

GENERAL PARALYSIS.

THIS discussion, which stood adjourned at the Quarterly Meeting held on November 23, 1928, was resumed at the Quarterly Meeting, February 14, 1929, under the Presidency of Prof. J. Shaw Bolton, D.Sc., M.D., F.R.C.P. (*vide* p. 1).

The PRESIDENT said that last time a good deal of attention had been paid to diagnosis, though considerable reference had also been made to the subject of treatment. Little, however, had been said on symptomatology, except by Dr. Smyth. Dr. Caldwell had referred to the question of there being a special neurotropic strain of spirochæte. And there were other pathological questions, such as whether acute cerebral syphilis should be regarded as general paralysis; and whether general paralysis was a pure or a mixed infection; also whether the pathological findings in general paralysis were pathognomonic, or were found in cases of dementia. The latter he did not think was worth discussing. Naturally, it was not the wish that members should tie themselves down to any particular subject; he hoped, for the benefit of the meeting, that everything possible would be mentioned.

Dr. C. HUBERT BOND said he rose to ask a question, which he hoped someone present would answer. It was in connection with cases of general paralysis treated by malaria in whom improvement had not occurred, but death had taken place, perhaps after improvement at one stage. In those cases had any spirochætes been found in the brain?

Dr. J. R. LORD, answering Dr. Bond, said the reply would be found in a special paper by Mr. Geary, published in the Mott Memorial Book, which described the work done in the Maudsley Laboratory on this subject. In 50 cases treated by malaria the spirochæte was not found.

Continuing, he said that he had purposely included No. 4 of the points for discussion; it was the foundation of our knowledge of cerebral anatomy, particularly of how the changes in the brain occurred in mental disease. The President had taught them that the cortical areas concerned in the dementia of general paralysis were the

same as those involved in every form of dementia. To the speaker this was a point of extraordinary interest. The theory was now suggested that the brain was damaged in the direction taken by the perivascular lymph-stream of the cerebral arteries. If such were so, the poison was not selective in its action, and the damage done depended upon an anatomical and mechanical, and not a biological factor.

The old theory of general paralysis was that it resulted from a premature using up of cerebral vitality due to excessive enjoyment of "wine and women," and a too full life. The new theory was that of a healthy brain which would have persisted in its health but for the circulation of a poison in a particular direction.

With regard to No. 3, "Is general paralysis a pure or a mixed infection," that was put in because it occurred to the speaker that when one introduced, for purposes of treatment, what was really an infection, one ought to know what other infections were present. One took a patient who was presumably a case of general paralysis; one knew that the syphilitic infection was present, but there might be half a dozen toxæmias operating in that case. Another case might be without additional toxæmias. The remedy was applied indiscriminately from this point of view. One case got better; another did not. Unless one knew exactly what toxæmia each case was suffering from before the remedy was applied, the results could not be correctly assessed. He would like to see a series of cases, in which the poison was purely spirochætal, treated by malaria; and another series in which there were other toxæmias (septic for instance) similarly treated, and the results compared. This might answer the question why the remedy did good in one case, and did not in another.

No. 2 was put in because of Dr. Smyth's paper. That gentleman had described cases of general paralysis in which the infection spread, not *viâ* the lymph-stream, but *viâ* the blood-stream, which was not necessarily in the same direction as the lymphatics. Some would say that these cases were not general paralytics, but cases of brain syphilis, and would respond to ordinary anti-syphilitic measures.

Dr. HAMILTON MARR said he had heard one of the speakers say that the diagnosis of general paralysis was quite an easy one—in fact Prof. Robertson said no disease of the nervous system could be diagnosed with such certainty as general paralysis of the insane. He, the speaker, took a diametrically opposite view. His own experience during the war was that out of 10 cases diagnosed as general paralysis, probably 9 were syphilitic pseudo-paralysis. He did not know that the profession had gone much further in their

discoveries since Krafft-Ebing laid down the dictum that general paralysis was due to "civilization and syphilization."

With regard to clinical diagnosis, two very important points made one suspicious that a case was not one of general paralysis, namely, the presence of hallucinations and the presence of "bulbar speech," as against the staccato and slurred speech of general paralysis. Of all methods of distinguishing between cerebral syphilis and general paralysis—and Sir Frederick Mott had agreed with him in this—the best was the colloidal-gold test. Even if the patient had hallucinations and bulbar speech, and if it was then found that the cerebro-spinal fluid reacted strongly to the colloidal-gold test, he would decide in favour of general paralysis. But even in those cases he did not refrain from anti-syphilitic treatment. The results justified this, for many such cases recovered.

The speaker did not regard the Wassermann test alone as pathognomonic.

Dr. F. A. PICKWORTH (Birmingham) said it was generally admitted that syphilis of the brain was an essential factor in the ætiology of general paralysis, but in the present state of our knowledge it would be a pity if other pathological investigations were neglected. The long period between syphilitic infection and the onset of general paralysis suggested that other factors were important. Abnormal agglutinin formation had been noted in general paralytics, suggesting intestinal infection as an accessory factor, and sphenoidal sinusitis (of which two specimens were demonstrated) as another.

