

616951

CEREBRAL SYPHILIS

A CLINICAL ANALYSIS OF TWENTY-SIX CASES

SEVEN WITH AUTOPSY.

BY

D.K. HENDERSON, M.B., Ch.B.,

Resident Physician,

Henry Phipps Psychiatric Clinic, Baltimore, U. S. A.

---

INTRODUCTION:

CAUSATION

HISTORY OF INFECTION

RE-INFECTION

IMPORTANCE OF CONTRIBUTORY FACTORS

TIME OF ONSET OF NERVOUS SYMPTOMS

MORBID ANATOMY

SYMPTOMATOLOGY - : ( SOMATIC SIGNS  
( PSEUDO-BULBAR PARALYSIS  
( MENTAL SYMPTOMS  
( ANOMALOUS CASES  
( CEREBRO-SPINAL FLUID

DIFFERENTIAL DIAGNOSIS

PROGNOSIS

TREATMENT

SUMMARY

BIBLIOGRAPHY.

## INTRODUCTION:

Syphilis is a subject which has always occupied an important place in medicine, but it is only comparatively recently that our knowledge concerning it has been much increased. Metchnikoff and Roux, Neisser and others have now succeeded in transmitting syphilis to apes, Schaudinn and Hoffman have discovered the spirochaete pallida, Wassermann, Neisser, and Brück have elaborated a bio-chemical reaction which is of the greatest practical importance in diagnosing syphilitic affections, and during the last year Noguchi has succeeded in obtaining a pure culture of the spirochaete pallida. Such a brilliant series of results lead us to the hope that the near future will increase our knowledge still further.\*

Syphilis shows itself in all manner of forms and attacks every kind of tissue, but in this communication I intend only to deal with it as it affects the nervous system and more especially as a factor in the causation of mental disease. The topic is one which is of extreme importance to the state, and of great interest to the physician. It is important to the state owing to the fact that recent studies with the Wassermann reaction have made it plain that syphilis is probably one of the most potent factors in the production of all degrees of congenital feeble-mindedness, and by most physicians it is recognised as the sole cause of general paralysis, locomotor ataxia, cerebro-spinal syphilis, and as a contributory factor in the development of many other organic conditions. If one just considers for a moment what a large

---

\* Since this paper was written Noguchi and Moore in the Journal of Experimental Medicine for February, 1913, have reported the demonstration of the spirochaete pallida in the brain cortex of 14 out of 70 cases of general paralysis which they have examined.

percentage of the inmates of our asylums, almshouses, and feeble-minded institutions are syphilitic either as a result of acquired or hereditary syphilitic disease one may form some estimate of the cost to the state for the upkeep of these hopeless victims. To the physician the disease as it affects the nervous system is a most fascinating one owing to the protean nature and elusiveness of its manifestations.

Syphilis of the nervous system is a relatively frequent disease as according to Dana 5-10 per cent of all those affected by syphilis develop an affection of the nervous system. Other observers put the average at from  $1\frac{1}{2}$  to 3 per cent. Mott asserts, however, that owing to the increased strain of living and owing to the conversion of a rural into an urban population syphilitic affections of the nervous system are greatly on the increase. Why the nervous system is affected in some individuals and not in others is a question which at the present time cannot be answered. Is it due to a very highly susceptible nervous system, or to a specially virulent type of organism? Mott quotes as the most striking example of its being a special neurotoxic virus the cases reported by Brosius of seven glass-blowers each of whom had a chancre of the lip; ten years later five of them again came under observation and it was found that four of them had developed either tabes or general paralysis.

It must be clearly understood that not necessarily everyone who has a syphilitic involvement of the nervous system shows mental symptoms, but I don't think I am rash when I say that probably about one half of them do develop

a psychosis which has many characteristic features. The role of cerebral syphilis as a cause of mental disease has, however, never been quite fully realised, and a glance through the literature is sufficient to show how scarce the systematic and detailed presentations of the subject really are. This neglect seems to me to be partly due to the fact that until a few years ago cases of mental disorder were studied almost entirely from a symptomatic point of view, any excitement being designated mania, any depression melancholia, while it was considered more or less waste of time to attempt to analyse the individual symptoms, and thus find out the main cause of the mental disorder. Even the most modern textbooks on mental diseases deal quite inadequately with this subject, and give us no idea of its importance or frequency. Such a state of affairs is all the more to be wondered at because of all organic affections of the nervous system syphilis is by far the one most amenable to treatment. My object in presenting this thesis is to try to prove that cerebral syphilis has a definite place in the organic psychoses, that there are certain symptoms and signs in cerebral syphilis which when taken together make up a symptom-complex which is characteristic of cerebral syphilis, and which allow us to differentiate cerebral syphilis from any other affection. It is true that in cerebral syphilis as in other disease entities, e.g. general paralysis, dementia praecox, etc. there are a certain number of cases that may be considered atypical, but a disease entity is formed by a majority of cases, and I would therefore state positively at the outset

that the vast majority of cases of cerebral syphilis do show a characteristic symptomatology which allow us to diagnose these cases from cases of general paralysis, arterio-sclerotic <sup>brain disease</sup> and other conditions.

This thesis is based essentially on the study of twenty-six cases, seven with autopsy, which I have personally observed. Twenty-four of these cases were studied in the clinical service of the Psychiatric Institute, Wards Island, New York, and the remaining two at the Royal Edinburgh Asylum, Morningside. In addition to these personally observed cases I have had the opportunity of examining the case-records of twenty-seven other cases of cerebral syphilis, all of which came to autopsy, from various of the New York State Hospitals.

#### Causation:

Since Schaudinn and Hoffman discovered the spirochaete pallida it has been generally accepted as the specific causal organism of syphilis, and has been demonstrated by a host of different workers in chancres, mucous tubercles and papules. In addition to having been found in the primary lesion spirochaetes have been found in infected glands far removed from the primary lesion, in the liver, spleen, and pia arachnoid of children with congenital lues, in syphilitic plaques in the aorta, and in practically every kind of syphilitic lesion.

Mott quotes Hoffman as showing that the cerebro-spinal fluid may be infective, as Hoffman successfully inoculated a monkey with the cerebro-spinal fluid obtained blood-free from a man suffering with a papular syphilide. Dohio and

Yanaka found spirochaetes in the spinal fluid in the case of a patient with a papular eruption, but a second examination was unsuccessful.

Nichols and Hough have very recently reported the exceedingly interesting case of a man, 25 years, who contracted syphilis in September, 1911, received two injections of 0.6 gm salvarsan, and was able to return to duty on December 24th, 1911. In May, 1912, the characteristic mental symptoms and physical signs of a syphilitic involvement of the nervous system set in. The cerebro-spinal fluid was examined for spirochaetes but none could be demonstrated. It was decided, however, to inject 3 cc of the untreated spinal fluid into each testicle of a full-grown rabbit. After a period of fifty seven days some clear rosy fluid was obtained from a resistant area which had developed in the body of the left testicle, and this fluid when examined with a dark-field microscope was found to be rich in active spirochaetes of the pallida type. Twenty four days later the testicle was excised and sections stained by the Levaditi method showed immense numbers of spirochaetes. These spirochaetes have now been transmitted to a second generation, and the incubation period was found to have dropped from fifty to twelve days.

The other testicle, up until date, has been unaffected. Nichols and Hough quote Babes and Panea, Gaucher and Merle, Rach, Sézary and Paillard, as others who have been successful in finding spirochaetes in the cerebro-spinal fluid.

In the tertiary stages of syphilis, however, the spirochaete has been exceedingly difficult to demonstrate, and has been found in small numbers practically only in gummata.

The explanation of their absence in tertiary lesions is probably due to the fact that tertiary lesions are as a general rule non-infective, and furthermore the organism may be in a latent or attenuated form. Strasmann, however, in 1910, reported a case in which for the first time spirochaetes were demonstrated in the central nervous system of an adult with acquired syphilis. The patient had first shown nervous symptoms 8 or 9 months after infection, and died after an illness which lasted for 18 months. The pathological diagnosis was meningo-myelitis, meningo-encephalitis, and Heubner's endarteritis of the great and middle-sized vessels. In the brain, spinal cord, meninges, and blood vessels large numbers of the spirochaetes of Schaudinn were found.

I am fortunate enough to be able to report a second case in which the spirochaete pallida has been found in the central nervous system (Photos 1 and 2). The patient was a married man, 47 years, who was admitted to the clinical service of the Psychiatric Institute on January 19th., 1910. He had contracted syphilis in August, 1909 - just five months previous to admission - was treated by a quack for two months, and then consulted a Dr. Logan for a severe vesiculo-pustular eruption, mucous patches, enlarged glands, and a serous discharge. Dr. Logan treated him with:

R <sub>x</sub> Hydrarg. bin.	gr. 1/16th
X Pot Iodid.	gr. X

Sig. T.I.D.

In addition he is said to have received mercurial inunctions twice daily. He improved for a time, but about three weeks previous to admission, even in spite of treatment, he started to complain of severe pain in the back of his head and neck,

became forgetful, spoke thickly, and on January 7th had a series of six convulsive seizures with loss of consciousness, but without any residual paralysis. During his hospital residence he had a dull, confused, untidy appearance, did not appear to realise or take any interest in his surroundings, but when roused cooperated fairly well in the mental examination. He was slightly euphoric, said that he was happy, but did not express any grandiose or peculiar ideas. No hallucinations could be elicited. He had a poor realisation of time and place, stated that he had been admitted to the hospital on a Sunday or Monday (Wednesday), that he had travelled all the way in a carriage (really in a boat), and that he had been in the hospital for three days (when he had only been for one). He was ~~able~~ unable to mention the main facts of his life correctly, but was quite unable to correlate dates. He made mistakes in doing the simplest calculations, had forgotten all the three retention tests after a period of three minutes, but yet did not realise that his mind was disordered, and said that he thought he was capable of working.

Physically, he had a scar on his penis, and old syphilitic scars on his body. He presented slight residuals of a right-sided hemiplegia, e.g. tongue protruded to the right, and right arm and leg slightly weaker than those on the left side. His tendon reflexes were equally exaggerated on the two sides; there was no sign of Babinski. He had a ptosis of both upper eyelids, pupils reacted promptly both to light and on accommodation, speech and writing showed confusion, but no special distortion. There was tremor of tongue, facial muscles, and hands.



The examination of the cerebro-spinal fluid showed 250 cells per cmm., positive globulin tests, and a positive Wassermann reaction both with the blood-serum and cerebro-spinal fluid.

His condition remained unchanged until the time of his death, ten days after admission.

The autopsy showed a syphilitic basal meningitis with miliary gummata, an acute softening in the left caudate nucleus, and a moderate degree of endarteritis.

A portion of the brain was sent to Professor James Ewing, Cornell University, who was able to demonstrate spirochaetes in a diffuse syphilitic process in the region of the left Sylvian fossa.

The case seems to me to be an extremely important one, therefore, on account of the fact that it developed such a short time after the initial infection even in spite of vigorous anti-syphilitic treatment, on account of its rapid course, and also on account of the fact that this is only the second time that spirochaetes have been found in the central nervous system.

#### History of Infection:

In many well-marked cases of syphilitic disease of the nervous system it is often extremely difficult to obtain a history of the primary infection. It is consequently extremely interesting to remember that in 1865 a Medical Commission appointed by the Admiralty to investigate the whole question of venereal disease gave it as their opinion that sores, both soft and hard, may be followed by every variety of syphilitic eruption. Mott has also stated

decisively that in his opinion soft sores are often syphilitic in nature. Such statements render it imperative for all venereal sores to be examined for the spirochaete pallida so as to be able to definitely rule out syphilitic infection.

Gowers in his Lettsomian lectures has stated that Radcliffe Croker collected 56 cases of tertiary syphilitic skin eruption and in eleven of these no history could be obtained of the occurrence of a primary chancre. Such being the case it is not to be wondered at that not infrequently one comes across cases with syphilitic involvement of the nervous system from whom it is impossible to get a history of primary infection. The question then naturally arises whether the nervous system is more likely to be affected after mild forms of the primary infection - so mild that the primary sore~~s~~ and secondary symptoms are entirely overlooked - or after the severer forms. It seems to me that it is in the mild cases that treatment is either neglected altogether, or else very imperfectly carried out, and it is therefore only logical to suppose that those are the cases which will be most likely to show some further progress of the disease either in the way of gummata, involvement of the internal organs, or nervous system.

A case that well illustrates the points just mentioned is the following: A married man, 33 years old, was admitted to the clinical service of the Psychiatric Institute on December 28th., 1909, presenting unmistakable signs, both physical and mental, of an acute syphilitic involvement of the nervous system. He himself and his wife were repeatedly questioned in regard to syphilitic infection but both absolutely denied

any knowledge of it. A letter from a doctor who had seen the patient outside, however, stated that on July 31st., 1908, the patient was suffering from mucous patches and condylomata, and five months later had a transitory right-sided hemiplegia, which rapidly cleared up under large doses of potassium iodide

In three of my cases all history of venereal infection was denied, in three no definite information could be obtained owing to the mental condition of the patient, one denied syphilis but gave a history of gonorrhoea.

#### Re-infection:

Another question in regard to the etiology of syphilitic conditions is the question of re-infection. Mott seems to hold the view that a person after having once acquired syphilis obtains an immunity and cannot be reinfected. McDonagh, on the other hand, states that there is no evidence to show that there is such a thing as syphilitic immunity either to one's own original or to a foreign virus, and gives as his reason why so few cases of reinfection are seen the fact that so few cases are really cured, i.e. they are syphilitic, and so cannot be reinfected.

The following case~~x~~ supports Mc Donagh's view and furnishes good evidence that reinfection is quite possible: An unmarried man, 42 years old, on January 18th., 1910, was admitted to the clinical service of the Psychiatric Institute in an excited, elated, but somewhat confused state. His memory for recent events was very poor, and from time to time he reacted to auditory hallucinations.

Physically, he complained of severe frontal headache; his optic discs showed a slight degree of neuritis. His

pupils were equal, regular, and reacted promptly to light and on accommodation. His speech was unimpaired, but in writing, letters were occasionally omitted; the tendon reflexes were equally exaggerated on the two sides.

