

SOME CLINICAL ASPECTS OF GENERAL PARALYSIS.

By W. D. NICOL, M.B., M.R.C.P., D.P.M.,
Medical Superintendent, Horton Mental Hospital; and
E. L. HUTTON, M.B., B.S., D.P.M.,
Assistant Medical Officer, Horton Mental Hospital.

THE employment of malaria as a therapeutic agent in the treatment of general paralysis has focused attention on the latter disease and has provided much material for thought. A discussion on the prognosis and treatment of general paralysis was sponsored by the Association at the quarterly meetings in November, 1928, and February, 1929. The Sections of Psychiatry and Neurology of the Royal Society of Medicine had a similar discussion at the same time, and quite recently the Neurological Section of the Royal Society of Medicine debated the unsettled problems of neuro-syphilis, when the President, in summing up, remarked, "Our problems still remain unsettled".

The general acceptance of general paralysis as an incurable disease with a fatal termination within a few years was undisputed before the days of malaria therapy. The occurrence of remissions following a course of malaria provoked much criticism and a good deal of scepticism. Numerous schools of thought came into vogue: some critics said that general paralysis was prone to remissions and so there was nothing new in witnessing these so-called cures; others maintained that the cases treated were not true cases of general paralysis, while others put forward the theory that changes had occurred in the clinical aspects of the disease, and malaria would never have achieved such results in the old types seen in the past.

In the inquiry undertaken by Meagher for the Board of Control the occurrence of spontaneous remissions without treatment was very definitely refuted. Of 624 untreated general paralytics admitted to mental hospitals in 1923, 90% had died by the end of 1927. He states that "remissions met with denote a transitory, illusory and imperfect improvement, and that complete remission of a year's duration is extremely rarely met with".

The other criticisms offered demand more serious attention: they concern the diagnosis and the possibility of a change in the clinical character of the disease.

Our own experience of general paralysis before the advent of malaria therapy is somewhat limited. One recalls the immediate post-war period at Hanwell, where male general paralytics hastened their last days by floating about on the surface of a water-bed (the use of these was discontinued after

1923, when malaria therapy was first employed at that hospital). Physicians with longer and more mature experience maintain that patients suffering from general paralysis now do not present the same clinical picture. It is difficult to explain this. One may ask, has the modern arsenical treatment of syphilis modified the subsequent development of neurosyphilis? We are not in a position to negate this last suggestion, but we would emphasize a factor of importance, namely, the genuine denial in many cases of a primary attack of syphilis, and consequently the undoubted lack of any antispecific treatment. Another point put forward is the importance of alcohol as a factor influencing the clinical picture presented. Alcoholism was frequently associated with the onset of general paralysis a couple of decades ago, and no doubt masked the symptoms. Has the diminished alcoholic consumption of the present-day generation altered the picture?

Laboratory aids in diagnosis were introduced first about 1910, and since the war have been adopted universally. It was first thought that diagnosis would be made easier, but on the contrary, reliance on the serological findings has led to confusion and wrong diagnosis, with consequent fallacious statistical results. While we agree that the true general paralytic, before treatment, must exhibit a positive Wassermann of the cerebro-spinal fluid, with increased cell content and protein, and, in most cases, a typical parietic curve, we must not lose sight of the reverse, and that is that a positive cerebro-spinal fluid does not necessarily label a case as a general paralytic. In other words, we meet with three clinical varieties, in which the serological findings are positive: (1) The true general paralytic, who should be diagnosed without the aid of laboratory findings, but in whom the Wassermann affords merely confirmatory evidence; (2) those doubtful cases in which there may be one or two vague mental symptoms or clinical signs possibly suggestive of general paralysis, and in which the presence of a positive result should indicate the possibility of general paralysis and the advisability of therapeutic measures; (3) those cases in which, in the course of routine examination, a positive serum is discovered, so demanding a lumbar puncture, yet in spite of positive serological findings they can in no way be regarded as suffering from general paralysis.

Clouston* was quite definite about general paralysis; he regarded it as a distinct clinical entity and defined it thus: "An organic disease of the cortical part of the brain characterized by progression, by the combined presence of mental and motor symptoms, the former always including mental enfeeblement and mental facility, and often delusions of grandeur and ideas of morbid expansion or self-satisfaction; the motor deficiencies always including a peculiar defective articulation of words, and always passing through the stages of fibrillar convulsion, inco-ordination, paresis and paralysis; the disease process spreading to the whole of the nerve tissues in the body, being as yet incurable and fatal in a few years."

* *Mental Diseases*, 6th ed., 1904.

Kraepelin* described general paralysis as "a progressive deterioration leading to complete undermining of the whole mental and physical personality, accompanied by peculiar irritative and paralytic phenomena".

Mott† summarized general paralysis: (1) Progressive dementia, usually accompanied by mental exaltation; (2) unequal, generally irregular, pupils, reacting sluggishly or not at all to light, but reacting to accommodation; (3) progressive paresis with tremors especially affecting the tongue and face muscles; (4) hesitant, tremulous, slurred speech, with elision of syllables, and similar affection of handwriting; (5) altered knee-jerks, generally exaggerated, sometimes absent on one side, more often on both sides.

The psychiatrists of the past diagnosed general paralysis without the aid of laboratory findings, yet, in all these descriptions quoted, the course of the disease, with its fatal termination, was stressed, and it was the subsequent development which doubtless confirmed the original diagnosis.

To-day the disease is no longer fatal, indeed a certain percentage of cases treated by malaria recover sufficiently to enable them to be discharged; in others the progress of the disease is arrested. Have we not, then, to view general paralysis from a different aspect? Our aim in this discussion is to present to you some of the clinical aspects met with in general paralysis, and to derive from a study of those signs and symptoms some information which may enable us to diagnose the true case of general paralysis which should benefit from malarial therapy, and elucidate those factors which influence the course of the psychosis and afford some assistance in prognosis.