He also pointed out the relation of the main discussion to similar problems in general medicine. Typhoid osteitis was not usually regarded as typhoid fever, although *B. typhosus* was the infecting organism. A clinical enteric fever was not called typhoid fever if the bacteriologist's report indicates a paratyphoid organism. Undoubtedly, pathological methods would eventually replace clinical diagnosis, and in this lay the hope of preventive medicine, but such could find general acceptance only when quite free from misunderstanding as to the value of these findings.

Dr. W. F. MENZIES (Cheddleton) said that it was with peculiar pleasure that he contradicted the President's summary of the discussion last time. He turned to p. 3: "This comparison made me feel reasonable doubt as to whether the malaria treatment had very much effect on the course of any cases."* Could anyone have reasonable doubt who had tried it? All their cases in North Staffordshire had already been most carefully treated; all the

* *Vide* p. 27.

syphilitic cases in the Stoke-on-Trent Venereal Disease Clinic were treated with tryparsamide and other remedies, and the Medical Officer of the Clinic told the speaker that he had begun directly after the war, *i. e.* 11 years ago, and that he could honestly say that he had never done any good by these methods to any general paralytic, whereas interstitial syphilis cases improved greatly.

He asked whether, in the old days, the President ever saw any eight successive cases of general paralysis improve though they were not treated at all. The speaker never did. If one in five or six improved without treatment, it was considered very good. The death-rate was 98%. But things were different now; there was disappointment if a malaria-treated case did not improve, even if a number of them could not be sent out—since they were not received until the disease was advanced. At that stage clinical diagnosis was easy; but it was recognized to be too late for malaria treatment to bring recovery. He had a case which began about five years ago, and the man was still at work, but he confessed that the best most of them did was to become useful demented.

He was anxious to get some information about the pathology—the gross, not the minute pathology. It was interesting to note, in cases of syphilis, the different parts of the aorta which were atheromatous. In syphilitic cases in which the main disease had fallen on the heart, where there was double aortic disease or something of that kind, the atheroma affected especially the aortic valves and the ascending arch. In many toxæmias it was localized to a spot close to where there was an abscess. In the last two years he had had two cases which were most instructive. Neither was a case of general paralysis. One had an abscess in the pulmonary glands, and there was a large local atheromatous patch, about 2 inches long, in the aorta, just opposite to where the pus had been secreted. Another case died of prostatic disease. In him a foul abscess had been going on for two or three years, and in that case the atheroma was confined to the lower end of the aorta, just where it divided. Clearly those were not blood affections; they must be lymphogenous—must be carried by the lymph-stream back from the abscess into the walls of the arteries. Could it be that the whole of the syphilitic infection was lymphogenous, not hæmatogenous at all? He was beginning to think so. In most cases of general paralysis the atheroma of the aorta was very widespread, but there was a tendency for most of it to occur in the splanchnic area, not in the thoracic aorta; whereas in cases of interstitial syphilis the tendency was for the thoracic descending aorta above the diaphragm to be affected. This was not a universal rule, because in many cases, not only

of general paralysis, but in cases of old syphilis, the whole aorta was atheromatous. But it was wonderful how often in interstitial syphilis it was the thoracic aorta which was the more affected, while in general paralysis it was the abdominal aorta. It seemed to suggest that the general paralysis infection was in the splanchnic area, and that it was lymphogenous.

He could not answer the question as to spirochætes in the brain. A fortnight ago he had an acute general paralytic, who died 14 weeks after his single bout of malaria with one rigor. The appearance of the organs was such as might have been those due to a malarial death. There was a large, dark red spleen, liquid blood, engorged kidneys, yet every second day in the last fortnight of that patient's life the blood was examined for malarial bodies and not one was found. After death, blood taken from the spleen did not show malaria parasites either. What was that death due to? The brain in that case was interesting. In his Presidential Address in 1920, he opposed the theory of Prof. Bolton that the prefrontal area wasted because it was the last developed. He, the speaker, contended that the reason was geographical, from the flow of the cerebro-spinal fluid, as one speaker (Dr. Lord) had already said. The case he had just referred to was one of very acute general paralysis of the insane; he had died after being delirious for only a few weeks. He had a narrow track of infection of the meninges, and there was some cloudiness where the cerebro-spinal fluid flowed up over the hemisphere, spreading in a fanwise direction from the cisterna magna and Sylvian fissure. It was not the prefrontal area which was affected, but the intermediate pre-central. He would like to be given some information on those points.

Dr. G. W. B. JAMES (London) said this discussion was being held at a very opportune moment, because the Psychiatry Section of the Royal Society of Medicine were, that week, having a two-day debate on the prognosis and treatment of general paralysis of the insane. In that discussion, which began two evenings ago, there arose some points which were worthy of notice by this Association.

The first, which was introduced by Sir James Purves-Stewart, was the question of the name "general paralysis." The speaker agreed with Sir James that the name was a particularly bad one. Sir James Purves-Stewart suggested the name "progressive syphilitic meningo-encephalitis."