Under anti-syphilitic treatment with mercurial inunctions a rapid improvement occurred, and by March 15th, he had completely recovered.

The point which I wish to emphasize about the case is the fact that after his recovery he gave a history of a syphilitic chancre which he had acquired in 1894. At that time he was in Berlin, and was treated by Professor Lassar for 13 weeks with bi-weekly injections of quicksilver.

A letter obtained from his doctor in New York states that he saw the patient about March, 1909, ten months before the development of mental symptoms, and that at that time the patient had an extensive rash over his body and mucous patches on his mouth and throat, which disappeared under treatment with bichloride of mercury and potassium iodide. He then neglected treatment, and the further symptoms ensued. There seems then from the above statements to be little reasonable doubt in regard to this patient's double infection.

Importance of other factors as causative agents:

Although a syphilitic infection is a sine qua non in the causation of tertiary lesions various other etiological factors are frequently met with which may act as contributory factors, e.g. alcoholic excess, physical or mental strain, and trauma. Some of the older writers for instance used to speak about cases of "traumatic general paralysis", but we now realize that in such cases the trauma simply helped to

light up the underlying syphilitic process. That these contributory factors may however seriously complicate a case and render the diagnosis extremely difficult is very well instanced by the following case: A bartender, 50 years, married, was admitted to the clinical service of the Psychiatric Institute on October 2nd., 1909. He had had syphilis at a date which could not be definitely specified, and had also been excessively alcoholic. Two years previous to admission he was hit on the left side of the head with a sledge-hammer and was rendered unconscious for a short period of time. Shortly after this a change was noticed in his disposition, he became forgetful, complained of severe headaches, and lost interest in things. Three months previous to admission he had a transitory diplopia, dragged his feet when walking, became delirious, imagined he was fishing, and acted at times as though he was picking insects off his wife.

On admission he was in a dull, complacent, mildly euphoric state, and took little interest in his surroundings. He answered questions promptly but made many contradictory statements and fabricated somewhat, saying that he had been in the hospital for six months (two days). He admitted having heard voices calling him names. He was disoriented for time and place, said that the month was August (October), and that the place was Staten Island (Wards Island). In giving an account of his life he made numerous contradictory, and inconsistent statements, and discrepancies occurred in his dates. His power of retention was rather poor, and in carrying out simple calculations several mistakes were made. He denied that his mind was in any way disordered, did not admit feeling

confused, and said that his memory was good.

Physically, his sense of smell was defective on both sides, the pupils were unequal, irregular, and reacted with small excursion both to light and on accommodation; the left side of the face was slightly flattened, but no difference could be made out between the two sides on movement; no speech defect; writing showed omission and transposition of letters. There was general muscular wasting of arms and legs; hand grips were weak, about equal; extensor power of the feet was diminished especially on the left side; the gait was unsteady, and Romberg's sign was slightly present; tenderness was elicited on deep pressure of the leg muscles; the left knee jerk was diminished, the right was normal. The examination of the cerebro-spinal fluid showed a marked pleocytosis.

During his hospital residence he continued to maintain the same dull, drowsy, complacent attitude, and died twenty days after admission.

From the clinical point of view, the case was one which presented numerous difficulties as the three etiological factors: syphilis, alcohol, and trauma, each seemed to have played a part in the development of the psychosis. The head trauma was no doubt the exciting factor in the case as following it there was a definite change in the patient's disposition. Whether or not the head trauma had made him more susceptible to alcohol is impossible to say but the polyneuritic features were prominent in the case, and associated with the mental picture of confusion and fabrications reminded one very much of a case of Korsakow's type of alcoholic psychosis.

From the history of transitory diplopia, the fact that his pupils reacted with limited excursion to light, that his writing was defective, and that he had a marked pleocytosis of the cerebro-spinal fluid, the picture was thought to be complicated by a syphilitic or parasyphilitic affection of the nervous system.

The autopsy showed a well-marked syphilitic meningitis and endarteritis (Heubner's type).

Time of onset of nervous symptoms:

Fournier and Heubner used to hold that it was exceedingly unusual for nervous symptoms to develop within the first year after syphilitic infection, but present day statistics prove them to have been wrong.

Naunyn, for instance, out of 325 cases, 70 with autopsy, has stated that syphilitic disease of the nervous system appears most frequently during the first year after infection, that this frequency decreases from year to year, and that cases of cerebral syphilis rarely occur more than ten years after primary infection. In 22 cases reported by Erb in which the date of primary infection could be definitely determined 59% appeared during the first three years, and 82% during the <sup>first</sup> six years after infection. Mott quotes Kahler as describing a case which occurred while the primary sore was still unhealed, and has himself reported a case of syphilitic basal meningitis which developed ten weeks after infection. He has also reported other cases which have developed four months after infection.

Nonne and Oppenheim each describe cases which have occurred within 3 to 4 months after the primary infection. Kinnier in 1888 described the case of a woman, 35 years, who was in a delirious mental state, had convulsive seizures, and at the same time had typical mucous plaques, enlargement of glands, a specific rash over her body, ulcers on her hips, and typical bullous syphilodermata.

Barrett has described the extremely interesting case of a man, 41 years, who in June, 1902, had a syphilitic infection. He was treated with mercury, and had occasional weeks of mixed treatment. In November, 1902, he was described as having severe headaches, was forgetful, dirty in his habits, "too stupid to eat". In December, 1902, he had a maculopapular rash, mucous patches, and enlarged glands. Later he relapsed into a stuporose state and showed cranial nerve palsies. The autopsy showed what Barrett calls a disseminated syphilitic encephalitis. Head, Gaucher, and Maloizel, Dutheil, Gowers, Harkness, Neu, Ogilvie, and many others have all described cases occurring within a few months after primary infection.

In 17 of my cases of cerebral syphilis in which I have been able to get an accurate history of the date of infection and the onset of the nervous symptoms the average interval elapsing has been six years, the shortest period being five months and the longest twenty-two years. In this case which occurred twenty-two years after infection, the diagnosis of cerebral syphilis was confirmed by autopsy.

From the above statistics, then, one can say with confidence that the majority of cases of cerebral syphilis do

occur within the first ~~two~~ ten years after primary infection. Some cases undoubtedly may and do develop later but they are relatively few in number.

In general paralysis, on the other hand, it is exceedingly rare to have cases developing during the first ten years after syphilitic infection. In forty five cases of general paralysis in which I was able to get an accurate account of the date of syphilitic infection, and the onset of the general paralysis, the average interval elapsing before the onset of mental symptoms was fifteen years.

#### Morbid Anatomy:

Anatomically three main types of cerebral syphilis have been differentiated: meningitis, endarteritis and gumma, but in each individual case there may be a combination of two or all of these elements. The endarteritic type is further subdivided into two forms (1) syphilitic endarteritis of the large cerebral blood-vessels as described by Heubner in his classical monograph in 1874, (2) the small or terminal vessel form of endarteritis described especially by Nissl and Alzheimer. This last form is much less well-known than that described by Heubner, but a number of cases are now on record some of which will be considered later in discussing the symptomatology.

It is principally due to the splendid histo-pathological work of Nissl and Alzheimer that we are now in a position to recognize the different forms of cerebral syphilis post-mortem, and with almost absolute certainty differentiate them from cases of either general paralysis, or arterio-sclerotic brain disease. Just as clinically, however, one occasionally meets with long-standing cases of cerebral syphilis showing

a diffuse intelligence defect which it is well-nigh impossible to say whether it is an acute syphilitic, or a general paralytic disorder, so also at autopsy cases do occur in which the most expert histo-pathologists hesitate to make a definite diagnosis.

I do not intend to discuss in detail the histological changes met with in cases of cerebral syphilis as they have already been most fully and accurately described by Nissl, Alzheimer, Mott, Nonne, Dunlap, and a number of others, but a word may be said in regard to those cases of late cerebral syphilis of the meningo-encephalitic form which are frequently so difficult to differentiate from cases of general paralysis. Dunlap has stated that these two usually distinct processes (cerebral syphilis and general paralysis) can come so closely together that no one can be too positive about which is actually present. The point which Dunlap especially emphasizes is that "whatever is found in the cortex of cerebral syphilis can be fairly definitely shown to be an extension of the process from the pia inward"; general paralysis, on the other hand, is essentially a disease of the cortex.

Other cases are sometimes met with at autopsy in which it is extremely difficult to say whether the vascular changes are of the nature of a syphilitic endarteritis or of arteriosclerotic brain disease. This difficulty was particularly emphasized by Gowers in his Lettsomian Lectures when he said: "As generally met with the disease is recent, and consists in a thickening of the wall, which is more limited than in atheroma, and less opaque. But when such a disease has been treated as by a course of iodide of potassium the thickening is less and the opacity greater, so that the condition re-

sembles more closely ordinary atheroma for which it may usually be mistaken". When such a condition of affairs exists, one can obtain great help in coming to a diagnosis by considering the clinical picture as a whole, paying special attention to the age of the individual, the history of syphilitic infection, and the character and rapidity of onset of the mental and physical signs.

In addition to such cases as the above other cases occur in which plainly there is a combination of an acute syphilitic with a general paralytic process. Many such cases have been reported in the literature, and an excellent example which has occurred in my own experience is the following:

A man, 38 years old, ten months after syphilitic infection developed a right-sided hemiplegia, from which he made a good recovery. He was again able to take up his employment, and worked efficiently for a period of five years. He then came under observation at the Psychiatric Institute for a depression, from which he made, in the course of a few weeks, what seemed a complete recovery. At this time he showed residuals of his right-sided hemiplegia, e.g. right face flattened, weakness of right arm and leg, hemiplegic gait, tendon reflexes more exaggerated on the right side, and continuous ankle-clonus on the right side. There was no sign of Babinski, no hemianopia, no disorder of sensibility, and no tremor of the facial muscles. His sense of smell was defective on both sides. His pupils were unequal, right larger than left, both irregular, the right reacted sluggishly to light, the left reacted promptly; both reacted well on accommodation. There was no disorder of speech or writing. The examination of the cerebro-spinal fluid showed from 15-30

cells with a No. 3 eye-piece and 1/12th lens. Unfortunately at this time no Wassermann examination was made. Two months after leaving the hospital he had a convulsive seizure, was unconscious for two days, and later is said to have expressed some grandiose ideas. About one month later when re-admitted to the Psychiatric Institute he behaved in such a strange excitable manner that at first it was thought that he might be malingering. He denied that he had ever been in the hospital before, denied knowing the physician's name, said that he thought that the physician was in the hardware business, and called the charge-attendant "Antony". Later he lapsed into a quiet apathetic state, and showed especially a very striking defect in his power of retention, e.g. one day after being examined by ten different physicians he had no recollection of having been examined at all. At no time did he express any grandiose ideas. His physical condition remained as noted above but a second examination of his cerebro-spinal fluid showed ten cells per cmm, positive globulin tests, and a positive Wasserman reaction both with his blood-serum and cerebro-spinal fluid. He died one year after admission following a series of three general convulsions.

The autopsy showed in addition to a syphilitic meningitis and endarteritis, a focal general paralytic process affecting the left temporal, supra-marginal, and angular gyri regions.

The case is one of extreme interest, and emphasizes in a very special manner the difficulties frequently encountered in differential diagnosis. Here we had a man who ten months

after syphilitic infection developed a right-sided hemiplegia from which he recovered sufficiently to be able to take up work again. Five years later he had a depression unaccompanied by any intellectual impairment, and without any physical signs suggestive of general paralysis. A few months later, however, following convulsions we have decidedly peculiar behavior and a mental condition of the nature of an acute organic reaction, e.g. marked retention defect, complete disorientation for time, place, and person, and a poor memory for recent events. The physical signs tended to support the view that the case was one of cerebral syphilis. It is now interesting to note that the positive Wassermann reaction both with the blood-serum and cerebro-spinal fluid was really the only point which indicated that the case might be one of general paralysis.

In such a case one can only speculate in a very vague way in regard to the time of onset of the general paralytic process. Was it simply an acute extension of the already existing syphilitic process, or had it been slowly progressive in nature? Without attempting to answer the question one would say that the striking thing about the anatomical picture was that the areas of predilection for general paralysis were essentially free.

#### Symptomatology:

In a disease exhibiting so many pathological types as cerebral syphilis it is only natural to suppose that the clinical signs and symptoms will be markedly erratic, will lack any uniformity, and will vary according to the predominating type. Some writers insist upon describing one

set of symptoms for the meningitic type, another set for the gummatous type, and still another set for the endarteritic type. It seems to me to be utterly valueless so to do, in the first place owing to the fact that practically in every case two or all the types are in combination, and secondly because the treatment is essentially the same in each case irrespective of the type.

The important thing is to try to recognise the disease in its earliest stage, and treat it promptly and systematically.

In considering the symptomatology I intend to take up the physical and mental symptoms separately and in some detail.

1. Somatic signs:

Headache: This is one of the commonest and earliest symptoms met with in cases of brain syphilis, and should be looked upon as a definite danger signal. It is of especial diagnostic value in those cases in which it is severe and persistent in character, and has developed a few weeks or months after the primary syphilitic infection. The great majority of my patients gave a history of having experienced severe headaches which were frequently described as stabbing or throbbing in character, and were localised usually to the frontal region. My experience, however, in regard to the nocturnal exacerbation of the syphilitic headache - which by some is held to be pathognomonic - has been different from that of most others as I must admit that in my cases it has been rarely present. Although the pain is not necessarily nocturnal in character it is rather striking to note that it is very frequently paroxysmal, that it may precede all other

symptoms by months or years, and gives the patient a strained anxious appearance. Patrick emphasizes the fact that headache is especially diagnostic of cerebral syphilis when "in sequence or association with other symptoms", e.g. severe headache preceding the onset of a hemiplegia, monoplegia, or cranial nerve palsy.

Sleeplessness as a direct result of headache is seldom absent.

Dizziness: Just as the majority of patients complain of headache they likewise complain very frequently of a feeling of dizziness or faintness without any definite loss of consciousness, but sometimes accompanied by a feeling of mental confusion. These attacks are probably due to cerebral vascular disorders, and accordingly are very much more common in the endarteritic type of cerebral syphilis than in the meningitic or gummatous forms. Fournier has called this condition the "habitual subvertiginous state", and according to Patrick believes that it is practically confined to cerebral syphilis.

