

in avoiding any interference with legitimate therapeutical methods, yet the use of the dry and wet pack is still considered as a method of restraint in their revised regulations of 1913.

These regulations demand still further consideration and it may be hoped that, whilst preventing the abuse of wet packing, they may be so framed as to encourage its employment as one of the most important and valuable means of treatment of the insane.

The Wassermann Reaction, and the Male Insane.
(Essay for which was awarded the Bronze Medal of the
Medico-Psychological Association, 1914.) By J. C.
WOOTTON, M.R.C.S.Eng., L.R.C.P.Lond., Assistant
Medical Officer, Cane Hill Asylum, Coulsdon.⁽¹⁾

INTRODUCTION.

PRIOR to the discovery of the Wassermann reaction it was practically impossible to obtain a correct estimate of the incidence of syphilis amongst the insane, owing to the infrequency of physical signs in specific cases, and the difficulty of obtaining reliable histories. Experience has shown that in a large number of cases a positive Wassermann reaction with the serum may be the only evidence of syphilitic infection; moreover, Dr. Mott (*Archives of Neurology and Psychiatry*, vol. vi) has shown that definite skin lesions are comparatively rare in general paralysis of the insane.

It is generally accepted that a positive Wassermann reaction on the serum may be regarded as specific evidence of syphilis, if leprosy, trypanosomiasis, and a few other diseases of rare occurrence in this country be excepted, and the test, therefore, affords an invaluable aid for the diagnosis of syphilis in cases presenting no physical signs. At Dr. Mott's suggestion I have directed my attention to the application of the test to the serum of cases admitted to Cane Hill Asylum.

Altogether over 550 specimens of serum have been examined, and 65 specimens of cerebro-spinal fluid obtained by lumbar puncture have been submitted to the test. The tests have been applied to the following cases:

- (1) All male epileptics resident in the asylum, 66 cases.
- (2) Chronic irrecoverable cases resident in the asylum, 150 cases.
- (3) Consecutive male admissions to the asylum, 284 cases.
- (4) All suspected cases of general paralysis.

DESCRIPTION OF METHOD EMPLOYED.

About 5 c.c. of blood was obtained by puncture of a prominent vein in the arm, generally the median basilic. The serum was separated by centrifugalisation, and inactivated by heating at 55° C. for thirty minutes.

The technique adopted for the performance of the test was that devised by Candler and Mann (*Archives of Neurology and Psychiatry*, vol. vi).

At the commencement of the research an alcoholic extract of the liver of a syphilitic foetus was used as antigen, but later the use of the heart extract-cholesterol antigen was adopted; from a considerable experience of this reagent the above authors confirm the statement of McIntosh and Fildes: that this may be regarded as a reliable and standard antigen. The hæmolysin used has been obtained by the injection of sheep cells into the rabbit, and fresh guinea-pig serum has been used throughout for complement.

(1) *Estimation of the Minimum Hæmolytic Dose.*

A series of tubes is prepared containing 0.5 c.c. of a 5 per cent. suspension of washed blood-corpuscles, and 0.4 c.c. of a 1 in 10 saline dilution of fresh guinea-pig serum, and falling doses of the appropriate hæmolysin; each tube is filled with saline to a 3 c.c. volume. The tubes are incubated for one hour, when the minimum amount of hæmolysin giving *complete hæmolysis* is noted; this quantity is the *minimum hæmolytic dose*. A suspension of sensitised cells is now prepared, each cubic centimetre containing 0.5 c.c. of the 5 per cent. suspension of washed blood-corpuscles, an amount of hæmolysin equivalent to four times the *minimum hæmolytic dose*, and saline to 1 c.c.

(2) *Estimation of the Minimum Complementary Dose.*

Into a number of tubes are introduced 1 c.c. sensitised cells and falling doses of guinea-pig serum diluted 1 in 20 with

saline. Each tube is then filled with saline to a total volume of 3 c.c. They are now incubated for one hour, when the minimum amount of guinea-pig serum (complement) giving *complete* hæmolysis is noted; this quantity is the *minimum complementary dose*.

(3) *The Wassermann Reaction.*

A series of four 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 0.4 c.c. of a 1 in 10 saline dilution of guinea-pig serum), 0.1 c.c. of a 1 in 5 saline dilution of antigen, a quantity of the cerebro-spinal fluid or inactivated serum to be tested, and saline to the constant total volume of 2 c.c.