General paralysis was surely decided and determined as a progressive syphilitic disease. There was scarcely any disease known to medicine occurring in a man of 40 to 45 years of age in which

accessory factors would not be present, and general paralysis was no exception to that rule. If one examined every man of 40 or 45 present that day he did not suppose one would fail to find some infection—his teeth, his tonsils, his accessory sinuses, his intestines, his genito-urinary system. And it was this septic factor which seemed to him to be so much over-determined. For general paralysis there had been introduced a satisfactory treatment by pyrotherapy, and it seemed to the speaker to be becoming increasingly important for the practitioner to be able to diagnose it at the earliest possible stage. One often heard, even to-day, of cases of a fracture or a suspected fracture, in which the medical man attending it omitted to carry out an X-ray examination, with the result that in some cases a prosecution for criminal neglect resulted. It seemed to the speaker that this question of general paralysis and its diagnosis might well become something of the same sort, *i.e.*, it might come to be considered neglect on the part of general practitioners to fail to do lumbar puncture and venepuncture when any case showed any sign or symptom which might be considered due to general paralysis, treatment at an early stage being so absolutely essential for success. He put forward this medico-legal point as one which might profitably be discussed.

With regard to the treatment itself, there were two schools—the blood-to-blood school and the mosquito school. His own view was that the blood-to-blood malarial infection was the better because one did not get so often a preliminary rise of temperature before the rigors commenced and malarial relapses after the treatment. The blood-to-blood infection was, in his experience, more easily controlled than was the mosquito infection.

Dr. A. A. W. PETRIE (Banstead) said he, too, wished to ask some questions. A very important question was, What criteria should be taken for submitting a patient to what was really a dangerous form of treatment? There seemed to be comparatively general accord that in what could be called 100% general paralysis certain pyrexial treatments were desirable. Pyrexial treatments seemed to have been, on the whole, more successful than chemical treatments, though some people spoke favourably of tryparsamide. One speaker suggested that tryparsamide was very good for interstitial syphilis, but pyrexial methods were obviously the best for general paralysis. The question of diagnosis came in, and he agreed with Dr. Hamilton Marr that sometimes that was a difficult matter. Usually one could easily diagnose the more obvious interstitial cases and the 100% general paralysis cases, but there was an intermediate class in which there was great difficulty in diagnosis, and in judging what kind of

treatment to adopt for them. One case, which he well remembered, was sent to the Maudsley Hospital by an eminent neurologist who had no connection with that hospital, diagnosed as delusional insanity. The patient was very self-absorbed and much dissociated. There was nothing to suggest that he suffered from syphilis. Somebody tested the patient's blood, but not with the expectation of finding anything. The Wassermann was strongly positive in both blood and cerebro-spinal fluid, and the paretic curve was present. He had no symptoms of general paralysis, and the question arose whether one had stumbled upon a person about to become a general paralytic, or whether the psychosis was coincidental. The patient was given a course of tryparsamide, and he improved very much mentally and went out. If he had remained well, probably some would have said it was not general paralysis. The speaker heard of him three years later, and his informant said the question whether he was suffering from general paralysis was answered, for he showed every clinical symptom, as well as the positive serological findings.

One, then, came to the opposite extreme—that of the case which showed clinical symptoms of general paralysis, and no change in the cerebro-spinal fluid until late in the disease. Should one give active treatment or not? He remembered a case in which the cerebro-spinal fluid gave a negative result on at least six occasions. The man died of typical general paralysis within six months. At the *post-mortem* the brain was characteristic, and only shortly before death was the cerebro-spinal fluid positive. That was the kind of exceptional case which made one doubtful how to classify general paralysis for treatment. Was it the general opinion that when cases did not present the characteristic symptoms of general paralysis, but were presumably cases of interstitial syphilis, or cases even of tabes which might turn later to general paralysis, such should have pyrexial treatment, or should one treat them merely chemically? Cases with a number of neurasthenic symptoms attending as out-patients were found to have signs of tabes. They sometimes developed later into cases of tabo-paresis. Should one merely give tryparsamide, or deal with them by the pyrexial method?

There was a strong consensus of opinion that malaria was the best available treatment. Whether it was the ideal treatment was another matter, and he thought the search for other methods of treatment should still go on. He had tried some of the other pyrexial methods. Typhoid presented good results, but did not give the intermissions which malaria did. He had quoted a series of cases treated with relapsing fever, and his experience made him say that, though the figures were somewhat comparable with those for malaria, the

results, on the whole, were not so good, and there was evidence that at times relapsing fever could be even more dangerous than malaria, and was not so easily controlled. In his experience with malaria and relapsing fever he had come across a type of general paralysis in which symptoms seemed to be aggravated by the treatment, and an occasional case seemed to get worse rapidly. That might be a coincidence, as patients might have been going downhill before the treatment commenced. Some declared that malarial treatment was safe, but he thought it would be generally conceded that it was a dangerous treatment, and one was only justified in employing it in cases in which the prognosis was grave. He asked for the opinion of others as to how far, when they were doubtful about a diagnosis, they felt justified in applying pyrexial methods of treatment.