Vomiting: Associated with a history of headache, dizziness and sleeplessness it is not uncommon to get a history of vomiting projectile in type, not in relation to meals, and not accompanied by a feeling of nausea; it is in fact the type of vomiting which is seen in cases of brain tumor.

Those symptoms which have been mentioned are what might be called the prodromal or danger-signal symptoms of a case of syphilis of the nervous system, and it is rare indeed not to get a history of one or all of them. They should immediately put one on one's guard and make one direct the further examination along fairly definite lines.

Anaemia: In 1888 Mc Call Anderson in his presidential address on "Syphilitic Affections of the Nervous System" before the medical section of the British Medical Association made the following statement: "The syphilitic subject is very likely to have lost his healthy appearance, and to have a dirty, earthy, sallow complexion, which is all the more marked the longer the poison has remained unchecked in the system. This peculiar form of anaemia is not constantly present but when pronounced it is very significant of syphilis to the skilled observer, especially if he knows the patient to have had a clear complexion in earlier years".

The above statement struck me as interesting because occasionally one does notice a peculiar "muddy" appearance in these patients which is different from that seen in health. One would hesitate, however, before accepting such a point as a diagnostic sign, or as being especially characteristic.

Polyuria and polydipsia:

These two symptoms are stated by a number of observers to be frequently present in cases of cerebral syphilis, particularly in cases of basilar meningitis. Oppenheim is stated to have found them present in eleven or twelve out of thirty six cases of syphilitic basilar meningitis. They were not prominent in any of my cases.

Temperature: The temperature in cases of cerebral syphilis does not, as a general rule, differ markedly from the normal, and on this account the temperature is of some diagnostic value in differentiating cases of cerebral syphilis from cases of tubercular or other infection of the meninges in which the temperature is usually considerably raised.

Strasmann, however, has reported two cases of uncomplicated cerebral syphilis in which the temperature was raised, and remained raised for a month; it is also well to bear in mind that during convulsive seizures the temperature, both in cases of cerebral syphilis and general paralysis, may rise considerably.

#### Cranial Nerve Affections:

Smell: In cases showing a mental disorder it is often found exceedingly difficult to test the sense of smell owing to defective cooperation either on account of suspiciousness or mental confusion; in nine of my cases I was ~~able~~ unable to come to any satisfactory conclusion in regard to it. Out of the remaining seventeen cases, however, I was able to demonstrate some disorder of the sense of smell in eight, i.e. in 47 per cent. Although the attempt was always made to examine each nostril separately it was sometimes found impossible to do so, so that the tests cannot be considered entirely satisfactory. Although then the statistics are small and the mode of examination not everything that could be desired the results are interesting and show how important a careful examination of the small function might be. ~~of considerable~~ ~~value in diagnosis.~~

Visual Apparatus: Eye symptoms of all kinds and degree are among the earliest and most characteristic symptoms of brain syphilis. Not infrequently a blurring or dimness of vision "seeing double", squint, drooping of an upper eyelid etc are often the first symptoms spontaneously complained of by the patient, and are often stated to have been transitory in nature. It is this peculiar "coming and going" of symptoms

which is especially characteristic. It has been estimated that in the absence of traumatism upwards of 90 per cent of all cases of ocular palsy in adults are caused by brain syphilis, tabes, general paralysis and brain tumor; by far the most frequent causes are brain-syphilis and tabes, and cases of tabes are as a general rule so characteristic that it is exceedingly seldom that they are liable to be confounded with cases of brain syphilis.

The whole question of eye-symptoms in nervous and mental diseases has recently been fully and exhaustively treated in the second edition of Professor Bumke 's monograph on the "Pupillenstörungen bei Geistes und Nervenkrankheiten".

Pupils: In all my cases the pupils have been described as unequal or irregular in outline. This observation, however, is not of any special diagnostic value as in the great majority of cases of general paralysis and tabes, and in a certain number of cases of arterio-sclerotic brain disease, senility, alcoholism, and toxic exhaustive states this same condition of inequality and irregularity is present.

In a previous paper on "The Diagnosis of Cerebral Syphilis" I laid great weight on the extreme rarity of the Argyll Robertson phenomenon as being a distinct help in differentiating cases of acute syphilitic brain disease from other organic affections of the nervous system. Since that time although I have not been able to greatly increase my case material I am now able to say that out of twenty-six cases of brain syphilis I have only been able to demonstrate the presence of Argyll Robertson pupils on two occasions.

Siemerling in an analysis of 1639 cases showing Argyll Robertson pupils found only 1 per cent to be due to syphilis of the nervous system. Mott has stated that although the Argyll Robertson pupil is a sign of syphilitic infection it does not occur in true syphilitic brain disease. J. Michell Clarke in an exceedingly interesting paper considers that the Argyll Robertson phenomenon has to be regarded as an example of "the selective action of a poison upon the central nervous system inasmuch as a special group of neurones having a definite and restricted function is picked out and put out of action". It is pointed out that other parasymphilitic affections offer other examples of similar selective action, e.g. the disease of certain fibers of the posterior roots in tabes. In cerebro-spinal syphilis such results are held to be conspicuously absent as the paralyzes there met with are due to gross lesions. In his series of sixty-nine cases of cerebro-spinal syphilis Argyll Robertson pupils were present in only five cases.

Purves Stewart states that experimental evidence has shown that the ciliary ganglion is the peripheral motor nucleus controlling the sphincter pupillae, and quotes Merina and as reporting twenty-eight cases of tabes ~~of~~ general paralysis exhibiting the Argyll Robertson pupil in which this ganglion was found to be invariably degenerated. "In one of them where the Argyll Robertson phenomenon was confined to one eye the ciliary ganglion was degenerated on that side alone, the ganglion of the other side being normal"

In twelve cases of cerebral syphilis with autopsy reported by Matthews the Argyll Robertson phenomenon could not be demonstrated. Hunt has reported six cases of cerebral syphilis

and has emphasized the fact that the Argyll Robertson phenomenon was always absent.

For the sake of comparison it is interesting to consider the frequency of the presence of Argyll Robertson pupils in general paralysis. Kornfeld and Bikeles found them present in 62 per cent of cases, Raecke in 58 per cent, Joffroy in 53 per cent, Siemerling in 60 per cent, Jolly in 52 per cent, and Westphal in 50 per cent (quoted by Bumke).

Out of a series of fifty-four cases of general paralysis examined by myself thirty-six or 66.2 per cent showed the Argyll Robertson phenomenon. In tabes the percentage of Argyll Robertson pupils is even higher than in general paralysis. These statistics prove very conclusively to my mind how very important in diagnosis the presence or absence of the Argyll Robertson phenomenon really is in diagnosis. Bumke is inclined to belittle it somewhat as a diagnostic aid<sup>c</sup> and speaks of an internal ophthalmoplegia as peculiarly diagnostic of brain syphilis. Internal ophthalmoplegia is, however, a comparatively rare symptom at any time, and therefore its use as a practical diagnostic agent must be extremely limited.

Rose has recently reviewed the literature concerning the presence of the Argyll Robertson pupil in non-syphilitic conditions, and found reports of its presence in some traumatic cases, alcoholism, one case of diabetes, one case of disseminated sclerosis, and some cases of seringo-myelia.

Farquhar Buzzard, however, has reported that absence of the light reflex, unilateral or bilateral, as a solitary ocular symptom might be a most important physical sign, not of syphilis

or of parasyphilis, but of the locality of a cerebral lesion. Buzzard backs up the above statement by the report of two exceedingly interesting cases with autopsy.

1st case: For several weeks previous to admission the patient had had severe paroxysmal headaches which later were associated with vomiting and slight double optic neuritis. Double sign of Babinski. The right pupil did not react to light, the left reacted sluggishly; all the other oculo-motor functions were normal. The autopsy showed a cyst the size of a hazel-nut lying in the 3rd ventricle attached to the choroid plexus, adherent to the fornix and blocking the Foramen of Munro.

2nd case: History of epileptoid spells for three years, and of headache and vomiting for ten months. She had an optic neuritis and slight hemi-paresis. Both pupils were completely inactive to light; there was no other form of ophthalmoplegia.

The autopsy showed in addition to a large frontal lobe tumor, a small cyst lying in the 3rd ventricle attached to the choroid plexus, impinging on the superior colliculus and the posterior commissure.

From the above observations Buzzard believes that absence of the light reflex is a valuable sign of gross disease in the 3rd ventricles or in structures immediately surrounding it, and that it not infrequently constitutes the first localising evidence of that disease.

When not accounted for by optic atrophy absence of the light reflex in cases where a brain tumor is suspected contradicts operation because it nearly always signifies that the tumor is too deep for eradication. Buzzard's observations <sup>have been</sup> ~~are~~ given at some length because they do not appear to be very

generally known, and because if correct<sup>they</sup> merit attention.

Optic Nerve: Ophthalmoscopic and perimetric examinations are imperative in every case of cerebral syphilis. By means of the perimetric examination one may be able to detect not only a concentric contraction of the visual fields, but also hemianopic disturbances which otherwise might not have been suspected.

Two of my cases showed a double optic neuritis, three showed a one-sided optic atrophy, and one showed a retinitis proliferans.

In regard to optic neuritis it may be well to remark that "it is simply a sign of increased intracranial tension and occurs par excellence in cases of brain tumor. It may, however, occur in nephritis, in lead poisoning, in diabetes, and in severe anaemia, and these affections have always to be excluded before thinking of some intracranial affection.

The optic atrophy seen in cases of cerebral syphilis has usually followed a previous neuritis; primary optic atrophy practically always means tabes, or general paralysis, or disseminated sclerosis. Untoff, for instance, thinks it highly improbable that a pure, progressive, primary atrophy of the optic nerve can occur in cerebral syphilis. The case which showed the double retinitis proliferans was that of a sailor, 38 years old, who in 1907 contracted a syphilitic infection, e.g. hard chancre, skin rash, sore throat. He received treatment for a number of months. About one year later he started to suffer from intense headaches, and his eyesight started to fail. He was again treated with mercurial ~~injections~~ inunctions; his headaches disappeared, but no improvement occurred in his vision.

Two years later (In February 1910) he was admitted to the clinical service of the Psychiatric Institute in a highly excited, irritable state, suffering from auditory hallucinations in which he heard people say that they were going to hypnotise him, syphilize him and kill him. He denied ever having had any visual hallucinations but sometimes from his conduct it appeared as if he really suffered from them. His memory and general intellectual functions were well preserved.

Apart from his eye symptoms he exhibited no special neurological features.

The examination of his cerebro-spinal fluid showed a negative cell count of 5 cells per cmm, negative globulin tests, and a negative Wassermann reaction both with the blood serum and the cerebro-spinal fluid. The case is interesting then on account of its showing an acute hallucinatory disorder in a man who apparently had been cured of the syphilitic condition of his nervous system.

A number of my cases showed a homonymous hemianopic disturbance, but these, with one exception, were cases in which the hemianopic defect was associated with a hemiplegia and will be considered later. The exception was a colored man, 38 years old, who gave a history of having contracted syphilis in 1901 for which he received three years treatment. In 1908 he noticed that he could not see anything on the right-hand side of his field of vision, his memory started to fail, and he became depressed. Later his sense of smell became very defective, and on May 15th, 1909 he had a stroke of paralysis, without loss of consciousness, affecting principally the left arm.

Mentally he presented a dull depressed state, made many

inconsistent statements, showed poor judgment, and had no true appreciation of his condition.

The patient died from lobar pneumonia on November 17th., 1909, but unfortunately permission for an autopsy could not be obtained.

3rd, 4th and 6th nerves: Of all the cranial nerves the 3rd seems to be the one by far the most frequently affected in syphilis of the nervous system. Fournier, Knies, and others have stated that in 75 per cent of cases its partial or complete paralysis is syphilitic in origin, but it is extremely rare to see a complete 3rd nerve palsy. In four of my cases the 3rd nerve was partially affected; one case showed a bilateral ptosis; two cases showed a unilateral ptosis; one case showed an internal ophthalmoplegia and in addition a paralysis of the inferior oblique muscle.

The 4th nerve was affected in the patient who had the internal ophthalmoplegia and the paralysis of the inferior oblique; in none of my other cases was the 4th nerve affected.

The 6th nerve was affected in only two of my cases.

Oppenheim in a series of 100 cases observed clinically, found the 3rd nerve affected thirty-four times; the 6th nerve was affected sixteen times; the 4th nerve was affected five times (quoted by Mott) .

Before leaving the consideration of the eye symptoms, one might mention that nystagmus is sometimes seen in cases of cerebral syphilis, and along with the other symptoms is sometimes helpful in diagnosis.

Other cranial nerves: Of the other cranial nerves the 7th nerve was affected in five, and the auditory nerve in four of my cases.

None of the other cranial nerves were affected except in association with a hemiplegic disorder.

Speech: In the majority of cases of brain syphilis the speech remains intact. In some cases an aphasia disorder may be present, but this is usually in association with a right-sided hemiplegia. Occasionally one comes across a case in which the aphasia disorder has occurred independently of the hemiplegia, e.g. N.G.F. ~~case~~ ~~case~~ ~~case~~ a right-handed man who had a left-sided hemiplegia and a motor aphasia. Aphasia disorders occur, however, quite frequently in cases of general paralysis of a focal nature, in cases of arterio-sclerotic brain disease, and in other conditions, and therefore their presence is not of any special diagnostic value.

The point which I wish to emphasize is that in those case of brain syphilis which do show a speech defect - those cases in which there is a hemiplegia - it is of the nature of a dysarthria, indistinct, monotonous, and absolutely different from the thick, slurring, distorted speech of the general paralytic .

Writing: In some cases the writing may be used as a help in diagnosis, but it is by no means a safe guide as so much depends upon the education or lack of education of the individual.

As a general rule in cases of cerebral syphilis the writing usually remains intact, but in a number of my cases it showed defects similar to those seen in cases of general paralysis. Although it is by no means a safe guide it is one which should never be omitted.