Unless otherwise stated, the material for this paper has been collected from approximately 100 consecutive admissions of each sex.

The early recognition of the disease is of paramount importance, but unfortunately most difficulty is presented at the onset, when physical and mental symptoms are indefinite. Pre-paretic symptoms in many cases pass unnoticed for long periods, and it is only when the fully developed parietic symptoms exhibit themselves that relatives seek advice, and on looking back can recall evidence of commencing mental disorder. An accident is not infrequently a precursor; changes in character, irritability, outbursts of temper, apathy or emotional instability are frequent; wandering, confusion and amnesia, poorly executed work and a gradual falling off in efficiency have been noticed. Insomnia or excessive sleepiness may be present—in fact some cases have been suspected of encephalitis lethargica. Slurring of speech is an extremely valuable sign, and often an early one. An unexpected fit, with no resulting paralysis, sometimes heralds the onset of the disease. A very sudden onset of grandiosity or gross confusion is relatively rare, but a phase of depression preceding the development of grandiose ideas is often observed.

It is only when the disease is fully established that it becomes possible to

* *General Paresis*, Kraepelin, Nervous and Mental Disease Monograph Series, No. 14, 1913.

† *Archives of Neurology*.

label the different types of general paralytics. The classical grandiose type, the manic and the depressed forms do not afford much difficulty in diagnosis. The simple dementing form is characterized by a general mental deterioration, but must be distinguished from a fifth type, the confused parietic. The differentiation between definite confusion and dementia presents great difficulty; both may show amnesia, disorientation, restlessness and faulty habits, yet the recognition of the confused type holds out a very fair prospect of recovery compared with the bad prognosis associated with the dementing case.

One must realize, however, that the classification of the patients into different types means no more than that in these patients certain symptoms dominate the clinical picture, so that we can accordingly label them as pure types, e.g., grandiose, confused, depressed, manic or simple dementing; or mixed types, grandiose with confusion, mania with simple dementia, etc.

The occurrence of these mixed types, and the transition of a patient during the course of his illness from one category into another, leads us to suppose that these differences in symptomatology do not so much represent different forms of the disease, as different events in the development of the disorder from its inception to its ultimately fatal termination.

If this is so, the thorough investigation of all the symptoms will lead to the correct classification of the patients, and thus to a truer appreciation of the actual pathological conditions present when the patient comes under observation. These findings may afford us the explanation for the failure of some seemingly recent cases to respond to treatment. For example, it often happens that the clinical picture of the simple dementing case is tinged with a strong grandiose or confused element, and one is apt to hold out false hopes of recovery because undue attention is paid to the obvious grandiosity or confusion, whilst the less obtrusive dementia is ignored.

The early discovery of physical signs should afford much help in arriving at a diagnosis. Whilst it must be borne in mind that most of the cases observed by us are drawn from the rate-aided classes, one has been informed quite spontaneously by intelligent relatives that slurring of speech has been noticed in some cases for a considerable length of time. It would appear that some of the physical signs—slurring of speech, tremors of the face, exaggerated tendon reflexes and pupil changes—occur really early in the course of the disease and are not later manifestations. In the women, slurring of speech is very common, occurring in 80%; the presence of tremors of the tongue, facial muscles and hands was nearly as frequent. Increased knee-jerks and Argyll Robertson pupils were present in about half the cases. In the men, slurred speech and tremors were less often observed (about 55%), increased tendon reflexes in about 25%, and pupil abnormalities with Argyll Robertson reaction in one or both eyes were recorded in just over 40%. The concurrence of tabes with general paralysis was present in 5 women and 6 men; in both sexes, absence of knee-jerks was noted in about 15%, but without any other evidence of tabes.

Rombergism, also not associated with tabes, is relatively common in the untreated male, but rare in the female.

Seizures occurred in 23 men and in 30 women, and in 3 of these cases, 2 women and 1 man, alcohol may have been a contributory factor. The number of seizures in these cases varied; in some no more than one fit is recorded, which may either have been the first symptom noted, or may have occurred at some later period in the course of the illness. In yet others, fits occurred in large numbers, and in some a condition resembling status epilepticus developed. The majority of the seizures noted seem to have occurred in the post-malarial phase, i.e., in later rather than in the earlier periods.

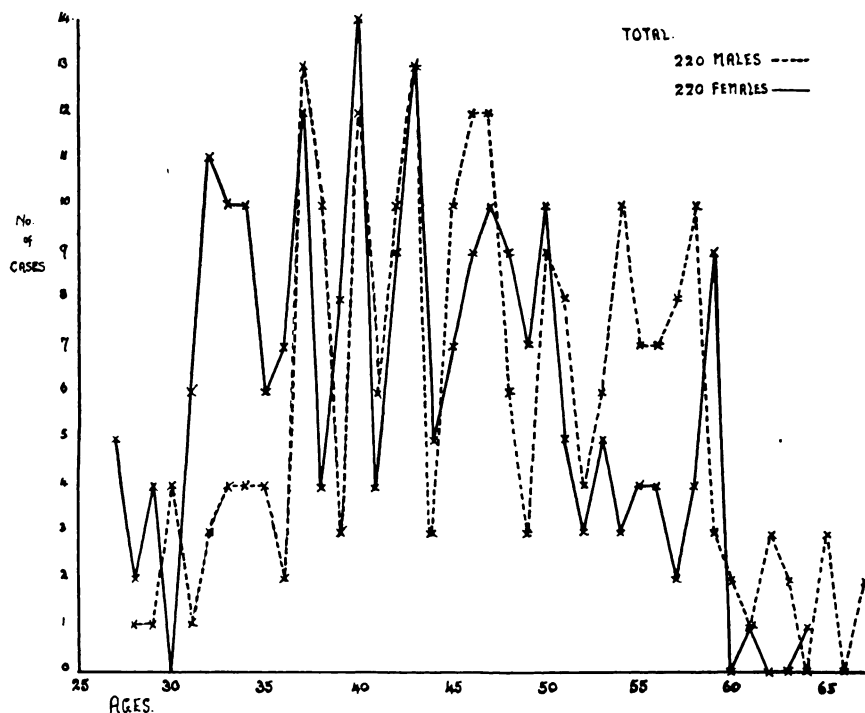
When seizures are correlated with the psychological findings there seems to be overwhelming evidence that seizures very rarely occur in the pure grandiose or confused types, that they occur most frequently in the pure dementing type, and that in whatever type they occur they are almost invariably accompanied or followed by some degree of dementia. Out of our total series only 3 cases—2 women and 1 man—made a good recovery. At the same time it must be borne in mind that just as the simple dementing type may run a very slowly progressive chronic course, so also do we find that some of these patients with seizures, if they do not succumb with exhaustion from very severe or prolonged convulsions, form part of the permanent hospital population for many years.