Dr. W. D. NICOL (Horton) said he might be able to answer one or two queries. Dr. Bond raised the question whether spirochætes had been found in the brain of general paralytics who had received the malaria treatment. Dr. Lord had answered that question. At the Maudsley Hospital many brains had been examined, and in only one brain were spirochætes found, and that was the brain of a juvenile general paralytic. The speaker had seen the brains in a number of cases which had had malaria treatment, though only of one or two who died immediately following malaria. Of the others some died 3, 4, 8 months or a year afterwards, and in each case the brain did not have the appearance of the untreated general paralytic. There was no thickening of the meninges, nor was frosting of the fourth ventricle observed.

Dr. James had stated that the blood-to-blood infection method of malarial inoculation was best. He, the speaker, had been associated for four years with Col. James with this treatment, and as a result he was strongly in favour of the direct mosquito infection. Infective mosquitoes were kept at Horton to supply the demands throughout England and Wales. One of the several reasons why he favoured mosquito infection was that one was certain in this way of getting a pure strain of benign tertian. If a strain were used through a series of patients, blood to blood, one did not always know what one was introducing from one patient to another. In this connection he would like to ask a question: If there were a series of patients, in whom the Wassermann was strongly positive, others with the reaction weakly positive, would a possible success be invalidated by introducing the strongly positive blood into a weakly positive patient?

The most important thing in mosquito treatment was the contro

of the malaria. Dr. James had said that blood inoculation was easier to control than mosquito inoculation—a statement which surprised the speaker. He had seen the mosquito inoculation done at Horton and other parts of England and Wales in a large number of cases, and his experience was that if they were watched closely they could be easily controlled. The whole secret of conducting malaria treatment on a safe basis was that when the case appeared to be getting out of control, one dose of 5 gr. of quinine should be given between the sixth and ninth days. After that small dose the malaria parasites disappeared from the blood in forty-eight hours. The patient did not have a remission till fourteen to eighteen days, and during that time his strength was returning. Another great advantage was that the strain of malaria was not lost. The remission was never so severe as the first.

It might be asked, What were the indications for bringing about an abortion of the fever? When should that be done? At Horton they had the decided advantage of a skilled pathologist doing parasite counts. By taking the blood-film and examining twenty-five fields under the microscope, using an oil-immersion lens and a No. 2 ocular, it was taken that if a patient had more than one parasite per field, or forty parasites to twenty-five fields, the malaria should be aborted by the small dose of quinine. It had only been necessary to do this in about 20% of cases. At Horton they had done 140 cases under research conditions, and in only 2 had he seen commencing jaundice. That, he thought, was largely because the malaria had been controlled before toxic effects had had a chance to develop.

Another important point was the taking of the temperature. It was very important that this should be taken every fifteen minutes when the rigors commenced, so as to avoid hyperpyrexia. Many men who had had experience said that albuminuria was in itself dangerous, but the speaker had not found it so. The majority of the cases, after six days of fever, had albuminuria to a slight degree, and he did not think that was an indication for stopping the treatment.

Dr. James also said that in mosquito-induced cases the malaria relapsed to the extent of 60%. Through the courtesy of Dr. Bond the report of the Board of Control on this treatment had been seen, and it seemed definite that mosquito inoculation gave better results than blood inoculation. This might be due to the fact that the malarial process was going on the whole time. Such relapses took place usually about six months later, and they did not cause much inconvenience. The fever being of a true tertian type, and causing little general disturbance, not having the severe character

of the quotidian fever experiences in the primary attack. There was no further trouble after quinine gr. v daily for ten days had been given.

In the case of benign tertian, if one wanted to give them a second course of treatment, it was found difficult to reinfect them owing to immunity. This has been solved by inducing quartan malaria. Last August Col. James was able to get a strain of quartan malaria from Hamburg. It was the least malignant form of the three species of malaria parasites. Some cases at Horton had been treated with it. The quartan strain had some advantages over benign tertian: the patient had fever every fourth day, instead of every second day, and thus obtained more rest between the rigors. The rigors themselves were less severe. The more debilitated type of patient could stand quartan malaria quite well; he could go on six or seven weeks without having anæmia. Many patients who stood quartan well would not have tolerated a week of benign tertian. Quartan malaria also afforded a great opportunity of treating those cases which were immune to benign tertian malaria. A number of cases treated with benign tertian malaria had been disappointing; their physical condition only improved, and not their mental state. Nearly twenty such cases had been repeatedly re-infected with benign tertian malaria and failed. On being given quartan malaria they had run a good course of that disease. It was too early yet to make any statement as to the results of this research, but at Hamburg Prof. Kirschbaum spoke very highly of the results, and claimed 50% of remissions by quartan malarial treatment.