Tremor: The tremors which one meets with in cases of cerebral syphilis may be of almost any variety depending upon

whether the anatomical condition is of a specially diffuse nature. Taken by itself tremor in cases of cerebral syphilis is of no diagnostic value, but I think it is important to note - even although it is a negative fact - that the tremor of lips and facial muscles, which is such a common sign in cases of general paralysis, is conspicuously absent in most cases of cerebral syphilis. I do not mean to infer that facial tremor is never present in cases of cerebral syphilis. It is sometimes present as markedly as in general paralysis, but it is relatively very infrequent.

Convulsions: It is a well-known fact that convulsions of any kind - if heart and kidney disease are excluded - coming on in a man between 25 and 45 years of age are most commonly the result of syphilitic involvement of the nervous system. Convulsive attacks are of course especially common in cases of endarteritis, but they are also by no means infrequent in cases of meningitis, particularly of the convexity, and in gummata. The convulsion may be very slight, may be simply limited to a special group of muscles, or it may be epileptoid or apoplectiform in nature. Gowers has stated that in cerebral syphilis the convulsive attacks frequently take place without loss of consciousness, and has reported that in one tenth of fifty cases examined by him this was actually so. Other points that may be emphasized in connection with the fits of syphilitic brain disease are that they are usually focal in nature, and tend to leave permanent residuals. In general paralysis, on the other hand, the seizures are typically general in character, are usually accompanied by loss of consciousness, and frequently leave no residuals; cases of general paralysis with permanent focal symptoms, however, are

by no means rare.

In fourteen of my cases there was a definite hemiplegia or residuals of such, two cases showed a hemiplegia plus an aphasia disorder, one case showed a hemiplegia with hemianaesthesia and analgesia, and four cases showed a hemiplegia with hemianaesthesia and homonymous hemianopia. I regret that I cannot state definitely in how many of my cases the onset of the hemiplegia was unaccompanied by unconsciousness owing to the fact that it is exceedingly difficult to get an accurate history along these lines.

In a great many instances it was the physical examination which was responsible for first bringing it to the notice of the patients that they were suffering from a weakness affecting one or other side.

At this point it might be well to take up the occurrence of pseudo-bulbar paralysis.

#### Pseudo-bulbar Paralysis:

Pseudo-bulbar paralysis is quite frequently met with in cases of cerebral syphilis, and out of my series of cases six have shown well-marked pseudo-bulbar symptoms. It may be described as a bilateral motor paralysis, the commonest cause of which is a bilateral softening or multiple small softenings in the region of the basal nuclei. The usual history is that the patient has had several hemiplegic attacks at first implicating the same side, and then latterly the other side is affected so that a bilateral spastic condition results. These patients speak in a thick, monotonous way, frequently have great difficulty in swallowing, coughing and blowing, and

really show the same subjective symptoms as in true bulbar but are differentiated from ~~the~~ true bulbar palsy by the absence of, atrophy of the paralysed parts, fibrillar tremors, and electrical changes.

Patients with pseudo-bulbar paralysis are particularly unstable emotionally and laugh or cry in an explosive way on the slightest provocation; during the laugh a peculiar inspiratory "crow" is heard.

The cases are of sufficient interest to warrant reporting.

F.J., a married man, 33 years old, denied any knowledge of syphilitic infection, but on July 31st, 1908, is stated by the family physician to have suffered from mucous patches and condylomata. Five months later he developed a right-sided hemiplegia, which rapidly cleared up under anti-syphilitic treatment. For one year he remained well, then again complained of headache, insomnia, double vision, severe sciatica, inability to walk straight and a feeling of weakness. His wife had noticed the gradual onset, without any unconscious spell, of a right-sided hemiplegia which first involved his right leg, then right arm, and right face. Saliva dribbled from the corner of his mouth. Mentally he became childish, had laughing and crying spells, and was untidy in his personal habits. On December 28th., 1909, he was admitted to the clinical service of the Psychiatric Institute. At that time he was in a markedly unstable emotional condition, and laughed or cried at the merest trifles. He, however, cooperated well in an examination, did not express any peculiar ideas, and to a certain extent realised that he was mentally sick. His power of retention of recent impressions, his grasp on current events and his ability to calculate were all found to be considerably impaired. The examination of his cerebro-spinal fluid showed

a very abundant cell-count, and it was interesting to note that 50 per cent of the cells were of the polymorpho-nuclear variety. Films were prepared but no micro-organisms could be demonstrated (Dr. Garvin)

During his hospital residence he continued to exhibit marked emotional instability, was mildly euphoric, and showed a gradual deterioration in his memory, and general intellectual functions. He had forgotten two out of the three retention tests in five minutes, could not tell the Governor or Mayor of New York, and made mistakes in doing simple calculations, e.g.  $9 \times 7 = \underline{54}$ . From time to time he complained of twitching of his tongue and of his left leg, but there was no convulsive seizure.

On March 16th., 1910, he had a transitory paralysis of the external rectus muscle of the left eye. His fundi at this time were reported to be normal, while a perimetric examination showed only slight contraction of the field of vision in the upper half of the left eye. On March 22nd., 1910 it was noted that he had a double sign of Babinski, and a double Ankle-clonus.

On April 27th., 1910, a second examination of his cerebro-spinal fluid showed 30 cells per cmm., but now there was no excess of polymorph leucocytes; globulin tests were positive; the Wassermann reaction was positive with the blood serum but negative with the cerebro-spinal fluid.

Later still he became bedridden, deteriorated mentally, and his laughter and crying were even more explosive, and more easily provoked than formerly.

He now showed a well-marked nystagmus in all directions of gaze, his speech was exceedingly thick, slurring and monotonous; jaw movements were slow and difficult; the tongue was protruded straight, it could be freely moved, and showed no atrophy or fibrillary tremor; he was unable to cough voluntarily. On September 12th., 1910, He developed a paralysis of the left side of the face, and of the external rectus muscle of the left eye, which disappeared under anti-syphilitic treatment.

On November 9th., 1910, Dr. Sohier Bryant (visiting laryngologist) reported a paralysis of the soft palate, and of the left vocal cord.

Finally the patient lost all control over his bladder and bowels, his speech became unintelligible, and great difficulty was experienced in swallowing. He died during the Summer, 1911, but unfortunately permission for an autopsy was refused.

W.E.J., a printer, 40 years, four years after syphilitic infection started to complain of headache, blurring of vision, tinnitus, and poor memory. He was treated with anti-syphilitic remedies, and for fourteen months was able to continue at work. Then again he became mentally confused, his memory became poor, his speech was noted to be defective, and he staggered when he walked.

On admission to the Psychiatric Institute on March 31st., 1909 he presented a dull, drowsy, apathetic appearance. He said that he felt weak, but that he was perfectly contented. He was approximately correctly oriented for time and place. His memory both for remote and recent events was somewhat

impaired, but he was able to give the main facts of his life correctly. He made mistakes in doing simple calculations, e.g.  $6 \times 9 = \underline{30}$ ,  $15 + 17 = \underline{36}$ . He had a fair realisation of his condition, and showed no special abnormality of behavior.

Physically: He complained of headache which was worst at night, and of shooting pains in his legs. His sense of smell was impaired in both nostrils. He complained of having seen double for two weeks previous to admission, and exhibited a paralysis of the left external rectus muscle of the left eye; his pupils reacted to light and on accommodation; his ~~speech~~ speech was thick, slurring, monotonous (bulbar variety); the right arm and leg were weaker than the left, the tendon reflexes were equally exaggerated on the two sides, and he had a double sign of Babinski.

On April 2nd., 1909, a lumbar puncture was performed and showed an abundant lymphocytosis.

On April 4th., 1909 he was noticed to drag his left foot in walking.

In May, 1909, he was feeling much better mentally but complained of weakness in the right side of his body, and said that his knife would occasionally drop from his right hand at meal times; the right foot was now dragged in walking. Gradually, under anti-syphilitic treatment, he began to show marked improvement both mentally and physically. He behaved naturally, became an efficient worker in the mat-shop, and was able to give a good retrospective account of his sickness. On April 5th., 1910, a second lumbar puncture showed a doubtful cell count of 7 cells per c mm., negative globulin reaction, positive Wassermann reaction with the blood-serum but negative

with the cerebro-spinal fluid.

The other physical signs also showed a marked improvement, so that eventually he was discharged in a very much improved condition.

C.G., a glass-blower, married, 39 years, was admitted to the Manhattan State Hospital on January 11th., 1901. In 1890 he had sustained a head trauma following which his disposition is said to have changed. He had also been exceedingly alcoholic. In 1899 he developed a left-sided hemiplegia (he was a right-handed man), and at the same time had a transitory attack of inability to speak which lasted for five days. Following this he started to behave in an outrageous way towards his wife and family, became forgetful, and had two additional strokes of paralysis which, however, were poorly observed. On February 26th., 1906, he was examined by Dr. Macfie Campbell, who found him to be considerably deteriorated mentally and without any true realisation of his condition. He showed well-marked residuals of a left-sided hemiplegia, but his plantar response was noted as flexion on both sides; his speech was stuttering, thick, and at times quite unintelligible; his pupils reacted well both to light and on accommodation.

During the night of March 1st., 1907, he is described as having an "attack of weakness", and in the morning was found to be able to utter only vowel sounds but understood gestures and questions. Later he became very emotional, laughed in a fatuous way, and at times would be exceedingly irritable. He was unable to blow out a candle, had great difficulty in swallowing, and saliva continually dribbled from his mouth.

On September 9th., 1909, Babinski's sign was found to be present on the left side, but on the right the plantar response was still flexion.

He eventually died from dysphagia.

The autopsy showed multiple bilateral small areas of softening in the region of the basal nuclei due to a syphilitic endarteritis obliterans.

W.D., a bar-tender, married, 42 years, fifteen years after syphilitic infection was admitted to the clinical service of the Psychiatric Institute on October 12th., 1910. For four years previous to admission he had been noticed by his wife to be irritable in his disposition, and in the Spring of 1910 was discharged from his employment on account of inefficiency. In August, 1909, he had complained of twitching in both legs which later disappeared under treatment (the kind of treatment could not be specified). During the Spring of 1910 he complained of dizziness and had two attacks of unconsciousness, after the second of which he gradually lost power in his left face, arm, and leg. His hemiplegic condition gradually became more and more marked, he had incontinence of urine, and became forgetful. At times he would become extremely irritable, would tell his wife to go to hell, and would laugh without reason. Just previous to admission he had a third attack of unconsciousness, but an adequate description of it could not be obtained.

On admission he showed an anxious, tearful state, but cooperated well in the examination, and expressed himself as hopeful in regard to his ultimate recovery. He misidentified the physician, called him Dr. Dean (Dr. H.), and said that he had known him for a number of years (which was false)

His memory for recent events was considerably impaired as he had no recollection of having had his photograph taken on admission, or of having been for several hours on another ward. He was able to give the main facts of his life correctly but had great difficulty in correlating dates, e.g. born in 1868, and came to U.S.A. in 1874 when 18 years old. He had a fair appreciation of time and place, did not express any absurd or grandiose ideas, and hallucinations could not be demonstrated.

Physically he presented residuals of a left-sided hemiplegia and also a diminution of touch and pain sense on the left side; there was no hemianopia. In addition his sense of smell was defective on both sides; both pupils were slightly irregular, reacted slowly to light but well on accommodation; hearing was impaired in the left ear; he had at times marked difficulty in swallowing, and saliva continually dribbled from the left side of his mouth; speech was thick, monotonous, and of the bulbar variety; writing showed some distortion of words; all the tendon reflexes were much exaggerated, and there was a double sign of Babinski.

The examination of his cerebro-spinal fluid showed 35 cells per c.mm., positive globulin test, and positive Wassermann reaction both with the blood-serum and cerebro-spinal fluid.

For some time following admission he remained in an emotionally unstable state, was irritable, cantankerous, and at times tearful, but gradually, under anti-syphilitic treatment, with mercurial inunctions, an improvement set in. On November 2nd, 1910, he expressed himself as feeling brighter, now realised for the first time where he really was, stated that

he must have been out of his mind and thoroughly appreciated his need of further treatment.

His hemiplegic condition gradually became less marked, the dulling of sensibility disappeared, and the pupils reacted quite satisfactorily.

Several months later a second examination of his cerebro-spinal fluid showed a negative cell-count, negative globulin reaction, and a negative Wassermann reaction both with the blood-serum and spinal fluid. His general physical and mental condition improved to such an extent that he was finally discharged as recovered.

W.S., 48 years, married, was admitted to the Royal Edinburgh Asylum, on October 9th., 1907. Previous to admission he is described as having been childish and confused, and had the delusion that he had lots of money which people were stealing from him. When examined in January, 1912, he showed a very unstable emotional condition, would laugh and cry in an explosive way without reason, and at times would become very irritable. He was very garrulous, went into great detail, but his memory showed numerous gaps both for recent and remote events. He showed very poor judgment, and had no insight into his condition.

Physically: The history in the case was very defective, but the physical examination revealed the following: The right side of his face was drooped, the right arm was not so strong as the left (right-handed man), but in walking the left leg was held stiff, and the left foot was dragged. The tendon reflexes were all exaggerated, but those on the left side were more exaggerated than those on the right. Babinski sign was present on the left side, and also an ankle-clonus; on the

right side the plantar response was flexion. Right eye showed an internal ophthalmoplegia, and a paralysis of the 4th cranial nerve; the left pupil reacted promptly to light and on accommodation; his hearing was markedly impaired in the right ear. His speech was thick and monotonous, and at times unintelligible; he had difficulty in swallowing, and saliva dribbled from his mouth.

The examination of his cerebro-spinal fluid was negative in every respect (Dr. Winifred Muirhead).

J.G., single, 35 years, was admitted to the Royal Edinburgh Asylum on August 21st., 1907. He denied syphilitic infection but for several weeks previous to admission had complained of severe headaches, and "terrible dizzy turns".

On admission he was described as disoriented for place, and confused in regard to dates; he had a slight paresis of the left side of his face.