In the case of the cerebro-spinal fluid the quantities range from 0.8 to 0.1 c.c., and in the case of the blood serum from 0.4 to 0.1 c.c. In special cases larger doses are employed in addition to those mentioned, *e.g.*, 1 c.c. cerebro-spinal fluid and 0.5 c.c. serum. When it is required to estimate exactly the intensity of the reaction a wide range of tests is made, containing doses falling to 0.01 c.c., by means of saline dilutions of serum or cerebro-spinal fluid.

The tubes are now incubated at 37° C. for one hour, when 1 c.c. *sensitised cells* is added to each tube. After shaking, the tubes are returned to the incubator for another 1 to 1½ hours, when the results are read off, and any special cases are placed in the ice-chamber for further investigation the next morning.

Control tubes are also put up to show that none of the individual reagents possess the property of vitiating the accuracy of the test.

This method efficiently checks the technique, and enables a quantitative expression of the results to be made; it is, therefore, far more useful and reliable than the single tube qualitative test.

The minimum complementary dose of the technique (which is generally represented by 0.01 c.c. of pure guinea-pig serum) is taken as a unit of complement, and the results expressed as units of complement absorbed per 1 c.c. of cerebro-spinal fluid or serum. In each tube there are four minimum complemen-

tary doses of complement, and when any quantity of fluid gives total prevention of hæmolysis, four units of complement have been absorbed. For example: If a tube containing 0·1 c.c. of cerebro-spinal fluid or serum shows complete prevention of hæmolysis, the reaction is recorded + 40, and similarly for tubes containing other fractions of a cubic centimetre of cerebro-spinal fluid or serum.

INVESTIGATION OF THE BLOOD-SERUM IN EPILEPSY.

The results obtained by the application of the Wassermann test to the serum of idiots and feeble-minded have formed the subject of many publications, but few have dealt with epilepsy. Dean (*Proceedings of the Royal Society of Medicine*, 1910, iii, p. 117) examined the serum of 330 inmates of an asylum for idiots at Potsdam, and obtained a positive reaction in 51 cases (15·4 *per cent.*): the 1 epileptic included in this series gave a positive reaction. The results obtained by Dean show that as the age period rises, so the percentage of positive results diminishes, for, whereas he obtained 21·27 *per cent.* positive reactions on patients ten years of age and under, this figure dropped until for cases sixteen to twenty years of age only 6 *per cent.* positive reactions were obtained.

In Denmark, Thomsen, Boas, Hjort, and Leschly (*Berlin klin. Woch.*, 1911, p. 891) examined the blood of 2,061 feeble-minded persons, of whom only 31 (1·5 *per cent.*) gave a positive Wassermann reaction; the series included 25 cases of epilepsy of ages from five to seventy years, and only 1 gave a positive Wassermann reaction. On the other hand, Fraser and Watson (*Journal of Mental Science*, October, 1913), from an examination of 205 cases of mental deficiency, conclude "that syphilis is the causative factor in a very considerable percentage of cases of mental deficiency of whatever degree of severity, as it is present in over 50 *per cent.*," also that "syphilis is the main causative factor in the production of that type of epilepsy which manifests itself at early ages. Syphilis is present in an equal degree in those cases in which the epilepsy is associated with mental deficiency, and in cases where no apparent mental defect exists."

Rees Thomas (*Report of the Commissioners of Lunacy*, 1912, p. 110) examined the blood of 91 males and 72 females con-

genitally deficient of all ages ; of these 12 males and 15 females also suffered from epilepsy ; he obtained a positive reaction in 8 cases, of which 3 were epileptics.

The variability of the results obtained by different workers apparently depends on the age of the cases investigated, and the series containing a large proportion of adult cases give a low percentage of positive reactions.

The cases I have had the opportunity of investigating were all male adult epileptics. Out of 66 cases examined, 5 were found to give a positive reaction, *i.e.*, 7.6 per cent.

WASSERMANN REACTION IN MALE ADULT EPILEPTICS.

Age at commencement of fits.	Number examined.	Number of positive cases.
Under 25	45	3
25-44	8	1
45 and upwards	6	1
Uncertain	7	—
	—	—
	66	5

My results are in agreement with those obtained by Stoddart (*Report of the London County Asylums Committee, 1912, p. 44*), who, from an examination of 184 adult epileptics of both sexes at Colney Hatch Asylum, obtained positive reactions in 14, 7.6 per cent.