Dr. WALK (Long Grove) regretted he had not been present at the last two discussions on this subject. He had, however, read Dr. Brander's paper, and with regard to the advice not to place too much reliance on pathological findings, he thought that was pushing at an open door. The mistakes in diagnosis mentioned in Dr. Brander's paper had all occurred round about 1910-12, and since then the tendency in medical teaching had been in the direction which Dr. Brander pointed out. Nowadays, with the present teaching, he did not think there was much danger of people placing too much reliance on laboratory findings alone. The great tendency was to correlate those with the clinical symptoms, and if that could not be done, the present teaching was for the clinical findings to have the predominance every time. On the other hand, as far as some of Dr. Brander's statements were concerned, he and some of his colleagues, with whom he had discussed the paper, felt they could not agree. It was felt that Dr. Brander was going too far in

emphasizing the absolute distinction between cerebro-spinal syphilis on the one hand and general paralysis on the other; that he was going further than the clinicians, who worked before the Wassermann test came out, had ever done. And on looking up the views of Sir Frederick Mott on the matter, one did not find that he maintained that one never found any tertiary lesions in patients who had general paralysis. It was agreed that in the majority of the cases no such lesions were found at *post-mortems*, nevertheless in a small number there were evidences of tertiary syphilis found in *post-mortems* on general paralytics.

With regard to juvenile general paralysis, even in the experience of the speaker and his colleagues they had seen cases of juvenile general paralysis who had signs of bodily syphilis as well. Dr. Brander had said that juvenile general paralytics gave a history of heredity only, but never showed signs of syphilis themselves. The speaker had seen cases running with the typical course of general paralysis, all the typical signs *post-mortem*, and yet had Hutchinson's teeth and similar lesions.

His purpose that day was to draw attention to some of the work which had been done, and some of the views which were held abroad about general paralysis and its nosology and treatment, and in particular some of the work seemed relevant to the first case which Dr. Petrie had described, that of the man who showed mental symptoms, and was accidentally found to have a Wassermann-positive blood and fluid. He was treated with tryparsamide, and went out later, and at a subsequent date turned out to be a general paralytic.

The speaker thought that several views concerning the pathology of general paralysis had not been mentioned. Dr. Caldwell had spoken of the neurotropic strain of spirochæte, etc., but there were other views. One he would mention was the view—which held currency especially in France—that the difference was one of reaction on the part of the patient, and that it could be correlated with the question of allergy; that the ordinary forms of syphilis were allergic, whereas general paralysis and aortitis and leucoplakia of the tongue were manifestations which were anallergic. It was held that the divergence showed early in some, and that these were potential general paralytics, and further, that such patients might show transitory manifestations of neuro-syphilis, either transitory nervous signs, or transitory mental disturbances without nervous signs, long before the onset of their general paralysis. It was possible that the case Dr. Petrie mentioned that day was of that kind. And that case illustrated another very important point, one which had come to the fore recently. It concerned the effect of anti-syphilitic

treatment on the development of general paralysis of the insane. Some work had recently been published from the Vienna clinic, which referred to the question of patients who were accidentally found to have changes in their cerebro-spinal fluid, patients who were in the latent period, who had had a primary and perhaps a few secondary lesions. Those patients were in an unstable state in which various factors might precipitate the onset of general paralysis. One such factor was anti-syphilitic treatment. It was said that if one took a patient in that latent period, it was possible to distinguish between potential paretics and other cases, not so much by a single examination of the fluid, but by repeated examinations extending over a long period. Starting from the fact that in the secondary stage 60% of syphilitic patients showed changes in their cerebro-spinal fluid, whereas later the number who showed them diminished until it went down to 20% or 10%, it was believed that patients in whom these reactions were diminishing were not likely to become general paralytics, whereas those in whom it was stationary or increasing would probably develop that disease. Therefore if one had a patient with no signs of syphilis, but who had positive findings in his blood and in his fluid, and he was repeatedly examined, over months and even years, one could show a tendency of these reactions to either increase or diminish, and such a patient should be treated as a potential parietic immune accordingly. Therefore it was possible that in the case that had been described, in which the patient had no obvious signs of paralysis, treatment by tryparsamide might have precipitated the general paralytic psychosis a few months later.

That brought one to the question of the treatment of early syphilis and its effect on the later development of general paralysis, which had recently been raised. Dr. Frost had drawn attention to that at the last discussion, and articles on the matter had recently appeared in the *Lancet*. It referred particularly to the work which had been done in Norway on patients who had been under treatment by Prof. Boeck, of Oslo. He practised until 1910, and he did not believe in mercury in treating general paralysis, laying it down that treatment by mercury and iodide was palliative only, and that it was harmful in that it lowered the patient's resistance. Therefore that authority merely gave them tonics to improve their general nutrition. It had been found since that only a very small proportion of those patients ever developed general paralysis of the insane. Apparently all patients who were under his care, if they had developed general paralysis, would have alternately come to one of two clinics in Oslo, but hardly any did come. Therefore the matter was followed up in greater detail, and it was found that the

proportion of cases who had been under Boeck's care and who developed general paralysis was very small—about one-tenth of the normal figure. The whole question of the effect of treatment on the future development of general paralysis seemed thus to have been raised in an acute form.