When examined in January, 1912, he showed a markedly unstable emotional condition, would laugh or cry in an explosive way on the slightest provocation, and at times would become exceedingly irritable. He could not give the day, month, or year, knew that the place was a hospital but could not tell its name. His memory for recent events was extremely poor, and he had forgotten all the three retention tests after a period of three minutes. His grasp on general information was exceedingly defective, and he made mistakes in doing simple calculations, e.g.  $6 \times 4 = \underline{20}$ . In contrast with the above he was able to give the main facts of his life correctly, and did not express any odd or peculiar ideas.

Physically he presented residuals of a right-sided hemiplegia, but in walking showed a double spastic condition, and

had a double sign of Babinski and a double ankle-clonus. His pupils reacted satisfactorily to light and on accommodation; speech was thick, slurring, and monotonous; there was some difficulty of swallowing and dribbling of saliva. The examination of his cerebro-spinal fluid was negative in every respect, and the Wassermann reaction was also negative with his blood-serum (Dr. Winifred Muirhead).

These cases have been fully reported not because they show any specially unusual features but because they demonstrate very clearly both the mental and physical characteristics of pseudo-bulbar paralysis. The first case of the series reported was particularly interesting owing to the fact that the first examination of the cerebro-spinal fluid showed that 50 per cent of the cells were of the polymorpho-nuclear variety. Such a large percentage of polymorpho-nuclear cells is practically unknown in syphilitic conditions, and of course immediately raised the question of a mixed infection. There was, however, no special elevation of temperature, and the examination of films prepared from the cerebro-spinal fluid failed to show any organism. Subsequent examinations of the cerebro-spinal fluid failed to reveal any excess of these cells.

Another point in the case which deserves special emphasis is the fact that there was a paralysis of one vocal cord. Fernier states that paralysis of one or both vocal cords in cases of pseudo-bulbar paralysis is extremely rare but reports Oppenheim, Siemerling and Munzer as describing such cases.

Mental Symptoms:

There has always been a great amount of uncertainty attached to the mental symptoms showing themselves in cases of cerebral syphilis, but now that we have come to the stage where we are trying to analyse the symptomatology of mental cases, of finding out what the symptoms really mean, and of allowing for the setting in which they occur, we may hope for a clearer formulation.

The main type of mental reaction is what has been described by Adolf Meyer and Hoch as an acute organic reaction and is characterised especially by mental confusion, delirium, hallucinations, and a memory defect for recent events. At first, however, these patients may complain of a certain nervous uneasiness, may feel dull, changed, "mixed-up in the head", and have difficulty in thinking. Their emotional condition frequently shows striking variations, without any definite cause; at one time they will be excited, irritable, resistive and surly, and at another time will show a depressed, anxious easily frightened state. In those cases where there is much increase of intra-cranial pressure dull, stuporous, apathetic states, usually with loss of control over the organic reflexes, show themselves, but a feature which might be emphasized is that when roused these patients are often able to give a fair account of themselves, and are found to be not nearly so demented as their appearance might suggest. Hallucinations of sight or hearing are very often prominent features, and resemble to a certain extent the hallucinations seen in chronic alcoholics in that they are often accompanied by a marked fear-reaction. Some patients show a marked difficulty of

comprehension due to a disorder of attention; delirious states occur with a very imperfect realisation of time and place, and a memory defect especially for recent events is one of the most important and diagnostic mental features. In those cases of cerebral syphilis showing a progressive deterioration diffuse memory defects analogous to those occurring in cases of general paralysis are present, but the characteristic memory defect met with in cerebral syphilis consists, as stated before, of an inability to retain recent impressions. It is ~~known~~ important to realise, however, that memory defects no matter of what nature when occurring in a setting of mental confusion have practically no value or importance in diagnosis. The judgment of the patient suffering from cerebral syphilis is usually relatively little disordered, he has as a general rule a good realisation of and insight into his condition, and his personality is usually well retained. The term "retention of personality" is used in the sense that these patients take some pride in their personal appearance, behave in a natural way like patients in a general hospital, and realise that they are sick. In general paralysis, as contrasted with cerebral syphilis, the patients are usually untidy in their appearance, dilapidated and often outrageous in their behaviour, and have not the slightest realisation of their condition. Certain anomalous features not infrequently show themselves in the mental picture but before describing these I will briefly report three cases to help to drive home the points already mentioned, and to emphasize the characteristic features of the disease.

F.P., single, longshoreman, 28 years, was admitted to the clinical service of the Psychiatric Institute on February 17th., 1909. He had contracted syphilis in 1904, for which

he had received about one month's treatment.

In November, 1908, he began to experience severe headaches localised principally to the frontal region; these gradually increased in severity so that in February, 1909, he had to give up work. He next began to complain of weakness in his right arm and left leg, became dull mentally, spoke only in answer to questions, and cried a great deal. He lapsed into a dreamy, confused state, had no idea of time or place, and was filthy in his habits.

On admission he was in a dull drowsy state, took no interest in his surroundings, and cried during the examination. He complained of feeling weak, thought that he had been in the hospital for fourteen days (really one), and could give no description of how he had travelled here. His power of retention of recent impressions was impaired. He denied ever having had any hallucinations at any time. His memory for remote events was excellent, and no discrepancies were elicited in his dates.

Physically he complained of headaches and dizziness. He could not differentiate the test solutions for smell; the left pupil was slightly more dilated than the right but they reacted promptly to light and on accommodation; his speech was monotonous but there was no gross disorder; his writing was almost illegible. His tongue was protruded towards the left, and there was a tendency to a sign of Babinski on the left side; his tendon reflexes were equally exaggerated; his gait was like that of a drunken man.

The examination of the cerebro-spinal fluid showed a positive pleocytosis.

The patient was immediately started on treatment with

mercurial inunctions and almost at once an improvement occurred. His headaches disappeared, he became less confused, started to take an interest in his surroundings, and to help in the work of the ward. In about a month's time he was able to give a good retrospective account of his trouble, and was practically in his normal condition. In October, 1909, he was discharged as recovered.

D.A., single, salesman, 21 years, was admitted to the clinical service of the Psychiatric Institute on August 31st., 1910. He had contracted syphilis about one year previous to admission. One month previous to admission he became nervous and failed to carry out his orders. Later he started to talk in a confused way, said that he owed money, and that people were hounding him. He complained of drowsiness, felt mixed-up in the head, thought that he was going to receive electricity, and die a painful death. He was sleepless and restless at nights, and had both auditory and visual hallucinations.

On admission he had a dull, confused, frightened appearance, and talked in a rambling, semidelirious way, e.g. Are you married? "No, single, I don't know where it is - with the gold buttons - I was in a restaurant - I am not so strong". Your address? "No I am not sick - but they gave me gas on the ship - I guess I shall sleep". He talked in a confused way about his cousin Eva, said that he was married (false), and that he had married Eva's brother. He said: "Detectives wanted to arrest me because they found out that I had syphilis". He reacted to hallucinations of sight. He could not be got to cooperate in an examination for special tests of memory, grasp on current events, etc.

Physically ~~of~~ he complained of severe headaches, but could not be got to cooperate in the tests for smell and taste. His pupils reacted promptly to light and on accommodation; the right side of his face was flattened, did not move so freely as the left, and he could not close the right eye independently; his speech showed slight ~~sticking~~ sticking but no distortion over difficult test words; his writing showed tremor and some confusion. The tendon reflexes were equally exaggerated on the two sides; marked tremor of tongue, facial muscles and hands.

The examination of the cerebro-spinal fluid showed 105 cells per c.mm., globulin reactions were positive, and a positive Wassermann reaction was obtained both with the blood-serum and cerebro-spinal fluid.

The patient was immediately started on treatment with mercurial inunctions, and in addition in November, 1909 received an intra-muscular injection of 0.5 gramme salvarsan. It was, however, not until about one year after admission that any striking improvement was noted in his condition. In July, 1911, he was <sup>noted</sup> ~~noticed~~ as being neat in his appearance, ~~would~~ greet<sup>ed</sup> the physician spontaneously, played a good game at checkers. He admitted having been frightened for several days previous to admission as he thought someone was going to shoot him, and spontaneously remarked that at that time he must have been out of his mind. He had an amnesia for certain events just immediately preceding his admission.

He was finally discharged in an improved state, but quickly relapsed, and now is in a somewhat apathetic <sup>mental</sup> state.

L.H., single, 26 years, was admitted to the clinical service of the Psychiatric Institute on May 29th., 1909. In 1902, four years after syphilitic infection, he lost the sight of his right eye due to an optic atrophy. About six weeks previous to admission he began to complain of severe headaches, and had four transitory convulsive spells each of which was accompanied by loss of consciousness. Following this he became "foolish-like", did not pay attention to what was said to him, and frequently had to be asked the same question over and over again.

On admission he was drowsy, confused, at times irritable and resistive, and wet and soiled himself. He frequently answered questions quite irrelevantly, complained of having become very forgetful, and reacted with fear to both auditory and visual hallucinations. He had a somewhat imperfect realization of time and place, and a poor memory for both recent and remote events (which was no doubt dependent on his state of mental dullness and confusion).

Physically he complained of headache and presented residuals of a left-sided hemiplegia. His right optic nerve was atrophied, and the right pupil did not respond to light; the left pupil reacted promptly to light, and both reacted on accommodation. There was no gross disorder of speech or writing. The tendon reflexes were slightly more exaggerated on the left side; there was no sign of Babinski.

The examination of the cerebro-spinal fluid showed an abundant pleocytosis.

The patient was treated with mercurial inunctions and potassium iodide, and showed a gradual improvement both men-

tally and physically.

On September 17th, 1909, a second examination of his cerebro-spinal fluid showed a negative cell count, and negative globulin reaction; the Wassermann reaction was not done.

He was finally discharged as recovered.

In addition to these three cases another case may be reported which showed in a very striking way the difficulty of comprehension, and the marked attention disorder frequently present.

A.L., steamfitter, 38, married, was admitted to the clinical service of the Psychiatric Institute on October 26th., 1910. He had contracted syphilis in January, 1909, for which he had received several months anti-syphilitic treatment with mercury. About six weeks previous to admission, however, he started to complain of frontal headache, dizziness, and sleeplessness, talked in a rambling way about Indians, China etc., so that it was quite impossible to carry on a connected conversation with him.

On admission he seemed bewildered but laughed and smiled easily, and when started on a topic could not be diverted from it, e.g. How do you feel? "I am away from Edison's six weeks or perhaps seven".

Have you any dizzy spells? "No, not what you get from the hospital - I don't know - I have no thoughts whatsoever - my wife gave me a can to get something, but when I got on the street I did not know anything".

Have you vomited? "The water was not so extravagantly good - then I went under the bridge which leads to the power house".

What day is it? "Where I work now I am paid \$3 for

eight hours work, etc. etc.". Even although his thought content was so greatly disordered as seen by the above samples there was relatively no disintegration of his personality, and he readily cooperated in the work of the ward.

Physically he complained of intense headache which was worse at night; his ~~ka~~ optic discs were muddy but there was no definite neuritis; his pupils were widely dilated but reacted promptly both to light and on accommodation; the right side of his face was slightly flattened; no speech or writing defect; the tendon reflexes were equally exaggerated on the two sides.

The examination of the cerebro-spinal fluid showed 123 cells per c.mm. positive globulin tests, and a positive Wassermann reaction both with the blood-serum and cerebro-spinal fluid.

Under anti-syphilitic treatment with mercury and potassium iodidix a marked improvement took place both in regard to his mental and physical condition, and he was finally discharged as recovered.

#### Anomalous Cases:

It has already been stated that most cases of cerebral syphilis develop acutely, and within a few years after the primary infection, but other cases do occur which develop slowly and insidiously; the patients show a gradual falling off in their general efficiency, and accordingly from the type of onset raise the suspicion of a general paralytic process.

Such a case was that of J. Mc C., 53 years, who had contracted syphilis twenty-two years previous~~ly~~ to the onset of any mental symptoms. For seven years previous to his admission to the hospital he had been so irritable in his disposition

that his wife finally deserted him. Gradually his earning capacity declined, he had several transitory convulsive seizures, and showed a gradual mental deterioration extending over a period of several years.

On admission to the hospital he was found to be apathetic and contented, showed an especially poor memory for the retention of recent impressions, and made many mistakes in doing simple calculations. He was also disoriented for time and place. He complained of headache and dizziness, and showed residuals of a right-sided hemiplegia. His pupils reacted well to light and on accommodation; his speech showed no gross disorder, but his writing showed tremor and mis-spelling. The tendon reflexes were more exaggerated on the right side, but no sign of Babinski could be elicited.

The examination of the cerebro-spinal fluid showed 7 cells per c.mm., negative globulin reaction, a positive Wassermann reaction with the blood-serum, but negative with the cerebro-spinal fluid.

The diagnosis of cerebral syphilis was confirmed by autopsy, which showed a chronic low-grade syphilitic leptomeningitis most marked at the base of the brain, and a syphilitic endarteritis obliterans.

Another case which serves to illustrate the gradual onset, and was also interesting in other respects was that of J.M., grocer, single, 40 years, who, eight years after syphilitic infection, and two years previous to admission, began to fall off in weight, complained of a feeling as if something was lying on his head, became downhearted, and was less efficient in business. A few days previous to admission to the Psychiat-

ric Institute he had a dizzy spell following which he became delirious.

On admission (June 15th, 1910) he was in a semi-delirious state, misinterpreted the situation, commented on the note-taking, thought he was in a market, and talked as follows: "Well, I guess all right - what is that dozen you are putting down there - no, no we don't need all that for a week - we don't want steak and nothing - want only a couple of items, etc. etc." He could not tell where he was, had lost track of time, and had a very poor memory for recent events. Auditory hallucinations were a prominent feature. He complained of headache and dizziness; his pupils reacted sluggishly but extensively to light and on accommodation; his speech was tremulous but without distortion, writing showed tremor and confusion. The tendon reflexes were equally exaggerated on the two sides. Tremor of tongue and fingers, but none of the facial muscles.

The examination of the cerebro-spinal fluid showed upwards of 100 cells per c.mm., positive globulin test, and a positive Wassermann reaction both with the blood-serum and cerebro-spinal fluid.

