cases and cases under treatment a marked retardation with partial haemolysis may result, such results are of importance but must be regarded with care and in conjunction with the history of the case. Positive results on the cerebrospinal fluid in general paralysis may have a range from + 5 to +400+, and the same in the serum in

syphilis, but the more marked reactions are generally the rule.

CONTROLS.

In all cases it is advisable to make tests on positive and negative controls at the same time, also control tests should be made from time to time that none of the individual reagents used possess the property of vitiating the accuracy of the test. The main danger lies with the guinea-pig serum, which if faulty shows obvious interference in the satisfactory estimation of the minimum haemolytic dose. If the animals are kept under healthy conditions this is a very rare occurrence.

Any material to be tested showing signs of decomposition should be rejected, and sera that show haemolysis should be regarded with caution.

- (1) Bordet & Roulens: "L'Antigen Syphilitique de l'Institut Pasteur, Bruxelles".
Comptes rendus de la Soc. de Biologie, 1919.
- (2) Candler & Mann: Archives of Neurology & Psychiatry. Vol. VI, 1914.