The speaker thought that these points were worth bringing up now, and that cases should be observed from that point of view.

Dr. DAVID RICE (Norwich) said he had only a few remarks to make in this discussion, and only in the hope that some others, like himself, who had no laboratory at their disposal, and who worked with a wholly insufficient staff to carry out the malarial treatment of general paralysis of the insane, might be encouraged to do something.

In tryparsamide the profession had, he thought, an agent with which, in the smaller institutions for which he was speaking, the staff could do something. They could make a contribution to the question whether chemical treatment was any good in the disease. For that reason he wished to mention a few cases.

He had had seven cases—5 men, 2 women. The first question which arose was whether the diagnosis was right. Were they treating general paralysis or cerebral syphilis? He would not discuss that for the moment, but those cases were all diagnosed clinically as general paralysis. When it was decided that a case was general paralysis, the blood at least was examined by the Clinical Research Association. There were, among them, six positive bloods, one being reported as having a negative or at least a very doubtful Wassermann and a positive Kahn; his cerebro-spinal fluid was returned as positive. None of the cases were juveniles; they were in the fourth, fifth and sixth decades of life. The shortest duration was one which dated back three months; six weeks before admission, and six weeks in the institution when the treatment was started. One of the female cases was a tabo-paretic. All those patients had ten weekly doses of 3 grammes of tryparsamide. In two cases his colleague found extreme difficulty in getting the material into the vein at all; the only untoward event which occurred was that one woman had much pain after the injection was made, in the neighbourhood of the vein; subsequent injections were made deep into the buttock in her case. Local reaction was practically absent, and there was very little systemic reaction; in no case was there a continuing rise of temperature following the treatment. It was as yet too early to speak positively of the results, especially after what Dr. Petrie had said about the subsequent development of general paralysis. He hoped he would be able

to get hold of some of his cases three years hence, but up to the present there had been definite improvement in every single case. No attention was paid to seizures. One of the men had been bedridden some weeks, and had had many seizures, nevertheless he was given a full course. Another, between 30 and 40 years of age, had had one seizure before the course was started, and he had a very severe one after the first injection. The question of the discharge of that patient was already arising, and the speaker was in a little difficulty about keeping him for further observation. One man, who had been bedridden, was now walking about the ward. The tabo-paretic patient had not recovered her knee-jerks, but she could now walk, whereas previously she could scarcely get about. There were two cases in men in the fourth decade, whose mental symptoms had cleared up very much; they showed better application in what they were doing, and there was a greater readiness to converse, and more sense in what they said.

If, immediately after a course, the cases appeared so promising, it seemed to be in favour of giving tryparsamide a good trial in institutions and places where at present the malaria treatment was impossible.

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Dr. G. DE M. RUDOLF (Cane Hill) said Dr. Nicol had raised one or two points about inoculation of malaria by mosquitoes. The speaker's own experience of that method was rather limited, but he had had experience of blood inoculations, and he thought it might be of interest to compare the statements Dr. Nicol made with parallel facts in the blood-inoculation cases.

He dealt with immunity to malaria. The speaker had inoculated over 200 cases, and had not yet found a patient who was immune to blood-inoculation with benign tertian malaria. Some cases had failed to take even after a third inoculation, but after the fourth, malaria had developed. A series of 12 cases, who had not improved sufficiently to be discharged, were re-inoculated with blood. Using the same strain of benign tertian malaria, he found that each of these patients tended to become more and more immune according to the number of inoculations. Eventually two, who had had five inoculations, showed neither parasites nor fever. On reinoculating these cases with a different strain of benign tertian malaria developed. So that until one had tried a case several times with one strain, and then tried it with other strains as well, one could not be sure it was immune.

The important point about giving quinine in small doses to stop the fever temporarily was that the amount required to do this varied with the different strains. The strain in use at Claybury, which was

started in August, 1923, and was still being carried on, needed two doses of 10 gr. of quinine to stop the fever temporarily. As a rule, patients relapsed in about a fortnight. With the Horton strain it was also found at Claybury, also that 5 gr. of quinine sufficed. If too much quinine were given, the infection would be stopped permanently. Thus, in this method of treatment it was necessary to know the peculiarities of the particular strain employed.

The point had been raised about not being able to use malaria because there was no laboratory available. All that one needed were a microscope, slides and Leishman's stain, now that blood or mosquitoes could be sent anywhere in the British Isles without the parasites dying. The furthest he had posted blood was from London to Dublin, and that consignment took quite well. The injection should be made not more than 30 hours after the blood had been drawn.

One other point Dr. Nicol mentioned he would like to refer to, namely, the method of counting the number of parasites in twenty-five fields in order to control the infection. Dr. Ramsay had been doing some parasite counts at Claybury, and he used ordinary smears, counting the parasites in the film. He started with twenty-five fields, counted those in various parts of the slides, and found, in the end, that to get accurate results one needed to count more like 500 fields of each film. Twenty-five fields were enough for rough clinical work, but the parasites were spread so unevenly in the smears that it was necessary to count many fields in order to obtain an accurate result.