In four of the cases giving a positive serum reaction, in order to exclude the possibility of general paralysis, lumbar puncture was done, and the cerebro-spinal fluid found to be negative. One positive case died before lumbar puncture could be done.

Mercurial inunction was carried out on two positive cases, D— and H—, and after three months continuous treatment the sera were again examined, and found to be negative.

In one case, O—, after similar treatment, the reaction was still positive, but not nearly so marked, but has now returned to its original intensity.

Another case giving a positive reaction on the serum was placed under treatment, but died before further tests were made.

The following are the details of the non-paralytic cases in which a positive reaction was obtained on the serum, and which were submitted to treatment :

H—. Fits since the age of eighteen. Teetotal. No family history of insanity, tuberculosis, or alcohol.

January 6th, 1905: On admission, æt. 25; pupils unequal; knee-jerks normal. *Mentally*, dull and confused.

April 6th: Developed rash on arms, legs, and back. Nothing typical.

May 9th: Pustular eruption.

August 11th: Skin well.

August 22nd, 1912: Serum + 13.

September 11th: Mercurial inunction commenced.

March 25th, 1913: Lumbar puncture. Cerebro-spinal fluid: Wasserman negative, no lymphocytosis.

July 8th: Mercurial inunction ceased.

July 29th: Serum negative.

August 27th: Serum negative.

June 9th, 1914: Serum negative.

There is no change in the patient's mental or physical condition.

O—. Admitted November 26th, 1911. Æt. 52. Married. He had blow over right eye with hammer sixteen years ago, and fits began six months later. Alcoholic. *Mentally*, ill-tempered, querulous, dull memory poor. Syphilis denied. Scar in groin.

November 7th, 1912: Serum + 40.

November 9th: Mercurial inunction begun.

April 8th, 1913: Mercurial inunction stopped.

April 22nd: Lumbar puncture. Cerebro-spinal fluid: Wassermann negative, no cells.

April 22nd: Serum + 8.

August 27th: Serum + 40.

Fits continue, but his general physical and mental condition has improved. It will be observed that the intensity of the reaction diminished with treatment, but since inunctions have been stopped it has gone back to the original intensity, indicating the desirability of further treatment.

D—. Admitted January 3rd, 1911. Æt. 31. Fits began when æt. 16. Married, one healthy child.

August 22nd, 1912: Serum + 20.

November 9th: Mercurial inunction begun.

April 8th, 1913: Lumbar puncture, Wassermann negative, no cells.

April 8th: Mercurial inunction stopped.

April 16th: Lumbar puncture, Wassermann negative, no cells.

July 29th: Serum negative.

August 27th: Serum negative.

June 9th, 1914: Serum negative.

In the above case the positive Wassermann reaction on the serum disappeared as the result of treatment, but there is no alteration in the physical and mental condition of the patient.

THE WASSERMANN REACTION IN GENERAL PARALYSIS.

A positive Wassermann reaction with the cerebro-spinal fluid, and with the serum, is now regarded as a constant feature in general paralysis of the insane. In the earlier days of the Wassermann reaction there was considerable variability in the results obtained by different workers. McIntosh and Fildes (*Syphilis from the Modern Standpoint*, London), from the literature give 98 *per cent.* positive serum reactions, and 85 *per cent.* positive reactions with the cerebro-spinal fluid in general paralysis. Plaut (147 cases), and Boas (139 cases) obtained a positive serum reaction in every case examined. Plaut obtained a definitely positive reaction with the cerebro-spinal fluid in 95 *per cent.* of the 147 cases examined. Candler and Mann (*loc. cit.*), from the examination of 191 cases, in which the diagnosis of general paralysis was verified by subsequent autopsy and microscopical examination, obtained a positive reaction with the cerebro-spinal fluid in 98 *per cent.*; on a series of 186 cases of general paralysis these authors also obtained 98 *per cent.* positive serum reactions.

I have found the reaction of the utmost value in clearing up the diagnosis in obscure cases; in this direction I have made about 100 serum reactions. In cases where a positive serum reaction was obtained, and the clinical signs were not definite, lumbar puncture was performed, and the cerebro-spinal fluid examined by the Wassermann test for cell contents, and for protein. In all the positively reacting cases that have since died the *post-mortem* findings have confirmed the diagnosis, and Dr. Mott was able to demonstrate spirochætes in nine out of fifteen of the brains sent to him.