If the conclusions which we have drawn from these cases are correct, then, although the occurrence of one or more seizures is no contra-indication to the use of malarial therapy, the benefit to be derived therefrom is likely to be more or less limited, depending to some extent on the co-existent dementia, and any history of seizures must therefore influence the prognosis in an unfavourable manner.

The age-incidence is represented on the accompanying chart. It includes 220 cases of each sex. No case is recorded before the age of 26. In the women there is a sharp rise soon after the age of 30; it is not till after the age of 35 that the incidence amongst males becomes really high. Between the ages of 35 and 45 the largest number of cases is observed, the peak being reached at 40. It will be noted how the peaks of incidence over this period coincide with the two sexes. After the age of 45 the incidence among men still remains fairly high, while in the women, apart from the period over the climacteric, there is a big fall in the numbers observed until the age of 59, when a presenile rise appears. This incidence agrees fairly closely with statistics quoted by Kraepelin, women being affected earlier on the average than men, but the incidence remaining high much later in the male. We are at a loss to explain the curious peaks with their four-yearly falls. With the large number of cases observed it seems more than a coincidence that this regular rise and fall should occur.

We do not propose in this paper to follow the clinical course of those

treated cases, but the change in psychosis following malaria therapy deserves notice. Kraepelin recorded that "the course of all forms of paresis may be altered, almost in an unforeseen manner, by two different events—paralytic attacks and remissions". A new clinical picture is now presented, and in our experience what was once a typical paretic may become metamorphosed into a schizoid personality, whilst in others a hallucinatory psychosis may supervene. There is no record of these phenomena occurring prior to malarial treatment. It is not uncommon for cases, which have failed to respond



to treatment, to develop a dementia characteristic of the schizophrenic, so that many of these cases, were their history not known, would be diagnosed as cases of dementia præcox. Hallucinations will occur during malaria fever, and subside soon after treatment has been terminated. The occurrence of hallucinations in the early untreated cases is not of serious import, but the development of an hallucinatory psychosis following treatment is definitely of bad prognosis. It is comparatively rare, and has been observed in only two men over a series of nearly 200 treated cases; in women it is a little more frequent. No case has recovered; it may persist for years, while in others a fatal termination has ensued in a comparatively short time.

Yesterday, at Springfield Mental Hospital, Dr. Worth allowed me to see a woman who was a patient in my hospital some years ago. Her case was of fairly recent onset. We gave malaria, and after three months she was in the convalescent villa. A few months later she relapsed. She had an acute hallucinatory psychosis, which abated for a time. She went out under the care of her mother, under Section 79, and remained out a year. She came back to us in 1927, very much worse, her physical condition rapidly deteriorating, and I thought she would die. She was mentally in a state of inaccessibility, and she had visual hallucinations. There was very marked hyper-extension of the fingers. She got into the habit of holding a photograph of her husband in the hollow of her hand and contemplating it with arm extended. She was later removed elsewhere and I did not see her for eight years. She is in a much better physical state than formerly, but is quite inaccessible; the nurse says she never talks, is faulty in her habits, and still looks at the photograph held in her hand and mutters, as she did eight years ago.

Other cases which do not recover either show temporary improvement and arrest of their mental symptoms or exhibit gradual deterioration; patients of grandiose or manic type will lose their essential characteristics, which become replaced by a simple dementia.

Another problem offered is by the patient who has been discharged in a good state of remission and subsequently relapses. During the past ten years 10 women and 6 men have come under observation. One woman returned after three years with a definite hallucinatory psychosis; she remains in the same state after five years. Others relapsed with a confusional attack, from which emerged a certain degree of dementia. Another patient, originally of grandiose type, who had remained well for over a year, returned in a depressed state, with somatic delusions of such a distressing nature that suicide had been attempted; he has remained in this condition for three and a half years. Some of the demented and depressed types have died subsequently; only two cases have gone out again in a fair state of remission; one had a mild confusional attack, and the other, after two years' remission, became acutely depressed and agitated, with a certain degree of confusion and no insight (in this latter case there was no evidence of a manic-depressive psychosis). Though physical signs of general paralysis may be present, they are less marked than on the previous admission; indeed were it not for the history, diagnosis would not be easy in some cases; in only one case has a relapse presented a typical grandiose picture with emotional instability, slurred speech and generalized tremors—this man received a course of sulfosin at another hospital in 1932 and apparently remained well for two years.

It is a matter for regret that some hospitals still preclude their general paralytics from receiving malarial therapy. We do not know why; unfortunately we have not received the benefit of any publication which could inform us

as to the fate of these untreated general paralytics. During the last ten years we have accumulated some evidence regarding untreated cases, and a brief analysis is worth considering. Thirty-two women and 23 men were not given treatment because of their poor physical condition on admission. Of the women, 10 were fulminating cases of the confused, manic and depressed types. The average age was 43, ages ranging from 33 to 56; all died within seven months of onset of symptoms. Of the remaining 22 women, 16 were simple dementing types, and 14 were dead within two years of onset of disease. In a few the disease had lasted up to seven years. Tabes was associated with only 2 cases. The average age of these non-fulminating types was higher, being 50, ages ranging from 37 to 59. It is noteworthy that 5 of the cases exhibited contractures in the latter stages of the disease. The incidence of fulminating cases amongst the men was higher—13 out of 23, 5 being associated with tabes; the average age was 47, ages ranging from 35 to 56. Grandiose, confused and manic types were present in only 5 cases, and it is interesting to record that apparently the remaining 8 cases, in spite of the short history, were of the simple dementing type. All these cases died within seven months of onset, some within a few weeks. The remaining 10 non-fulminating cases all died within three years of onset and, with the exception of one grandiose and one depressed case, were of the dementing form; the average age was higher, being 55, and 2 had associated tabes.