Dr. GLEN DUNCAN (Severalls) said that at Colchester every male patient admitted was subjected to a thorough search for syphilis of the nervous system by neurological examination, by examination of blood-serum, and by a complete examination of the cerebro-spinal fluid, including the Wassermann and Sigma reactions. Taking about 80 cases of neuro-syphilis discovered by those methods, a considerable number could be said to be general paralysis. But there were 30% of cases who could not be described as general paralytics, and a fair number who were in an intermediate position in which he could not decide to his satisfaction whether they should be described as general paralysis or not, and he very much doubted whether anyone else could.

From that, and the results of treatment, he gathered that to attach the label "general paralysis of the insane" to a case tended to hamper not only one's investigations in psychiatry in general, but also one's treatment of cases. He mentioned 50 cases treated with malaria, of whom 41 were general paralytics, and 20 were successful. Considering the duration of the symptoms before coming under-

treatment, he found that in those who did well it was (contrary to what was quoted generally and contrary to one's previous impression), twelve months, and in those who did not do well it was eleven months; that was contrary to the prevailing belief that what was needed was the early case. Rightly, the early case was sought for in treating general paralysis by malaria and other means. By that was meant the case which, clinically, gave the impression of being an early one; in other words, there should be more dependence, from the point of view of prognosis, on the severity and rapidity of advance of the disease before coming under treatment than on the duration in months prior to starting treatment.

That brought him to remark on the pathology of this condition. Could the neuro-pathologist say that general paralysis of the insane was a specific definite pathological condition, which could not be confused with any other condition, such as meningo-vascular syphilis? He did not think so. Neurologists told him there was nothing specific to the one condition as compared with the other. When he was a student, neurologists told him there was no such disease as general paralysis, or tabes, or gumma of the brain; that it was syphilis, its locality being the central nervous system. In isolating off certain patients and labelling them general paralysis of the insane, physicians were confusing their minds, and were not doing their best with regard to the treatment. It was that which caused great discrepancies and differences of opinion. From those three points of view—the pathology of syphilis of the nervous system, the duration of the symptoms, and the difficulty in diagnosing intermediate cases—perhaps it would be well to drop the term "general paralysis of the insane," with the present conception of it, and attempt to take a stand on the basis of neuro-syphilis in each individual case, asking to which form of treatment it was amenable, or likely to be amenable.

In reply to a question by the President, Dr. DUNCAN explained that very careful examinations, serological and other, had been made on 80 male neuro-syphilitic patients admitted. In at least 30% of these the condition could not be diagnosed as general paralysis; of the remaining 70% a considerable number exhibited intermediate symptoms.

Dr. McRAE (Ayr) wished to ask one or two questions. A great many of the remarks made regarding the nature of the pathology of the disease had already been made years ago. The older school raised many of these points which were being raised to-day. First of all, Was syphilis the cause of general paralysis? Was it a special toxæmia? Was it a secondary infection? He was still wondering whether these questions had yet been answered.

One speaker thought that cure depended on the duration of the disease. What had duration to do with it at all? It depended on the degree of toxicity and other factors. How often could the statements of relatives be relied on, or, in any greater degree of certainty, the clinical information afforded by the general practitioner in attendance on the case, as to when the symptoms for which the patient was sent to the mental hospital developed? It was difficult to get any history. It was extremely difficult to get a reliable history. Therefore when one talked about the duration of the disease, the question was whether the given duration was of any value.

The question of the strain of the malarial parasite was raised by one speaker, who had been carrying on a strain for five years. He wondered whether the bacteriologists would agree that that strain at the end of five years could bear, as regards toxicity, the slightest resemblance to its original state. If one carried on the strain long enough the toxicity disappeared. Had the people who were working with strains of malarial parasites any method of standardizing toxicity? Before one could dogmatize one must know the toxicity of the organism. Enough stress had not been laid on that point. One speaker had said that the evidence of cure by malarial treatment was that, after death, no opacity was found on the surface of the brain, and there were no granulations to be found in the floor of the fourth ventricle. But were there ever any granulations or opacity in that case? In other words, was it general paralysis?

Dr. LORD said that the reference to cases to which the speaker had alluded was not a question of cure. The question was asked whether there were *spirochaetes* in the brain, and the reply was in the negative. Only one case had granulations in the fourth ventricle.

Dr. BOND said the remark was made in reply to a question from himself. It was not a matter of cure at all.

The PRESIDENT said he thought that the reply implied cure.

Dr. LORD replied that it could not be so; the cases had died and were not cured.

Dr. DONALD ROSS paid a tribute to the excellent summing up which the President had made on the last occasion. He regretted that there was a slight discrepancy in the remarks attributed to himself. The figures he mentioned in connection with the positive Wassermann—77 and 7—were wrongly given as percentages; they should be total figures out of 400.* His reference to the diagnosis

* This correction was made in the report.—Eds.

of general paralysis in the war had also been misunderstood. What he had meant to say was that in the war cases one was struck by the early appearance of the paralysis following the onset of infection ; it appeared much sooner than had previously been observed.