In some cases the test enabled a diagnosis of general paralysis being made in cases in which it was not suspected previously.

The following cases present points of interest :

M—, æt. 21; single; labourer. Admitted December 23rd, 1911. Regarded on admission as adolescent mania. No external signs of syphilis.

The occurrence of a slight seizure occasioned a Wassermann test being made; a marked positive result was obtained on both the cerebro-spinal fluid and serum, with lymphocytosis. A closer inquiry into the history revealed the fact that the mother had numerous

children still-born, miscarriages, and children dying in early infancy. There is no family history of insanity, and the father denies syphilis.

The diagnosis of juvenile general paralysis was thus confirmed, and is in accordance with his present mental and physical condition.

The patient has since died ; the autopsy revealed the typical lesions of general paralysis.

H—. This case was admitted first to the asylum February 25th, 1904, æt. 43 ; he was acutely melancholic, having made several attempts at suicide, and an alcoholic. He recovered, and was discharged six years later. He was re-admitted three years later, January 24th, 1913, with melancholia. At this time, and previously, there was no suggestion of general paralysis. He denied syphilis, and there were no external signs. Within a few months, however, he had a seizure. The Wassermann test then made was markedly positive on both serum and cerebro-spinal fluid, with lymphocytosis. Since this the diagnosis of general paralysis has been confirmed by the patient's typical physical and mental symptoms. Patient now admits having a "sore" shortly after intercourse, when aged fifteen.

The patient has since died ; the autopsy revealed the typical lesions of general paralysis.

A number of other cases for many years have been regarded as chronic general paralytics, but the serum and cerebro-spinal fluid gave a negative Wassermann reaction, and some have been discharged from the asylum, and to the best of our knowledge have remained normal.

In all these cases, there was a marked history of excessive and chronic alcoholism, and they must be considered as cases of alcoholic insanity, or Korsakow's syndrome, simulating general paralysis. The following case is an example :

B—, admitted January 30th, 1909, æt. 34. He served in the army nine years at home and abroad. Last few years has been a carman.

Family history.—Father was always a very heavy drinker. Mother insane, æt. 25, under asylum care prior to birth of patient. Three brothers and two sisters are alive and well. Patient had been married five years before admission ; no children, no miscarriages. Up to time of marriage he had always drunk heavily, and had lived a loose life, but denies syphilis, although admitting frequent risk of infection ; he admits gonorrhœa.

On admission.—Incoherent and unintelligible at times ; memory very defective ; grandiose ideas. Habits wet and dirty. Speech slurred. Inguinal glands shotty. Gait ataxic. Romberg sign marked. Facial muscles tremulous. Pupils small, react to accommodation, but not to light.

Since admission.—He has improved mentally and physically. He has had no seizures, and he never had anti-syphilitic treatment.

March 11th, 1913 : Cerebro-spinal fluid : Wassermann negative, no lymphocytosis.

March 4th : Serum negative.

August 27th : Again tested : cerebro-spinal fluid negative, no lymphocytosis. Serum negative.

November 13th, 1913 : Again tested : serum negative.

April 21st, 1914 : Again tested : cerebro-spinal fluid negative, no lymphocytosis. Serum negative.

June 30th, 1913.—He has considerably improved, his condition being as follows : Pupils small ; right slightly larger than left ; both react sluggishly to light and to accommodation. Knee-jerks normal. Romberg sign absent. Reflexes normal. Gait normal. Speech is not good, many words being clipped, but this may be partly accounted for by the absence of teeth. He is grandiose only as to his muscular development. He is clean in his habits and occupies himself usefully. Mentally, he is decidedly childish, and is easily provoked.

June 30th, 1914.—The patient has now considerably improved.

I was able to obtain a specimen of blood from the wife of this case, and the Wassermann reaction was negative.

THE EXAMINATION OF THE SERUM OF RELATIVES OF GENERAL PARALYTICS.

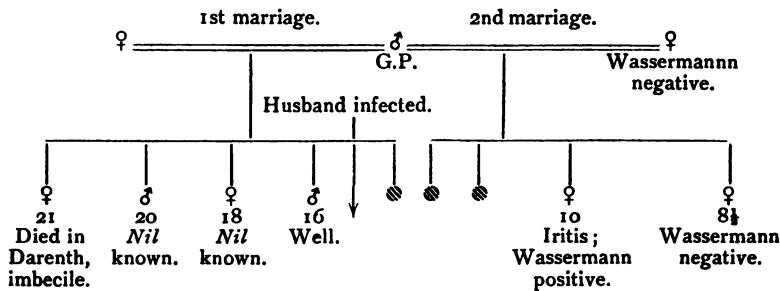
During the last few months the family history of general paralytics, and other cases giving positive serum reactions, have been closely investigated, and wherever possible the serum of their wives and children has been tested. The importance of this work is shown by the few results so far obtained. In some cases it is of great satisfaction to be able to report a negative serum reaction to the wife, and in others giving positive reactions to be able to advise them to place themselves under treatment.