The interpretation of the clinical facts of the cases collected can afford some assistance in prognosis. No good recovery amongst the women has occurred after the age of 50, and only 3 men over 50 have shown a good remission. A most constant feature is the length of time that elapses between the date of malarial treatment and the time of discharge. Every good remission is ready for discharge from hospital within six to nine months after treatment. We feel certain that one can say, with a good deal of assurance, that if a patient is not well enough to be discharged within that period, the hope of ultimate recovery must be abandoned. The occurrence of seizures in general paralytics should be viewed with concern; though a few cases in which seizures have been exhibited have been discharged, it is quite evident that the large majority of cases steadily deteriorate. It is the differentiation of the clinical types that affords most information regarding the chances of recovery.

In both sexes one cannot fail to be impressed with the very high recovery-rate in the pure confused, grandiose or manic types. Though in a series of 100 cases of each sex the numbers are necessarily small, it is clearly borne out that this high rate of recovery is due to early diagnosis and early treatment. Of 14 women exhibiting grandiose, manic or confused types, the average duration of the pre-paretic or parietic history was just over three months. Only one case failed to respond to treatment, and in this case there was a prolonged history of alcoholism; she has now become demented, with grandiose

delusions. Of the true simple dementing types no patient gave a pre-paretic or parietic history of less than five months, and two who had a history of five and six months respectively were dead within a year, suggesting that they were fulminating types. Amongst the men, however, two made good remissions, having a short onset of a few months. Nevertheless, the vast majority of simple dementing cases, whether men or women, fail to respond to treatment, and we attribute this to the long pre-paretic history with which these cases are associated.

The classification of types becomes more difficult when one finds grandiosity, confusion or dementia co-existing, but it has seemed advisable to us to introduce these mixed types, paying attention to the relative importance of the different symptoms.

When one considers these mixed types, the results are equally disappointing; nearly all cases remain deteriorated or demented. The majority have a long pre-paretic or parietic history, but one does meet with cases of a short duration which show an unsatisfactory or even fatal result, and indeed in the fulminating cases the brevity of the onset possesses an ominous significance. Therefore in these cases the presence of symptoms indicating the existence of definite mental deterioration will prevent our giving an unjustifiably hopeful prognosis, based on the fallacy that we are dealing with an early and therefore recoverable case. The rate of onset cannot, in itself, be regarded as a reliable prognostic aid; the type of symptoms must also be considered.

Since the discovery of spirochætes in the brain tissue in cases of general paralysis it seems rational to regard the symptomatology of this disorder as due to the abnormal functioning of the brain cells affected by the infective process.

This abnormal functioning may be due either to irritation of the cells, or to their destruction; moreover, although irritation may ultimately lead to destruction, one would not expect the reverse process to occur; a cell that has been destroyed must cease to function, and cannot give rise to symptoms dependent upon a pathological activity. Further, the irritation may subside without causing any permanent damage, whereupon the concomitant symptoms will disappear, and a cure, or at any rate a remission, may occur. This, however, can never happen when destruction has actually supervened, and these cases will therefore show a permanent if not a progressive defect.

If one regards the symptomatology of general paralysis according to this hypothesis, is it not possible to consider that the grandiose delusions, the attacks of confusion and the maniacal outbursts are produced by certain irritative phenomena occurring in the brain cells, and that the progressive dementia is, on the contrary, due to actual irreparable destruction of the brain tissue? We have recorded the good recovery-rate associated with pure grandiose, confusional or manic types, and the poor result of the case which has once shown signs of a true dementia. Moreover, though these pure types, if not treated early, will become demented, it is rare for a simple dementing case to develop

grandiosity or mania, and even though grandiose delusions or mania may arise comparatively late in the development of the simple dementing type, there is no evidence among our records of a simple dementing patient whose mental state became such that he could be classified as a pure grandiose or manic type. Similarly with the mixed types, the grandiose and demented, the confused and demented, or the manic and demented, it is rare to meet with a good recovery, and even where improvement occurs there is always some permanent defect.

Differences in symptomatology may also be produced by two other factors connected with the development of the disease, namely, the rate at which the pathological changes occur, and the extent of their distribution. In the fulminating cases it would seem that the extent of the lesion, and the rate at which it develops, are so great that the whole course of the disease is run in an extremely short space of time. In some of the simple dementing cases it would seem that the changes occur so slowly and involve the brain tissue so gradually that the change in the patient's personality is not noticed for a long period of time, and a fatal termination does not occur until many years after the onset. In yet other cases one obtains histories of recurring attacks of confusion or restlessness, or even of grandiose ideas coming on suddenly, lasting for a varying length of time and then apparently clearing up, but as one sees also in cases of disseminated sclerosis, ultimately causing permanent and progressive damage.

We have often thought that there would be striking differences evident between the male and female general paralytic. It is generally accepted that the disease is far more common in the male. It is only during the last three years that male paralytics have been treated at Horton, but females have been transferred for treatment for the past ten years, so it has been possible to observe a large series of women. The age-incidence is earlier in the female; fulminating types occur in both sexes, but it would appear that they are more common in men. In examining our series under discussion to-day the grandiose, confused and mixed grandiose confused type appear twice as common in the male. The simple dementing form gives a similar incidence in each sex. The deficiency of the grandiose confused type in the female is made up by a few depressed and manic types, but the chief number comprises a mixed manic dementing form, which does not appear among the male cases at all. In the untreated male cases, however, a mixed manic form was a common symptom, and no doubt gave rise to a fatal termination. Though our cases are too few, we still have the impression that the physical disturbances met with in general paralysis are more severe in the male. While the female presents much the same mental symptoms, she is not so seriously ill, and in consequence it would appear that she can withstand malaria therapy better, and so give an apparent superiority over the male as far as results are concerned.