Under anti-syphilitic treatment considerable mental and physical ~~xxxx~~ improvement took place, but the examination of his cerebro-spinal fluid always continued to give positive results.

The patient was able to be discharged, but owing to the fact that the spinal fluid results were hardly if at all modified by the anti-syphilitic treatment the case must be looked upon with considerable doubt.

Grandiose ideas:

At one time it was thought that the expression of grandiose ideas of a rather fantastic nature occurring in a setting of euphoria and associated with physical signs pointing to a syphilitic involvement of the nervous system was more or less pathognomonic of cases of general paralysis. The expression of grandiose ideas, however, is not by any manner of means foreign to the mental picture of cerebral syphilis, and is much more common than is generally realised. In one of the cases reported by Matthews, confirmed by autopsy, the patient said that he had \$100,000, and 75 horses, and was markedly euphoric. Head has reported the case of a young man, 21 years, who four years after primary infection became exalted, bought motor cars for which he could not pay, careered about the country at night, and behaved in an altogether spendthrift manner. Under vigorous anti-syphilitic treatment with inunctions a cure was effected. Mc Bride has quoted a case where the patient said that he was the Duke of Argyle, that he was a special favorite of Queen Victoria's, and wrote letters to her calling her "his dearest love". Welsh in a paper entitled "A Degenerative Form of Syphilitic Insanity" states: "The grandiose ideas seen in these cases frequently are of the same type as are seen in general paralysis". A large number of the cases whose records I have had the privilege of examining have expressed a feeling of well-being, and have boasted of their abilities. Three of my own cases are sufficiently noteworthy to be briefly cited:

J.C., 55 years of age, was admitted to the Psychiatric Institute with a complete right-sided hemiplegia, but stated that his head felt clear, that he was happy, that there was

nothing the matter with him, and that he had come to the hospital to join the Order of Foresters. He was drowsy, had lost track of time, constantly wet and soiled himself, but continued euphoric and stated that he had \$10,000 (which was false). The autopsy showed a syphilitic endarteritis obliterans, and a moderate degree of syphilitic meningitis.

N.G.F., 36 years of age, eight months previous to admission in 1902, developed a permanent left-sided hemiplegia, and had a transitory attack of motor aphasia. At the present time (June, 1911) he is somewhat unstable emotionally, and talks in an extremely disconnected and grandiose way. At times he has called himself King of the Universe, the Supreme Being, a millionaire, etc. Notwithstanding the fact that his utterances are so fantastic he remains bright and alert, has a ~~keen~~ keen appreciation of time and place, and takes a great interest in what goes on around him.

In addition to his left-sided hemiplegia he has a double sign of Babinski, and a double ankle-clonus; his pupils show the Argyll-Robertson phenomenon; his speech and writing are excellent and show no defect even when tested with difficult test-words. The examination of his cerebro-spinal fluid showed 50 cells per c.mm., doubtful globulin reactions, and a negative Wassermann reaction both with the blood-serum and cerebro-spinal fluid.

J.M.B., 60 years, for several weeks previous to admission had been noticed by his wife to be "not quite right", talked big, and told his wife that she would be a very rich woman some day. He then later became excited, restless, and very elated, ordered \$50 worth of provisions to be sent to the Lincoln Hospital, said that he was going to marry a nurse,

that he would buy his wife "brand new silk clothes", and that he himself was a Real Estate Agent. He presented physical signs pointing to a syphilitic involvement of his nervous system.

These three cases it seems to me should teach one not to be too easily led astray by the expression of grandiose ideas, but where they occur to carefully study the constitution of the individual, and the setting in which these grandiose ideas occur. If the patient is mentally confused they mean absolutely nothing, but if the sensorium is clear they point more to general paralysis than to cerebral syphilis, although as stated previously and as the three cases reported show they are not at all uncommon in the latter disease process.

Confabulatory states:

Another anomalous feature that sometimes occurs in cases of cerebral syphilis is the presence of a confabulatory state similar to that seen in cases of Korsakow's type of alcoholic psychosis. Kraepelin and Nonne remark on its occurrence, and cases have been reported by Chaslin and Portocalis, Roemheld, Ferchmin and Mooers. The condition is of sufficient interest and rarity to warrant one reporting a case which showed this confabulatory state to a marked degree.

J.C., a native of France, 40 years, was admitted to the clinical service of the Psychiatric Institute on January 7th., 1910. He had always been temperate in the use of alcohol, and had held his positions satisfactorily. He denied ever having had syphilis but gave a history of gonorrhoea five years previous to admission. For several months previous to admission he had been silly and confused, had lost control

of his bladder, ordered expensive things, and talked nonsense.

On admission he was puzzled and confused, had imperfect control of the bladder, and some difficulty in swallowing. Subjectively he had a general feeling of well-being. The striking features about his condition were his complete dis-orientation for time and place, his extremely poor power of retention, and the fact that he fabricated freely, and was extremely suggestible; he could not retain any simple test for more than a few seconds, thought that he was in a naval academy, that the most demented looking patients imaginable were his fellow-students, recognized the physician as a Frenchman, and although repeatedly corrected day after day for many months, called him his "cousin Claude", thought that the charge-attendant was a professor of mathematics, and so on. He was able to give the main facts of his life correctly, and although he had practically no realisation of his condition yet his personality as reflected by his general behavior and manner was well retained.

Physically he presented residuals of a left-sided hemiplegia; his sense of smell was very defective on both sides; vision in the right eye was entirely lost due to a post-neuritic atrophy, and the pupil did not react to light or on accommodation, the left pupil reacted to light and on accommodation; he had a central nystagmus; his speech and writing even over difficult test-words was excellent.

The examination of his cerebro-spinal fluid showed 400 cells per c.mm., positive globulin reactions, positive Wassermann reaction with the blood-serum but negative with the cerebro-spinal fluid.

He has been treated for months with anti-syphilitic

remedies but no material change has occurred in his condition.

Before concluding this discussion of the symptomatology of cerebral syphilis I wish to direct attention to those cases of syphilitic endarteritis obliterans of the small blood-vessels which were first described by Nissl and Alzheimer

Nissl has described one case, Alzheimer has described in all about nine cases, and more recently Sagel and Ilberg have each described a case.

The clinical features are very varied, are difficult to recognize, and seem to depend on the acuteness and diffuseness of the process. The difficulties of diagnosis may be readily appreciated if one glances at the diagnoses in the last six cases reported by Alzheimer; one was diagnosed as epilepsy, one as catatonia, one as general paralysis, two as stationary paralysis, and only one as cerebral lues. Sagel's case was also clinically a very atypical one, and was rendered more difficult than usual on account of the fact that the psychosis developed while the patient was in an anaemic condition, and was suffering from a carcinomatosis of stomach and liver. The mental condition consisted essentially of a confused fearful state with hallucinations of sight. Attention is drawn to the fact that although the histological examination of the brain made the diagnosis of syphilis of the small blood-vessels certain, there never at any time had been any convulsive seizures. Ilberg's case was that of a woman, 22 years, who had always been somewhat dull and peculiar, and who came from a poor stock. Her illness started with convulsions, but later she showed a catatonic state characterised by negativism, cerea flexibilitas, stereotypies impulsiveness, and hallucinations. During the life the diag-

nosis was unclear, an atypical case of general paralysis, a mental disorder associated with diffuse brain syphilis and catonia were all considered.

The autopsy showed a syphilitic endarteritis of the small blood-vessels.

None of my cases have shown this condition of syphilitic endarteritis of the small blood-vessels; in obscure cases such a diagnosis must always be thought of.

Cerebro-spinal Fluid: In a former paper on the cerebro-spinal fluid published in March, 1912 I reviewed the results which I had obtained in the cytological, chemical and serological examination of 118 cases of mental disorder, twenty of which were cases of cerebral syphilis.

In 19 of these 20 cases of cerebral syphilis a pleocytosis was obtained; in 15 out of 19 cases a positive globulin reaction was obtained; 16 cases were examined by the Wassermann reaction using the Noguchi modification, 94 per cent of which gave a positive reaction with the blood serum, but only 50 per cent gave a positive reaction with the cerebro-spinal fluid. A pleocytosis and positive globulin reaction are found almost invariably in both cerebral syphilis and general paralysis; they point simply to there being an inflammatory involvement of the nervous system, and cannot be used with any degree of certainty in differential diagnosis. With the Wassermann reaction, however, a different state of affairs exists. It has already been pointed out how in cerebral syphilis only 50 per cent of my cases gave a positive Wassermann reaction with the cerebro-spinal, whereas in general paralysis 90 per cent positive results were obtained from an examination of 53 patients - a difference of 40 per cent.

Much more striking differences have been reported by Plaut, Nonne, and numerous others.

Here then we have a point which should be of considerable help to us in differential diagnosis but it must be remembered that it is one which cannot be absolutely depended upon. All we can say is that, in the cases which show a positive Wassermann reaction both with the blood-serum and cerebrospinal fluid, the diagnosis of general paralysis is more indicated than one of cerebral syphilis. We are in no position to draw up hard and fast rules in regard to the exact significance of the Wassermann reaction as many cases of cerebral syphilis - according to my experience those of a very acute nature - do give as strong a positive reaction with the cerebro-spinal fluid as with the blood-serum; it is the long-standing, non-progressive cases which tend to give the negative reactions. In each individual case the Wassermann reaction should be closely correlated with the clinical findings, and definite conclusions should only be based on carefully examined autopsy material.

Several cases may be referred to:

A. Mc K. had a negative cell count, negative globulin reactions, a doubtful Wassermann reaction with the blood serum, and a negative reaction with the cerebro-spinal fluid. The patient was a young man, 26 years, who eighteen months after the primary infection suddenly developed a right-sided hemiplegia, and a motor aphasia. He had been systematically treated with anti-syphilitic remedies for a long period of time. Although he was admitted in an irritable, excited state yet during his hospital residence he showed no signs of an active syphilitic process.

J. Mc C. had a cell count of 7 cells per c.mm., negative globulin reaction, a positive Wassermann reaction with the blood serum, but negative with the cerebro-spinal fluid. This was the case in which the mental symptoms developed twenty two years after the primary infection, and which on account of the insidious nature of the onset brought up the question of general paralysis. The clinical diagnosis of cerebral syphilis was confirmed by autopsy.

In two of my cases the examination of the cerebro-spinal fluid was performed by Dr. Winifred Muirhead, Royal Edinburgh Asylum, who reported negative results throughout. These two cases both showed pseudo-bulbar symptoms, and had been non-progressive for several years.

In 1907 Alzheimer perfected a method for the differential estimation of the cells of the cerebro-spinal fluid by which he hoped to receive help in coming to a correct diagnosis in certain forms of nervous and mental disease. Using Alzheimer's method Dr. Winifred Muirhead and myself at the Royal Edinburgh Asylum examined a series of fifty-four cases principally of mental disorder with a view to seeing how far we could use it as a diagnostic aid.

Rehm had used Alzheimer's method over a large and varied material, and had come to the conclusion that plasma and gutter cells were present in the cerebro-spinal fluid of general paralytics more constantly and in greater numbers than in other forms of nervous or mental disease. Furthermore, Rehm was unable to demonstrate plasma cells at all in cases of tabes dorsalis. Our results did not entirely confirm those of Rehm.

Our series of cases included twenty-six cases of general paralysis in all of which plasma cells were found varying in number from 1.5 to 16 per cent; gitter cells were found, in all but three cases, in small numbers.

In the four cases of cerebral syphilis examined by us we were unable to demonstrate either plasma or gitter cells but this was probably due to the fact that each one of our four cases had been non-progressive for several years, and each gave a negative quantitative cell count. Other observers, e.g. Rehm, Hough, have found plasma cells and gitter cells present in the cerebro-spinal fluid in cases of cerebral syphilis but apparently not in such large numbers or so constantly as in general paralysis. It seems to me, however, that at present we have not quite sufficient evidence to allow us, by this method, to draw distinction between general paralysis and cerebral syphilis especially when one considers that the percentage of plasma cells in general paralysis varies all the way from 1.5 to 16 per cent.

Owing to the fact that Rehm was unable to demonstrate plasma cells in his cases of tabes dorsalis it was thought that here we had a sure sign which would allow us to differentiate between cases of tabes dorsalis with a mental disturbance non-paralytic in nature, and cases of general paralysis. In two out of three cases of tabes dorsalis examined by us we were able to demonstrate the presence of plasma cells. The case in which we failed to find plasma cells had been non-progressive for a number of years and also had a negative quantitative cell count, negative globulin reaction, and negative Wassermann reaction both with the blood serum and cerebro-spinal fluid.

From our results then we may say that although Alzheimer's method is the best one yet devised for a careful estimation of the cell types in the cerebro-spinal fluid it has not as yet been proved of any special value in enabling us to differentiate between disease processes which we include under the term organic psychoses.

#### Differential Diagnosis:

As has already been mentioned general paralysis is the condition more than any other which is apt to be confounded with cerebral syphilis. The points of difference between these two affections have already been fully gone into, and it is not my intention to again recapitulate them, but the matter might be focussed a little by emphasizing one or two main points.

An onset occurring within the first few years after syphilitic infection especially when accompanied by a history of headaches, dizziness, sleeplessness, and cranial nerve palsies practically always means an acute syphilitic process of the nature of a meningitis, endarteritis, or gumma; general paralysis, on the other hand, comes on in a slow insidious way <sup>usually</sup> ~~using~~ with a history of falling off in general efficiency, outrageous behavior, mental dulness, and a diffuse memory defect. In other words the onset in cerebral syphilis is usually with somatic signs, whereas in general paralysis the mental symptoms tend to predominate. In cerebral syphilis the mental picture is of the nature of an acute organic reaction and consists essentially of confusion, disorientation, a poor memory for recent events, frequently hallucinations, and delirium; in addition it is well to note that the personality is well retained and that the patient has a good reali-

sation of his condition. In general paralysis one has what may be called a chronic organic reaction characterised by a general intellectual deterioration, a diffuse memory defect, absurd delusions, and total lack of insight.