It is to be regretted that such great difficulty attends this work, for often our good intentions are misunderstood, and we are met with a curt refusal on the part of the relatives. We have found, however, that some of the relatives are aware of the fact that they may be infected, and readily assent to the examination of their blood.

Plaut (quoted by Mott, *Archives of Neurology and Psychiatry*, vol. vi, p. 10) investigated the families of 54 general paralytics, and found that 31·6 *per cent.* of the wives gave positive serum reactions ; 37·5 *per cent.* of the husbands of paralytic women were positive, and in only 38 *per cent.* was a transmission of the syphilitic infection to the spouse or offspring not found. The cases with a history of syphilis, and clinical evidence of transmission of syphilis, were remarkably

few. Of the 26 certain, and 8 probable infected children, not one was treated with anti-syphilitic remedies, and in only one was a syphilitic rash diagnosed, and this did not receive any treatment; in all the remainder not one had been thought to be suffering from congenital syphilis.

The few cases I have so far been able to investigate do not enable me to give any statistics regarding the incidence of positive Wassermann reactions amongst the relatives of general paralytics, but my experience bears out Plaut's findings. A number of the spouses have given negative serum reactions, but positive serum reactions have been obtained in many cases in which there were no signs or suspicion of syphilis. The following cases are of interest:



T. A.— Admitted April 18th, 1914. General paralysis. Serum + 40+; lymphocytosis and Nonne Apelt +.

Father insane; suicide. Mother consumptive. A brother and a sister alcoholic. Another sister was seduced, and now a prostitute. The whole family heavy drinkers. Patient married twenty-four years of age, and had four children. He then contracted syphilis, and had mercurial treatment for several months. He infected his wife, who was also treated. She later had a still-born child, and died from septicæmia. The patient married again. His second wife had first two miscarriages, then gave birth to a girl, now æt. 10, who has iritis, and a positive serum reaction; within eighteen months another girl was born, now æt. 8½, whose serum reaction is negative. The serum of the wife now gives a negative Wassermann reaction.

T. H.— General paralysis confirmed *post-mortem*. Admits syphilis contracted fifteen years ago at age of twenty-two. Alcoholism marked. Married six years. Wife infected, and had been under treatment for two years. No children living; three still-born.

W—, æt. 51. Advanced general paralytic. Has an epileptic sister. Contracted syphilis twenty years ago. Married. Wife is infected, her serum giving a markedly positive Wassermann reaction, and is now under treatment. Two children, males, æt. 20 and 18 respectively, said to be well, and to show no signs of infection, but so far I have been unable to test their serum.

I am indebted to my colleague, Dr. E. S. Littlejohn, for permission to quote the following case under his care :

I. D—, female, æt. 23. Admitted October 5th, 1913. Diagnosed as general paralysis on admission. Serum, positive Wassermann reaction; cerebro-spinal fluid, positive Wassermann reaction, positive lymphocytosis, and positive Nonne Apelt reaction.

None of her family show signs of syphilis, but the father, who denies syphilis, gives a markedly positive Wassermann reaction with the serum; the serum of the mother is also markedly positive. They had four children :

Patient, girl, æt. 23. General paralysis.

Girl, æt. 21. Serum, positive Wassermann.

Boy, æt. 19. Serum, negative Wassermann. Tested on two occasions.

Girl, æt. 17. Serum, positive Wassermann.

THE INCIDENCE OF SYPHILIS AMONGST THE CHRONIC IRRECOVERABLY INSANE.

With a view to ascertaining the prevalence of syphilis among the chronic cases resident in the asylum, 150 cases, taken at random from male patients of all ages, all of several years residence and considered incurable, were investigated. General paralytics were excluded from the series of cases, and a positive Wassermann reaction was obtained with the serum in twelve instances, *i.e.*, 8 *per cent.* In none of these cases was there a history of syphilis obtained, neither could any evidence of skin lesions be found.