Lastly mention must be made of those cases which have associated psychosis,

but in which there exists positive findings in the cerebro-spinal fluid. The clinical picture does not present the features of general paralysis. On searching the symptoms presented, we find they are suffering from schizophrenia, manic-depressive insanity or some chronic delusional state. In many cases there is a complete absence of physical signs; in others there may be some pupil irregularities or an Argyll Robertson reaction; in no case was slurred speech ever observed. When malarial therapy was first commenced at Horton in 1925, cases with positive findings in the cerebro-spinal fluid were transferred for treatment; some of them had already been under certificate for seven and eight years. Their physical condition was good, and they were quite fit to withstand malaria. We cannot believe that general paralytics would have been in this state at the end of such a prolonged period. These chronic cases, though treated by malaria (because of the serological findings), remain in their chronic mental state; apart from their being ten years older, their physical state remains much the same. Other cases suffering from manic-depressive insanity, and exhibiting the typical history of remissions and recurrences in the course of their psychosis, have also been treated. They have been discharged, but in several instances they have relapsed, true to the type of their mental disorder. We have endeavoured to establish general paralysis as a true clinical entity; we cannot see the justification for the belief that the original conception of general paralysis no longer exists. Healy,* in a thesis presented last year, maintains that patients who develop mental symptoms with neuro-syphilis would in any case develop a psychosis. Surely, just as alcohol will react in different ways on individuals, so will the toxin of syphilis produce different types of general paralysis according to the extent and site of invasion. In these associated psychoses, however, syphilis cannot be regarded as an ætiological factor; the patient happens to have had syphilis at some previous period in the course of his life. One has actually seen the typical picture of general paralysis superimposed on a pre-existing psychosis, and since malarial therapy has been introduced, one has been able to demonstrate the remission of general paralysis in some cases, only to lay bare the underlying mental disorder.

A far more difficult question to answer is, Are these patients suffering from an associated psychosis to be regarded as potential sufferers from general paralysis? Too little is known in our present state of knowledge regarding the serological changes accompanying the development of general paralysis. Has the cerebro-spinal fluid always been positive since the primary attack of syphilis, or has it recently changed from a negative to a positive reaction? We know tabetics exhibit positive findings without displaying any signs of mental disorder. At the same time some tabetics will develop later into tabo-paretics. Malaria is disappointing as a therapeutic agent for tabes; it is disappointing, too, in its application to these associated psychoses with presumably latent syphilis. Yet, on the other hand, have we in malaria a prophylactic weapon which will prevent

* *Syphilis in Relation to Psychosis*, F. H. Healy. Birmingham: Oman, 1934.

the subsequent development of general paralysis? We know that in many cases following malarial therapy all serological findings become completely negative; this has occurred in treated cases of general paralysis, and can in no way be correlated with the clinical recovery, as it is found both in good remissions and in failures to respond to treatment. In those psychotics who cannot be regarded as suffering from general paralysis, has the production of a negative cerebro-spinal fluid by malaria rendered them immune against the possible development of the disease? Unfortunately we are not in a position to say.

Mental symptoms associated with focal neurological signs, such as ptosis—a permanent paresis—again must not be confused with general paralysis; here ordinary antispesific measures are adequate and successful; in fact it was the very refractoriness of ordinary antispesific measures in the pre-malaria treatment days that often confirmed the diagnosis of the paretic. In most cases a history of a primary infection can be obtained, and the length of time elapsing in the cerebral syphilitic between the original infection and the later onset of symptoms is generally under five years, whereas in the general paralytic, if a specific history can be elicited, the time factor is very much longer.

We are forced to the conclusion, then, that malaria is definitely indicated in the treatment of the true case of general paralysis. Whether it should be employed as a prophylactic agent in psychotics, or non-psychotics for that matter, who show evidence serologically of previous syphilitic involvement, and presumably of the nervous system, is at present a matter of surmise.

As far as general paralysis is concerned, the advent of malarial therapy has marked a great advance in the treatment of a disease which previously had a hopeless prognosis. The admission-rate of sufferers from this malady was extremely high. It is a pity one cannot estimate the incidence. Is it on the increase or decrease? From all statistical reports the incidence of syphilis appears to be declining, in which case one must assume that even though the small percentage of syphilitics who ultimately develop general paralysis may remain constant, the sum total must be decreasing. Unfortunately the Board of Control are not in a position to tell us the fate of all cases suffering from general paralysis. It has become fashionable to treat many cases without certification and in general hospitals; during the last decade many hundreds have been so treated. We commend the interest shown by the Board in collecting statistics from the mental hospitals, but until the Ministry of Health or some general hospital organization undertake a similar inquiry into their treated cases, we shall not be in a position to settle some of these problems of neurosyphilis. We must still face the fact that treatment in many cases is disappointing. A large residue of these disappointments is accumulating in our mental hospitals, but even discounting those fulminating cases, the recovery-rate, which has remained fairly constant since treatment was started, will never reach higher proportions until this disease is diagnosed earlier by the physicians and treatment commenced immediately.

Discussion.

The PRESIDENT remarked that this paper had proved most interesting. Dr. Nicol had had a very large experience in recent years in treating cases of general paralysis; the paper now submitted had been very well prepared and placed before the meeting, and great help would be found in the statistics.