In regard to the physical signs the one which seems to me to be of most value is the bilateral presence or absence of the Argyll Robertson phenomenon. It is rare indeed that Argyll Robertson pupils are found in cases of cerebral syphilis, whereas they occur relatively frequently in cases of general paralysis; in cerebral <sup>syphilis</sup> the speech and writing are seldom distorted, and tremor of the facial muscles is rarely present. Other differential symptoms between cerebral syphilis and general paralysis such as the type of convulsions cranial nerve palsies, and the Wassermann reaction, have already been sufficiently referred to.

It must be frankly admitted that in neither affection can one rely on any pathognomonic sign, but I venture to say that if the above-mentioned points are kept clearly in mind <sup>the</sup> wrong diagnoses will be exception.

Arterio-sclerotic brain disease non-syphilitic in origin is another condition which may have to be ruled out. As a general rule it is comparatively easy to do so owing to the fact that it usually comes on in individuals over fifty years of age, and is characterised by an irritable, emotional mental state, and a memory defect of a lacunae nature; in addition the examination of the cerebro-spinal fluid shows almost invariably a negative cell count and negative globulin reaction, while the Wassermann reaction is negative both with the blood-serum and cerebro-spinal fluid.

Another disease which sometimes may cause the diagnosis to be in doubt is disseminated sclerosis, but here again the cerebro-spinal fluid findings should almost conclusively differentiate between the two processes as in disseminated sclerosis the results are, except for an occasional positive cell count, almost uniformly negative.

Prognosis:

The prognosis in cerebral syphilis may be said to depend on four main factors: (1) the early recognition and manifestation of the disease (2) the age of the individual (3) the pathological type (4) the amount of systematic treatment.

There can be no doubt that, just as in other disease processes e.g. tuberculosis, the earlier the disease is recognised the better are the chances for ultimate recovery.

Those who have expressed themselves on this subject agree in saying that those cases have the most hopeful prognosis which occur within the first few months or years after the primary syphilitic infection. That has been my experience also, but that excellent results may occasionally be obtained with cases which have developed more than ten years after primary infection is well exemplified by the case of pseudo-bulbar paralysis, already reported, which developed fifteen years after infection in a man 42 years old.

Another case which developed sixteen years after primary infection is also interesting from the same point of view. M.H., 45 years, was admitted to the clinical service of the Psychiatric Institute on January 17th, 1911. In August, 1910, he had had a transitory convulsive seizure following which he became dull, drowsy, and somewhat childish.

On admission he was dull and apathetic, but showed no special psychotic features. His power of retention of recent impressions was somewhat impaired, but on the whole his memory was well retained, and he had an excellent realisation of his condition.

Physically he complained of headache and dizziness, and presented residuals of a left-sided hemiplegia e.g. left face flattened, tongue protruded to the left; weakness of the left arm and leg; knee-jerk was more exaggerated on the left side; Babinski sign was present on the left side, and the abdominal and epigastric reflexes were absent on the left side. When his sense of smell was being tested he said spontaneously "I can't smell anything". His pupils reacted promptly to light and on accommodation; his speech was thick but there was no distortion even of difficult test-words; writing showed omission of letters and words. Tremor of tongue, hands, and facial muscles.

The examination of the cerebro-spinal fluid showed 141 cells per c.mm., positive globulin reaction, a positive Wassermann reaction with the blood-serum but negative with the cerebro-spinal fluid. He was treated at first with mercury salicylate grain I intra-muscularly once a week, and later with mercurial inunctions and potassium.

On February 16th., 1911, the examination of the cerebro-spinal fluid showed 35 cells per c.mm., and positive globulin reaction.

On April 24th., 1911, a third lumbar puncture showed 11 cells per c.mm., negative globulin reaction, a positive Wassermann reaction with the blood serum, but negative with the cerebro-spinal fluid.

He has also shown a very marked improvement in his general condition.

Such cases it seems to me should help to engender a spirit of hope in regard to the treatment and prognosis of cases which perhaps at first sight look somewhat discouraging. In addition to emphasizing the fact that here we had a recovery and an improvement in cases developing respectively 15 and 16 years after infection, it is noteworthy to remark that the patients were both over 40 years of age. The prognosis should always be considered less favorable when a patient is over 40 years of age owing to the fact that vascular changes of a fibroid type are then apt to have set in and consequently the recuperative power of the individual is considerably impaired.

Of the various forms of syphilitic disease of the nervous system those of a meningitic and gummatous nature are by far the most amenable to treatment; the most that one can hope for in vascular disorders, especially those which have given rise to areas of softening, is to arrest the further progress of the disease.

Fournier out of 90 cases gives his percentage of recoveries at 33.3 and Rumpf out of 34 cases at 35.2 per cent. Mickle has stated that one fourth recover, another fourth improve considerably, and half die or survive with grave disease. The most striking statistics are those recently reported by Krower who, out of a series of 59 cases treated with anti-syphilitic remedies, states that 35 cases completely recovered, 11 showed considerable improvement, 4 moderate improvement and 5 died. Out of my series of 26 cases, 6 have recovered, 4 showed considerable improvement, 6 remained un-

improved and 10 died.

When one remembers that the majority of cases which one had to deal with were in an advanced stage of the disease the above statistics should be considered as quite encouraging.

In every case, however, no matter how flattering the recovery or improvement has been the danger of a relapse is a very real one and should be guarded against by strongly urging the patient to refrain from excesses of every kind. Provided that systematic and thorough treatment can be carried out I would strongly urge the adoption of a more hopeful attitude towards this type of case than has heretofore been held.

#### Treatment:

Great differences of opinion have existed, and unfortunately still do exist, in regard to the best method of treating syphilis. The ideal method would be the prophylactic one of refraining from exposure to primary infection, but as that is a plan which probably will never be generally accepted it is our duty to adopt some practical means of curing, or of arresting the further progress of the disease.

Before the introduction of salvarsan the two ~~drugs~~ drugs most frequently relied on in the treatment of syphilitic diseases of the nervous system were mercury and potassium iodide. Mercury has now been conclusively proved by Metchnikoff and Roux to have the power of destroying the spirochaeta pallida, and therefore it must be regarded as a genuine anti-specific remedy. Potassium iodide apparently has no such anti-specific power, and in the treatment of syphilis is simply an adjuvant to the mercury helping to eliminate the

products disorganised by the mercury. On account of this eliminative faculty Gowers used to recommend that mercury and iodide be not given together as by doing so the iodide would tend to hinder the retention in the system of sufficient mercury to act upon the processes of the disease. Gowers also strongly believed in giving only small doses of the iodide usually from 7 to 15 grains, asserting that larger doses especially in endarteritic conditions were dangerous owing to the power they possessed of tending to increase the coagulability of the blood.

In a recent "Discussion on Syphilis" reported in the Proceedings of the Royal Society of London, Jonathan Hutchison, D'Arcy Power, Lane, Mc Donagh and others express somewhat divergent views in regard to the best mode of administering mercury, but all unanimously agree that to get really good results it must be employed in a thoroughly systematic way.

I have principally employed the inunction method and have found it extremely satisfactory; it is painless, and is much less liable to set up gastro-intestinal disturbances than the intra-oral method. The method of procedure was as follows: From  $\frac{1}{2}$  - 1 drachm of Unguent. Hydrarg. was prescribed to be rubbed into a different non-hairy part of the body daily for six successive days. A warm bath was given after every series of rubbings, and no mercury was given on the seventh day. Such a series of rubbings must vary with the individual case, and should be continued until the gums feel sore. Usually after about four weeks the mercurial treatment was stopped and the patient was prescribed potassium iodide in 15 grain doses three times a day.

By this method of alternating the drugs one can keep up anti-specific treatment for a long time without any ill effects; it really carries out Gower's dictum that specific treatment should be "brief, renewed, but not continuous".

In certain cases where it is necessary to bring the patient quickly under the influence of the drug intramuscular injections are exceedingly useful, and in the case of private patients are to be preferred for the following reasons: (1) the method is cleanly (2) the dose of the drug can be carefully regulated (3) it is not an almost constant proceeding as with the inunction method.

Many different preparations may be used but the creams of calomel and metallic mercury as recommended by Lambkin, Power and others appear to be among the best.

Although mercury is an excellent drug to employ there are a certain number of cases which are especially resistant to it, and who despite it develop syphilitic affections of the nervous system. One such case in my own experience was that of F.C., 46 years, who was admitted to the clinical service of the Psychiatric Institute on November 9th, 1909, in a confused, delirious mental state.

Physically he was poorly nourished, was markedly salivated, and complained of severe headaches. His pupils were unequal, irregular, and Argyll Robertson. (Cooperation was poor). The right side of his face was paralysed; his tendon reflexes were equally exaggerated on the two sides; the examination of the cerebro-spinal fluid showed a marked pleocytosis. A letter from the patient's family physician stated that the patient had contracted syphilis in 1904, e.g. chancre, skin rash, and falling out of hair, for which he was systematically

treated for four years with mercury and potassium iodide. Several weeks previous to admission he began to suffer from intense headaches and was ordered potassium iodide grains XX three times a day, bichloride of mercury pills grain  $\frac{1}{4}$  three times a day, and in addition hypodermic injections of mercury salicylate grain I every week. This treatment was continued up until the time of his admission to the Psychiatric Institute. He died nine days after admission.

The autopsy showed a well-marked syphilitic meningitis and endarteritis (Heubner's type).

Such a case as the above focuses the question as to whether we are dealing with a specially virulent type of organism or with an individual who has a very highly susceptible nervous system. It is in such cases, namely those that are exceedingly resistant to mercury that salvarsan appears to have its greatest value. When salvarsan was first introduced it was thought that at last a certain cure for syphilis had been discovered, but its early promise has not been quite realised. That it is an exceedingly valuable remedy cannot for one moment be questioned, but the results from its administration will have to be followed for a number of years before one will be entitled to express a definite estimate of it. The intravenous method of administration is now in most favor.

Shortly after the drug was first introduced and while it was still in its experimental stage I treated several cases of cerebral syphilis by 0.5 gramme injected intra-muscularly. No appreciable benefit resulted from any of these injections but the probability is that it was not the drug but the method of administration and the dosage which were at fault. The technique of administration and of dosage have now been

carefully worked out , and beneficial effects almost invariably follow its use in every form of syphilitic disturbance with the exception of general paralysis, and to a less degree locomotor ataxia.

The custom now is to give a series of intra-venous injections at a few days interval until from 2 - 6 grammes have been introduced. Mc Donagh asserts that the whole secret of the intra-venous method of ~~administration~~ administering salvarsan is to employ only distilled water which has been re-distilled a few hours before the operation; by taking this precaution all unpleasant symptoms such as vomiting, rigors, headache can be wholly avoided.

Neo-salvarsan has recently been coming into vogue; it is recommended on account of its having no after-effects, and because much larger doses can be given at shorter intervals owing to its being more rapidly excreted, and less toxic than salvarsan.

At the meeting in London already referred to everyone spoke highly of the value of salvarsan as a therapeutic agent, but this proviso was added: only as an adjuvant of mercurial treatment, the hypothesis being that "salvarsan kills adult and free spirochaetes, while it has little effect upon those which do not lie to close apposition with the blood and lymph paths, upon immature forms, or upon those in an intra-cellular stage". At the present time then one would say that the best results are probably being obtained by using a combination of mercury and salvarsan.

Whichever method is used the effect of treatment can now be gauged with a fair amount of accuracy by means of the examination of the cerebro-spinal fluid and blood serum.

More recently still Ellis in the Rockefeller Institute, New York, has been employing a method of intra-spinal treatment with which he has been obtaining splendid results, particularly in cases of cerebro-spinal syphilis, and tabes dorsalis. His results have not as yet been published but I have had the privilege of examining a number of his cases and records and can vouch for the beneficial effects of the method of treatment employed by him. The rough details of his method of treatment are as follows: One hour after the patient himself or a definitely syphilitic patient has had an intra-venous injection of salvarsan, a certain amount of blood, usually about 50 cc is withdrawn and centrifuged so as to free the serum from red blood corpuscles; the serum is then heated at a temperature of 56° C. for half an hour after which it is injected intra-spinously into the patient to be treated. By using this method the cerebro-spinal fluid findings have been greatly influenced, and in addition the "lightning pains" of tabetics have been greatly alleviated.

Since the methods above outlined, on the whole, prove so satisfactory, one need hardly consider the strenuous surgical methods recommended by Horsley. Horsley has stated that if improvement does not occur in the case of a gumma from six weeks medicinal treatment that it should be removed surgically. He sees an analogy between the subdural and intra-peritoneal spaces, and upon this basis, in cases of acute meningitis, chronic pachy-meningitis, and syphilitic optic neuritis, recommends opening into the subdural space and irrigating with sublimate solution (1 in 1000).

In conclusion I would like to enter a plea for a more thorough airing of the question of sex hygiene and for the

instruction of both boys and girls in the dangers and common after-effects of venereal disease. If medical men in general would adopt a more straightforward attitude in regard to the question of continence, and would use their influence ~~af~~ in favor of it a great deal would be accomplished in the way of the prevention of venereal disease, and its severe after effects.

Summary:

1. This thesis consists of the systematic clinical analysis of twenty-six personally observed cases of cerebral syphilis in seven of which the diagnosis was confirmed by autopsy.

2. Cerebral syphilis plays an important part in the production of mental disease, and should occupy a more prominent place among the organic psychoses than it heretofore has done.

3. The spirochaeta pallida has for long been surmised to be the causal organism, but it was not until 1910 that Strasmann first demonstrated its presence in the central nervous system of an adult with acquired syphilis; the second case is reported in this thesis.

Trauma, alcoholism, and physical and mental strain are important contributory factors.

Reinfection with syphilis is quite possible provided the initial infection has been thoroughly cured.

4. Anatomically three main types of cerebral syphilis are differentiated, viz: meningitis, endarteritis, and gumma; clinically this differentiation is seldom possible, and is without practical value as the treatment is the same

in all irrespective of the type.

5. The majority of cases of cerebral syphilis develop within the first three years after primary infection, and rarely more than ten years after infection; this is in striking contrast to cases of general paralysis and locomotor ataxia which almost invariably develop at a period more than ten years after infection.