THE INCIDENCE OF SYPHILIS AMONGST CONSECUTIVE MALE ADMISSIONS.

Since January 1st, 1913, the Wassermann test has been applied to the serum of consecutive male admissions to Cane Hill Asylum; in only 8 cases was the test not made. Altogether 284 sera were examined, and a positive reaction obtained in 89 instances (31 *per cent.*).

Of the 89 positively reacting cases 61 were general paralytics. Excluding these cases a positive serum reaction was obtained in 28 cases of the 223 non-paralytics examined, 12.5 *per cent.*

Mackenzie (*Fourth Report of Scottish Western Asylums Research Institute*) reports the examination of the blood of 786 insane persons. Of that number 234 were supposed from

clinical examination to be general paralytics, and of these 221 gave a positive Wassermann reaction. Altogether of the 786 cases examined 347 gave a positive reaction. Excluding general paralytics, he obtained a positive reaction in 126 cases out of 552, a comparatively high percentage of 22·8. A systematic examination of patients admitted to his wards at the Victoria Infirmery showed that 15 *per cent.* gave evidence of syphilis.

All general paralytics in my series of admissions (61 cases) gave a positive Wassermann reaction, and so far in no instance have I found the Wassermann diagnosis to be incorrect.

Of the 28 non-paralytic cases giving positive serum reactions I was able to obtain a history of infection in 8 instances. The remaining 195 cases giving negative serum reactions included 6 cases that gave a definite history of syphilis, the reaction having passed off as the result of treatment, or attenuation of the virus.

SUMMARY.

(a) The blood of 66 male adult epileptics has been submitted to the Wassermann test, and a positive reaction obtained in 5 instances, 7·6 *per cent.* This figure agrees with that obtained by other workers investigating similar cases, and the adult feeble-minded. The investigation of adult cases probably does not give a correct estimation of the causal relationship of syphilis and epilepsy, as the examination of juvenile cases probably shows a much greater incidence of positive serum reactions, the reaction passing off as the age advances.

(b) The Wassermann reaction has been found of the utmost value in the diagnosis of general paralysis of the insane. Illustrative cases are quoted.

(c) The investigation of the blood-serum of the relatives of general paralytics so far has shown that a good proportion showing no physical signs of syphilis are nevertheless infected. Illustrative cases are quoted.

(d) The blood-serum of 150 male cases of some years' residence in the asylums, and regarded as incurable, has been investigated, and a positive reaction obtained in 12 instances, *i.e.*, 8 *per cent.*

(e) The blood serum of 284 consecutive male admissions

has been tested, and a positive reaction obtained in 89 instances, *i.e.*, 31 *per cent.* Excluding general paralytics, a positive reaction was obtained in 28 cases out of 223, 12·5 *per cent.*

(f) Altogether 439 non-paralytic male adult cases have been examined, and a positive reaction obtained in 41 instances, 9·3 *per cent.*

In conclusion I would express my indebtedness to Sir James Moody for the facilities he has given me to do this work, to the Asylums Committee for the regular leave of absence during the last eighteen months, which has enabled me to visit the Pathological Laboratory of the London County Asylums and carry on this work, to Dr. Mott for his suggestions and encouragement, and to Dr. Candler and Mr. Mann for their unfailing kindness and assistance.

(¹) A preliminary report of this work was published in the *Archives of Neurology and Psychiatry*, vol. vi.

Intrathecal Treatment of General Paralysis. By EDWARD MAPOTHER, M.D.Lond., F.R.C.S.Eng., and THOMAS BEATON, M.D., B.S.Lond., Assistant Medical Officers, London County Asylum, Long Grove, Epsom.

THE purpose of this article is rather to present a general review of the methods of intrathecal treatment of general paralysis, and the results obtained thereby, than to record our own limited and necessarily inconclusive experience.

Although these methods have been used more extensively, and apparently with greater success, in the treatment of tabes and of cerebral syphilis than of general paralysis, we have confined ourselves, for the most part, to their application to the latter disease, as having a more special interest for alienists.

It is now accepted as proven that general paralysis is a form of syphilis of the brain dependent upon the presence of the *Spirochæta pallida*; not only is the Wassermann reaction almost invariably positive in the blood and cerebro-spinal fluid of patients whose cortex *post-mortem* shows the changes characteristic of general paralysis, but, furthermore, the organism can be demonstrated, in a majority of cases, to exist