He thought all members realized that there were two schools in the matter of diagnosis of general paralysis. He himself was one of the older school, and he always said that many of the cases which he had seen diagnosed as general paralysis did not display the symptoms of the original classical disease. In the old days when he was with Dr. Bevan Lewis, many of the cases of general paralysis were diagnosed in the mortuary. In more recent times he had seen many autopsies on the brains of supposed general paralytics, and many of the old signs were not present.

With regard to the so-called recoveries from general paralysis, some relapsed, but he often thought there might be either a superimposed dementia, or even dementia præcox following the condition originally diagnosed, and hence he sometimes wondered whether the original diagnosis was right.

There were many present who had worked at general paralysis, and he hoped they would expound their views.

Dr. F. L. GOLLA remarked that Dr. Nicol's paper was exceedingly interesting to him, for he saw the other side of that gentleman's work. All the remitted cases from the London mental hospitals were sent to him at the Central Pathological Laboratory, where they were kept under observation, some being seen once a month, some once a week, some once every two months, extending over an indefinite period. He felt that one got so departmentalized in one's view, seeing only the late cases, and not having the advantage Dr. Nicol enjoyed of seeing them in the pre-treatment stages, that he found it very illuminating to hear how these cases appeared to the clinician at hospital in the active period of the disease. In all the cases which Dr. Nicol and others sent to the laboratory there was one thing which was very apparent. They had people who went back to their skilled duties—civil servants, actors, etc.—but he thought that of few could it be said that they were the people they had been before the onset of their mental illness. One thing neurologists were beginning to learn—and it would alter views on neurological and pathological processes—was the extraordinary adaptability of the nervous system. He reminded his hearers of the experiments of Graham Brown, in which, after ablation of extensive cortical areas causing hemiplegia in a monkey, it would recover from the hemiplegia. After a time one operated on the opposite side, again taking away the cerebral cortex and causing contralateral hemiplegia. The animal recovered from that, and in the end one had a monkey which was practically as skilful in what it did as it had been before. Lashley had done the same in the case of rats. As long as the visual area was not interfered with, it was very difficult to distinguish the three-fourths decorticated rat from the normal rat. In these respects the speaker did not think there was any gap between the animal and the human. Once when he, Dr. Golla, was working with the late Sir Victor Horsley, the latter operated on a man who had fits commencing with a twitching of the thumb of the right hand. The operation consisted of taking away the whole of the hand area. The epilepsy was thereafter cured; the man had a complete flaccid paralysis of the hand, but after a few months he recovered from this, and when the speaker saw the man two years afterwards he could only say he was not quite as good at tennis as he had been before his motor area was taken away.

Therefore it was beginning to be understood that the central nervous system was an organ of which it could be said that if it could not do a thing in one way, it would do it in another. This question arose in connection with the treatment of general paralysis by malaria; once the original affection had been cured by malaria, it was a matter of performing functions in some other way than had been

customary before. It was that which made the problem which Dr. Nicol had tackled so difficult. If one could say, by observation in a case, that there were certain symptoms indicating irritative phenomena, and other symptoms indicating destructive phenomena, and that, when the results of syphilis had been dealt with by malaria treatment, one would be left with the destructive phenomena only, it should be possible for the clinician to say which case would undergo complete remission, and which case would not. But unfortunately the problem was much more complex than that; it was necessary to find some method of assessing how great the destruction had been, and whether it was so great that no other portions of the cerebrum could take on the functions of the parts which had been destroyed. That was why, in the treatment of tabes by malaria, the results had been so unsuccessful; there were no other structures to take on the function of the destroyed tracts in the spinal cord. In cases in which one was dealing with cerebral symptoms it was a more complex arrangement, and it was difficult to assess the amount of damage likely to occur. The speaker saw these patients year after year, and noted a gradual improvement in function; this did not represent recovery of damaged nerve-cells, as the damage had existed some months and was irreparable, but the patient had been able to use other methods of arriving at the same result. That was the true key to the question concerning the amount of improvement there would be after malaria treatment. Progress went on in some of the cases for three or four years, and improvement was not due to suppression of the trouble, but to the patient bringing into play other mechanisms.

There were so many other points in the paper that he had not thought it possible to deal in a short time with more than one—one in which he had had experience. No doubt some of the others present would speak on other questions.

Dr. W. M. MACALISTER said he had thoroughly enjoyed Dr. Nicol's paper. He thought that his statistics represented, fairly accurately, the experience of all engaged in the speciality, and especially those who had taken an interest in this method of treatment. His own connection with it began in 1923, when, almost for the first time in this country, the use of malaria as a therapeutic agent was introduced, and he found it very interesting to keep in touch with one or two cases which were treated at that time. One of them in particular formed, to him, a complete answer to the question whether malaria treatment was justifiable, and was, indeed, the only thing to do in a case which could be definitely diagnosed as general paralysis. The case he wished to refer to was that of a police officer who was retired on a pension as soon as his condition was diagnosed as general paralysis. The medical officer of health who retired him had a "soft side" for the policeman, and represented to the authorities that this man, in view of his service, ought to get the highest possible pension. That was granted, in anticipation of the usual length of the course of general paralysis, namely, death in two or three years. To the disgust of the local authority, the man was still alive at the present moment, and for all these years had been drawing the maximum pension, and, in addition, he was supplementing it by working a private inquiry agency, which he controlled single-handed for two or three years with so much success that he had had to call in assistance from four others. The man said it was better to be a recovered general paralytic with a good pension than to be a non-general paralytic with policeman's pay.

He quoted that case as one of several with which he had kept in touch, and though he began as a sceptic in regard to the whole matter, he was now convinced of the value of the treatment.

He had been much interested in Dr. Golla's remark with regard to one portion of the nervous system taking over at second-hand, as it were, a function which had previously been carried out by some other part of the nervous system. He believed there was more in it than even that. His own experience in the matter led him to suggest that where there was apparent destruction of nervous tissue it was often only apparent, not real. In some cases the degree of recovery was so remarkable that there could not have been destruction of nervous tissue. The time

limit within which recovery could take place was too short to allow re-education of the nervous system to take on function second-hand. He thought—though he was without any proof on the matter—that there occurred an impairment of function resulting from œdema or some similar phenomenon of a local character, which, under treatment, disappeared, so allowing the original tissue to once more function.