6. In regard to the physical signs the Argyll Robertson phenomenon is the one on which most weight should be laid in differential diagnosis as it is rarely present in cases of cerebral syphilis. Other important features are (a) an acute onset with headache, dizziness, and vomiting (b) cranial nerve palsies (c) convulsions without loss of consciousness but usually followed by permanent focal symptoms (d) intactness of speech and writing (e) absence of facial tremor.

7. The mental symptoms of cerebral syphilis are of the nature of those seen in acute organic reactions and consist of confusion, delirium, amnesia, hallucinations, retention defect, and a poor memory for recent events; in addition there is relatively little disintegration of the personality.

8. The Wassermann reaction must be considered in relation with the clinical picture in each individual case; when the Wassermann reaction with the cerebro-spinal fluid is negative the diagnosis of cerebral syphilis is indicated.

9. It is frankly admitted that there is no pathognomonic sign for cerebral syphilis, but if the nature and character of the onset, and the above mentioned physical and mental symptoms and signs are correlated, a disease entity is formed which has every right to be considered characteristic

10. Cerebral syphilis not infrequently causes pseudo-bulbar paralysis, and six cases of this affection have been here reported.

11. Anomalous features, among which may be mentioned euphoria and grandiose ideas, and confabulatory states, are more common in cerebral syphilis than in generally recognised; special attention must be paid to the setting in which these features occur because when occurring in a setting of confusion they mean practically nothing.

12. Recent statistics confirm one in the opinion that the prognosis of cerebral syphilis as compared with other organic affections of the nervous system is relatively good; the most favorable cases are those which develop soon after the primary infection, and those of a meningitic or gummatous type.

13. Mercury, no matter in what form administered, is an exceedingly valuable drug in the treatment of syphilis provided that it is given in a systematic way. The best results are, however, probably obtained by combining mercurial and salvarsan treatment. Potassium iodide acts simply as an eliminative agent and has no specific action on the spirochaeta pallida.

The only safe treatment is prophylaxis.

BIBLIOGRAPHY.

- Alzheimer, "Hist. Studien zur Differentialdiagnose, d. pro. Paralyse" Jena, 1904.
- Alzheimer, "Die syphilitischen Geistesstörungen". Allg. Ztsch. f. Psych., 1909, LXVI, 920-923.  
— Zentralb. Nervenheil. u. Psych. 1907, No. 239.
- Anderson, "Syphilitic Affections of the Nervous System", 1889
- Arsimoles and Halberstadt, "Sur quelques Syndromes Mentaux dans Syphilis Cerebrale". Rev. Neur., No. 21, Nov 15 1912.
- Barnes, F.M. Bull. #4, Government Hospital, Washington.  
— "Mental Disorders associated with Brain Syphilis". Am. Jour. Insan., April, 1912.  
— "The Syphilitic Psychoses". Med. Rec., Oct. 19th., 1912
- Bikeles, Deutsch. Zeitsch. f. Nervenkk., 1901
- Bristowe, "Syphilitic Affections of the Nervous System", Lancet, 1893, pp. 71, 181, 186.
- Buzzard, Brit. Med. Jour., 1910, Vol. II, p. 1319
- Campbell, C. Macfie, "The Diagnosis of General Paralysis" Jour. of Verv. and Ment. Dis. Mono. series. No. 9
- Chance, Burton, "Oculomotor Paralysis accompanied by Facial Palsy". Am. Jour. Med. Sc., August, 1909.
- Chaslin and Portocalis, Jour. de Psychologie, 1908, p. 303
- Clarke, J. Michell, Brit. Med. Jour., 1903, Vol. II, p. 1634  
— "The Argyll Robertson sign in Cerebral and Spinal Syphilis". Brit. Med. Jour., Feb. 11th., 1911.
- Claude, H., and Levy-Valensi, "Syphilis Cérébrale avec lésions multiples", L'Encephale, 5, 28, 1910  
— "Sur un cas d'amnésie à prédominance antérograde au cours d'un syphilis cerebro-spinale fruste" L'Encephale 6, 1, 287, 1911.
- Collins, Joseph, N.Y. Med. Jour., 1903  
— "Syphilitic Diseases of the Nervous System", Jour. Am. Med. As., April 23rd., 1910
- Dana, Text book of Nervous and Mental Disease, 7th ed.
- Dawson, "The Relation of Acquired Syphilis to Insanity" Jour. Ment. Sc., 1898

- Dewey, "The Psychoses in Cerebral Syphilis", Jour. Am. Med. As., Oct., 1901.
- Dock, G., "The advantage of using Potassium Iodide". Jour. Am. Med. As., Nov, 1909.
- Dowse, T.S., "Syphilis of the Brain and Spinal Chord", 1879
- Dunlap, C.B. N.Y. State Hosp. Bull., Vol. 5, No. 3, Nov. 1912 pp. 449-451
- Dytheil, "Contribution à l'étude de l'Hémiplégie Précoce à la période secondaire de la Syphilis". Rev. Neurol. Vol. 18, 1909, P. 904.
- Ellis, A.W.M., "Secondary Syphilitic Meningitis", Jour. Am. Med. As., Oct. 5th., 1912.
- Fairbanks, A.W., "Cerebral Syphilis in Children" Jour. Am. Med. As., March 9th., 1907.
- Ferchmin, Zeit. f. d. g. Neur. ~~xx~~ u. Psych. Referat. Bd. LV Heft X, p. 1116
- Fournier, "La Syphilis du Cerveau"
- Ferrier, Allbutt and Rolleston's System of Med. Vol. VIII, p. 186.
- Gaucher and Maloizel, "Syphilis Secondaire rebelle au Mercure" Rev. Neurol., Vol. 15, 1907
- Gilbert and Lion, Arch. gen. de Med., 1889, Vol I
- Gowers, Lettsomian Lectures, 1890  
 ——— Clinical Lectures on Diseases of Nervous System, 1895
- Haenel, H. "Beitrag. zur Kenntnis der Syphilis der Centralnervensystems". Arch. f. Psych. u. Nervenhk., Heft II, 1900.
- Harkness, J. Graham, "Early nerve involvement in Syphilis" Jour. Am. Med. As. 58, 478, 1912.
- Harttung, "Cerebrale Lues". Deutsch. Med. Wochen., 1907 XXXIII, p. 2199.
- Head, Henry, "Syphilis of the Nervous System within six years of Infection" Proc. Roy. Soc. of Med. Neurol. Soc., Vol 32, 1910
- Hecht, D'Orsay, "The Treatment of Syphilis and Para-syphilis of the Nervous System". Med. Rec., June 12th, 1909
- Hendersøn, D.K., "The Diagnosis of Cerebral Syphilis", Rev. of Neur. and Psych., May, 1911  
 ——— "The Cerebro-spinal Fluid", Rev. Neur. & Psych, March, 1912.

- Hjelman, Neurol. Centralb. 1894, p. 342
- Horsley, "Surgical Treatment of Intra-cranial Tumor", Brit. Med. Jour., Dec. 10th., 1910.
- Hunt, E.L., "Cerebral Syphilis", Jour. Am. Med. As., May 7th 1910
- Hutchison, Jonathan, Proc. Roy. Soc. of Med., Vol 5, No. 9, Oct., 1912.
- Ilberg, G. "Ein Fall von Psychose bei Endarteritis luetica cerebri". Zeit, f. d. g. Neur. u. Psych. Orig. II, 1, 1910.
- Jallet, E., "Contribution à l'étude des Troubles Psychiques au cours des periodes secondaire et secondotertiare de la Syphilis". Rev. Neurol. Dec 15th, 1912, p. 684.
- Kaplan and Casamagor, "The Neuro-Serological Findings in Tabes and General Paralysis" Arch. Int. Med., Feb 15th, 1912
- Kaplan, "The Laboratory Differentiation between General Paralysis and Cerebro-Spinal Syphilis", Am. Jour. Insan., Oct., 1912
- King, "Paresis and Syphilis", N.Y. State Hosp. Bull., May, 1912
- Kinnier, "Syphilitic Insanity", Alien. and Neur., Vol IX 1888.
- Knoblauch, "The Differential Diagnosis of Cerebral Syphilis" Monat. f. Psych. u. Neur, 1909, XXXI
- c/ Kopczynski, Deutsch. Zeit. f. Nervenhk., 1901
- Kraepelin, Psychiatrie, 8th Ed.
- Kaewer, L. "Zur Diagnostik der Hirnlues", Zeit. f. d. g. Neur u. Psych. Refer. B. II, Heft IX, p. 836.
- Lane, Ernest, Proc. Roy. Soc. of Med. Vol 5, No. 9, Oct, 1912
- Marcus, "Beitrag zur Lehre von den luetischen Geistesstörungen. Allgm. Ztsch. f. Psych. 1909, LXVI, 924-928
- Matthews, A.C. "A Study of the Clinical Manifestation of Cerebral Syphilis", N.Y. State Hosp. Bull., May, 1912
- Mickle, "Syphilis of the Nervous System"? Brain 1895, p. 98  
 ——— Brain, 1898, pp. 232 and 405
- Middlemass, Jour. Ment. Sc., Jan., 1894
- Mooers, Emma W., "A Case of Syphilis of the Nervous System Presenting Clinically an Amnestic Symptom-complex with autopsy" Am. Jour. Insan. Vol LXI, July, 1904

- Mott, F.W., Archives of Neurology and Psychiatry, Vol I  
 ——— "Syphilitic Diseases of the Nervous System", Brit  
 Med. Jour., June 12th, 1909.  
 ——— "A System of Syphilis", Vol IV, Oxford Univ Press  
 1910
- McBride, J.H., "Mental Symptoms of Cerebral Syphilis", Jour.  
 Am. Med. As., Feb 2nd, 1901.
- Mc Donald, William, Am. Jour. Insan., April, 1906
- Mc Donagh, Proc. Roy. Soc. of Med., Vol 5, No. 9, Oct, 1912
- Naunyn, "Zur Prog. u. Ther. der Syph. Erkrank. des Nerven-  
 systems", Leipsic, 1888.
- Neu, C.F., "Report of Ten cases of Brain Syphilis", Alien. and  
 Neur., August, 1910.
- Nicholls and Hough, "Demonstration of Spirochaeta pallida  
 in the Cerebro-Spinal Fluid"., Jour. Am. Med.  
 As., Jan. 11th, 1913, Vol Lx, No. 2
- Nissl, "Zur Lehre der Hirnlues", Allgm. Ztsch. f. Psych.  
 ——— "Hirnlues", Monat. f. Psych. u. Neurol., 1909, XXVI  
 1909, 178.
- Noguchi, "A cutaneous reaction in Syphilis", Jour. Ex. Med.  
 Vol. XIV.
- Noguchi and Moore, Jour. Exp. Med., Feb. 1913
- Nonne, Max, "Clinical Diagnōsis of Syphilogenous Diseases  
 of the Nervous System", Jour. Am. Med. As. July  
 24th., 1909.  
 ——— Syphilis und Nervensystem, 1909  
 ——— Deutsch. Zeit. f. Nervenhk. B. 43, Heft 3 - 6
- Nonne and Holzmann, Deutsch. Zeit. f. Nervenhk. 1909, Vol 37  
 p. 195.
- Ogilvie, G., "The Time of Onset of Syphilitic Disease of the  
 Nervous System", Lancet, 1895, 1, 1368.
- Oppenheim, Text book of Nervous Diseases (Trans. by Alex.  
 Bruce) 1911
- Patrick, Hugh T., "The points of distinction between Cerebral  
 Syphilis and General Paralysis", N.Y. Med J., 1898  
 ——— "The Somatic Signs of Brain Syphilis", Jour. Am.  
 Med. As., Oct 26th., 1901.
- Plaut, Felix, "Sero-diagnosis of Syphilis", Jour. of Nerv.  
 and Ment. Dis. Mono. series, No. 5
- Power, D'Arcy, Proc. Roy. Soc. of Med., Vol 5, No. 9, Oct, 1912
- Ranke, Neur. Centralb. 1908, XXVII, 1082.

- Roemheld, "Ueber den Korsakoffschen Symptomen complex bei Hirnlues". Archiv. f. Psychiatrie, Vol XLI, Bo. 22 1906, p. 703
- Rose, Felix, "La Signe d'Argyll Robertson dans les Affections non Syphilitiques". Sem. Med. No. 49, Dec 4th, 1912
- Russel, Risien, Brit. Med. Jour., 1910, Vol. II, p. 1317
- Sachs, B., N.Y. Med. Jour., 1899
- Sagel, W., "Ueber einen Fall von endarteritischem Lues der Kleineren Hirngefäße" Zeit f.d.g. Neur.u. Psych. Orig. I, 1910.
- Salager, E. "Syphilis et Confusion Mentale", L'Encephale, 1907 2, pp. 101-106
- Schaffer, K., Neur. Centralb., 1904, XXIII, 1026-1039  
"Beitrag zur Frage des Pseudo-paralysis Syphilitica Zeit. d.d.g. Neur. u. Psych., 1910, III, 203, 221
- Seglas, J. "Meningo-encephalite syphilitique, Accidents epileptiques, amnesie retro-antegrade" L'Encephale, 1909, II, p. 330
- Siemerling, E., "Zur Syphilis des Centralnervensystems" Archiv. f. Psych., 1890, XXII.  
Berl. Kliss. Wochen., 1896, No. 44
- Spiller and Camp, "Syphilitic Paralysis of the Trigeminal Nerve", Am. Jour. Med. Sc., March, 1910.
- Strasmann, "Zwei Fälle von Syphilis des Zentralnervensystems mit Fieber der zweite met positivem Spirochätenbefund in Gehirn und Rückenmark" Deutsch. Ztsch. f. Nervenhk. 1910, Vol 40, p. 367
- Stursberg, Deutsch. Ztsch. f. Nervenhk., 1910, Vol 39, p 458
- Turner, Aldren, Allbutt and Rolleston's System of Medicine, Vol VIII
- Weber, "Zur prognostischen Bedeutung des Argyll Robertson-schen Phänomens" Monat. f. Psych. u. Neur., 1907 Bd XXI, H. 3, p. 271
- Welsh, "A Degenerative form of Syphilitic Insanity", Jour. of Ment. Sc., 1899, p. 302
- Wigglesworth, Jour. of Ment. Science, 1893.