Dr. DAVID BLAIR remarked that he had been greatly interested in Dr. Nicol's paper, and thought the observations made by Dr. Golla highly educative. At the first blush it seemed as though Dr. Nicol was right in suggesting that even cases which seemed very demented before the treatment was started were only suffering from a toxic condition and that there was no real destruction of cells.

But in his (Dr. Blair's) experience, before any case could be diagnosed with conviction in a mental hospital, considerable destruction of nerve elements with accompanying dementia had already occurred. It was the startling improvement in advanced cases of the disease after malarial treatment that he found so remarkable. The change in the physical condition of the patient, the relief of tremors and inco-ordination, impressed them all. The first case of malarial treatment in which he was interested was a very typical general paralytic whom he had used for the purpose of demonstration to students. Before malarial treatment was given the condition was so advanced that the patient was unable to walk and was confined to his room. His habits had become very filthy. He was given malarial treatment and carefully watched. After a time he made a dramatic recovery and was apparently quite his normal self. Of course in these days they regarded this seeming recovery with great suspicion. The patient was discharged and remained out of hospital six months. He then returned in another phase of the disease. He was acutely depressed, but his delusions and hallucinations had gone, and he had fairly good insight and apparently little dementia.

Speaking of general paralysis, from forty years' experience, he was not prepared to admit that remissions and long remissions were so very uncommon in the days preceding malarial treatment. Many years before the war he had a patient who was in a very advanced stage of general paralysis. The patient—a lady—had been a very typical case, both mentally and physically. The disease ran a rapid course and she became bedridden and very dirty in her habits. Incidentally she contracted typhoid fever and became very ill. A large bed-sore appeared on her back; it sloughed and almost exposed the sacrum. It seemed as though she could not recover. However, she gradually got better. Later her husband came to see her and she insisted on being taken home. He took her home, but so soon as she saw another woman in charge she became excited, and smashed the furniture, so nurses had to be sent to bring her back. She then continued in the hospital six months. There was a very slight defect of speech, which the patient ascribed to her teeth, but there was nothing about her to suggest she was not well. At the end of the six months she was taken home again and she continued to look after her husband's home for fully twenty years.

Dr. P. K. McCOWAN said he also wished to thank Dr. Nicol for this paper. He only rose as he wanted to mention the question of prognosis, to throw some doubt on the grave prognosis given in respect of the simple demented forms; he did not think the outlook in those cases was quite as bad as the authors of this paper made out. When improvement was found in such a case the tendency was to think there had been a mistake, the amnesia and disorientation which had been attributed to dementia being instead the result of confusion. For this reason there was a tendency to put the good results of the simple dementia forms into the confusion category, and to conclude that confusion responded well to malaria therapy, while simple dementia was practically hopeless. But in recent years, by being more critical of himself with regard to this question, he had been surprised how many cases of the simple demented forms did quite well.

Dr. DAVID SLIGHT (Montreal) said that he also had been greatly interested in the paper and in the discussion. His work lay in a general hospital. He did not know what was the usual practice in Britain, but in Canada, in the medical wards, a Wassermann test was done on the blood of every patient as a matter of routine, and he saw many cases picked up from the general medical, and even from surgical wards, and ultimately diagnosed as general paralysis, with symptoms of no nervous change and few mental changes, also with doubtful serological changes.

Reference had been made to two schools, and he was reminded of what happened in regard to brain tumours. Most of the observations made in the past with regard to brain tumours were not considered valid to-day; it was not the custom now to wait until optic neuritis occurred or the patient was comatose, and then carry out decompression. A ventriculogram was now employed, and various other modern aids. So in general hospitals they could make a diagnosis of general paralysis early, at a stage long before the patient was certifiable. But these cases might raise a doubt; some of the cases had had accidents, and they came later for study, and the only changes demonstrable were those in the cells such as one might see in confusion psychosis and other mild conditions.

With regard to cure or the amount of damage, it was revealing to see what might happen in neuro-surgery. Two years ago he collaborated in a piece of work in which a study was made of the possible changes in patients who had large areas of the brain removed—the whole left frontal lobe back to the speech area, or the right frontal lobe, or the temporal lobe—and no change could be observed by the ordinary clinical tests. Men were able to go back to their work in large stores, minus a right frontal lobe; they were able to play games, and nothing abnormal was observed by friends. It was necessary to ask what standards of test must be applied. If social tests were applied, such as being able to return to work, and being able to carry on as usual in the family, there seemed no room for question that with malaria therapy much could be done in very many cases. It was true that the changes might be mild; the patient might not afterwards be able to initiate new ideas, he might not have the same artistic sense as before, but, as psychiatrists, those present were not interested in these fine differences of character. From the clinical standpoint one could get 100% recoveries. Therefore if one could take out the whole frontal lobe and remove twenty million nerve-cells, it did not seem very material that in general paralysis many nerve-cells might have been destroyed.

He had been greatly interested to hear Dr. Nicol's suggestion as to the dementing cases. It was a matter of clinical diagnosis, but, as one understood the term "dementia", he would agree with Dr. Nicol that if a clinical picture had established itself which deserved the name "dementia", it meant irrevocable damage over a large area of the brain; and the degree of recovery taking place could not be so good as in the cases indicated by confusion and maniacal symptoms. In general hospitals one could see cases at an even earlier stage, when the changes were such that the patient was not certifiable; and unless and until the relative experiences were obtainable from men practising in general hospitals—those who had the opportunity of picking up from among other patients cases of general paralysis, at a stage when the psychiatrist did not see them—many of the ideas concerning this disease would not lead to very fruitful results. His opinion was that very much had been learned from these new developments in neuro-surgery and from the methods of neuro-pathology which had been spoken about.

It was also necessary to take account of the question of the degree of cure. He was on a visit to Germany four years ago, and he found there one doctor who was sceptical about the malaria treatment of this disease, and that physician pointed to a large workhouse which was full of so-called recovered cases of general paralysis. He, the speaker, found that the cases had lasted two or three years before they had been certified, and that was not a fair test of the results of malaria therapy.

He had been surprised to learn that there were, at the present time, any

hospitals which deprived their general paralytic patients of the benefits of malaria therapy.

He cordially congratulated Dr. Nicol on his interesting paper.

Dr. RALPH NOBLE said he would like to support the remarks just made by Dr. Slight, both in praise of the paper, and in what he had said concerning the treatment of these cases by malaria in general hospitals. It was being used in general hospitals over and over again, and this Association should be grateful for that, and not in any way critical. It was a matter of satisfaction that in this country more beds were being devoted to psychiatric work in the general hospitals themselves. The more this development could proceed, the better for the patients in general, and for the medical profession in particular. He thought it would be generally agreed that it was a development which the Association should encourage in every way.

With regard to the methods of treatment, he saw, while in America, general paralysis cases being treated by various thermal methods other than malaria—for example by diathermy, and by means of the electric heat box. The General Electric Company had devised an apparatus for the latter purpose. Malaria, the speaker considered, gave the treatment in a more efficient way, and the treatment by this means was more under control than by any electrical means. He did not think electrical methods for this disease ought to be encouraged.

Dr. RUBY O. STERN also thanked Dr. Nicol for his and his colleague's paper. She would like to know whether in his very large experience of the malarial treatment of general paralysis Dr. Nicol found aortitis of more frequent incidence than without that treatment; also the effect the presence of this condition had upon the decision whether or not to give malaria, and whether it materially affected the prognosis.

She had been interested to hear that the slurring of speech and tremor were comparatively early phenomena, as she considered that these symptoms bore a relation to changes in the basal ganglia. In a series she examined, some patients died a few weeks after the induction of malaria. There were few changes in the cortex, little deterioration of nerve-cells, and not much inflammatory change. The changes in the basal ganglia, however, were more intense, and they were related to changes of speech and to tremor. She would like to know whether, in treatment by malaria, the tremors cleared up and the character of the speech materially changed.

Dr. NICOL, in reply, said he wished, first, to thank all present, especially those who spoke, for the kindly way in which this contribution had been received. It was a joint effort to explain some of the questions connected with the clinical aspects of general paralysis.

He had been interested in Dr. Golla's remarks on the experiments of Graham Brown, and in the theory he put forward suggesting that those tissues of the brain which were unaffected by the disease took on the functions of those which had been destroyed by it, the amelioration of the patient's mental condition being produced by a gradual process of re-education. While agreeing that this theory might in part account for the mental improvement which occurred in successfully treated cases, the speaker felt that the time-limit observed in the case of good recoveries could not be ignored; this was a constant factor, patients being ready for discharge six to nine months after the termination of the malaria.

This first course of malaria was all-important. At Horton they had an opportunity of employing different species of malaria, of ringing the changes between quartan and benign tertian, or malignant and benign tertian, and so on. The result was that the second course of malaria given was quite as severe as the primary attack. He and his colleagues had given second courses of malaria to over a hundred cases who did not respond satisfactorily to the first treatment, and in no case had there been any appreciable subsequent improvement. So one

was forced to the conclusion that if a patient did not respond to treatment after the first attack of malaria, a second course of fever afforded no hope of the patient's clinical recovery.

He agreed with Dr. Blair that physical improvement was more common than mental improvement. Dr. McCowan maintained that the simple dementing case would recover after treatment. The speaker was in some doubt as to whether this was so, but was in agreement over the extreme difficulty of differentiating between apparent dementia and confusion. He thought that when recovery occurred in cases exhibiting some dementia before treatment, these should be regarded, not as belonging to a pure simple dementing type, but to a mixed group.

During the discussion, the question of the incidence of aortitis in these cases had been raised. It had been asked whether patients with this disease ought to be precluded from the treatment. His experience at Horton was that one seldom came across aortitis clinically. He admitted that at post-mortem examinations one found aortitis, the aorta often being in a deplorable state, and one was led to ask why there were no symptoms of it clinically during the patient's life. Severe syphilitic aortitis seemed more common in men than in women, but unless one could spot it clinically—and it was difficult to do that—the case should be given the opportunity of having treatment. He could recall only one or two cases in which severe aortitis was present clinically and for this reason malaria was withheld. One such case which had twice been under care at Horton had died only three days previously. The Wassermann reaction of both blood and cerebrospinal fluid was strongly positive. This man held a responsible position as a parliamentary reporter, and was highly educated. On his first admission to Horton in August, 1933, he was in a euphoric maniacal state for several months. He was never treated with malaria. He was given a course of bisoxyl and tryparamide, and by February, 1934, was in a state of good remission and was discharged. His physical signs—absent tendon reflexes (knee-jerks and ankle-jerks) and Argyll Robertson pupils together with his mental symptoms suggested general paralysis as a possible diagnosis. He returned to his work as a reporter, and was seen from time to time by Dr. Golla at the Maudsley Clinic. In February of this year he returned to Horton in an extremely depressed state with well-marked delusions of a somatic nature, and died a few days ago. The clinical course of the case was much more suggestive of a manic-depressive psychosis than of general paralysis, and the microscopical examination of the brain rather supported this view, for none of the characteristic histological changes were found. The case seemed of particular interest because of the bearing which it had on the question of the occurrence and significance of aortitis in cases of general paralysis.

In their paper Dr. Hutton and he had put forward a plea for the evaluation of signs and symptoms as a means of differentiation of pure and mixed types. They felt that from the point of view of accurate prognosis, they must take into consideration not only the symptomatology of the case, but also the duration of the disease; these two things must be considered together. In this way clinicians should be able to anticipate the response of cases to treatment, instead of having to wait six to nine months before being in a position to give that answer.