One speaker had mentioned the views obtaining in France. He would utter a caution as to the views of any one school in that country. He recalled how, at a meeting a few years ago to celebrate the centenary of Bayle, who first described general paralysis of the insane as a clinical entity, a most acrimonious discussion took place, of a kind which was fortunately rare in this country.

The speaker went on to refer to the significance of early signs of disordered behaviour, sudden peculiarities, such as, in one case, in a man previously entirely respectable, a sudden impulse to run about the place pulling all the door-bells and embracing all the ladies. They were all accustomed to see such instances, which should be regarded with grave suspicion in every case, and general paralysis of the insane should be expected later.

Dr. Rice had mentioned the impossibility of applying malarial treatment in small and remote places. Few places were more remote from civilization than Western Argyll, yet malarial blood had been conveyed successfully down there, a thermos flask being used, and injection taking place within an hour of its receipt.

The PRESIDENT then proceeded to sum up the discussion. He said that Dr. Bond had opened by asking the question whether, in cases of general paralysis treated by malaria, where death had followed, the brain had been examined for the presence or absence of spirochætes. He was replied to by both Dr. Lord and Dr. Nicol.

The speaker was rather puzzled by quite a number of Dr. Lord's remarks, and was doubtful whether or not that speaker had read aright Dr. Smyth's paper. Dr. Smyth certainly did not say that general paralysis was a lymph infection,* but he specifically referred to the fact that the parts of the brain affected were those parts which were the last to be developed and were the most unstable portions of the brain. Dr. Smyth in particular referred to the types of cases in which spirochætes could be found and the regions of the brain in which they were when found. In acute confused cases of general paralysis he stated that he did not find the spirochætes. He said that in cases with exaltation and grandiose ideas, with extraordinary behaviour and ordinary physical signs, he did find

* Abstract from Dr. Smyth's paper : " The main course of the cerebro-spinal fluid is upward. Hence, from a purely mechanical aspect, it is probable that spirochætes, having gained access to the subarachnoid space, take the line of least resistance and are carried along the perivascular spaces of the anterior and middle cerebral arteries in the majority of cases, although some might be carried back along the posterior cerebral artery, etc."—Ed.

the spirochætes, and also where they were. These were the cases which had been found to improve under tryparsamide and also under malarial treatment. The speaker had not quite followed Dr. Lord's remarks *re* multiple infections, so he was afraid he must leave them at present.

The next speaker was Dr. Hamilton Marr, who strongly dissented from the remark by Prof. Robertson that general paralysis was an extremely easy disease to diagnose. He must say that in this respect he agreed with Dr. Marr. Dr. Marr had referred to the fact that after the war he found many cases which would have been ordinarily diagnosed general paralysis, but which were really not cases of general paralysis; they were a pseudo-paralysis. This agreed with Dr. Ross's statement that after the war general paralysis appeared to follow early upon syphilitic infection. The speaker also remembered how readily these cases remitted, and how responsive they were to treatment with arsenic and mercury. They were of the type referred to by Dr. Marr.

Dr. HAMILTON MARR: It was actually during the war; the cases were sent from the Front.

The PRESIDENT next referred to the statement of Dr. Pickworth that while general paralysis might be and probably was caused by syphilis, other pathological factors intervened which modified the disease. Dr. Pickworth had spoken particularly of infection through the sphenoidal sinus.

He could hardly make any remarks with regard to what Dr. Menzies had said, because he rather thought that Dr. Menzies was endeavouring to extend his (the speaker's) nether extremity!

Dr. James made a most interesting reference to certain branches of the subject that had not been dealt with. He referred to the discussion at the Royal Society of Medicine now proceeding, and mentioned that Sir James Purves-Stewart regarded "general paralysis" as a bad name and suggested some other. Something of that kind had already been said in the course of the discussion, and he thought it was Dr. Duncan who had suggested that the term "general paralysis" be given up. But if the term "progressive encephalitis" were taken they would get into great trouble. Dr. James rightly said that general paralysis was a progressive syphilitic disease, and he referred to the various accessory factors which necessarily existed in all men over forty, and which naturally might be over-rated. Dr. James considered it necessary to make an early diagnosis from the point of view of possible pyrexial therapy. In such treatment Dr. James preferred blood inoculation to mosquito inoculation and gave his reasons. He was replied to later by Dr. Nicol on that point.

Dr. Petrie's remarks had interested the speaker very much. He had specifically asked what criteria were necessary if such a serious thing as treatment by malaria was to be carried out, and he had pointed out the absolute necessity for accurate diagnosis. Dr. Petrie had referred to a case of delusional insanity treated by tryparsamide which was only diagnosed accidentally. Dr. Petrie had indicated how difficult it was to classify cases which were not classical, and he had asked whether one was justified in undertaking such very serious treatment as malarial therapy in cases which were not classical. He used the term "pyrexial methods," because at the Maudsley Hospital and at Banstead relapsing fever had been tried.

Dr. Nicol had replied to the question put by Dr. Bond, stating that spirochætes were found in a certain number of these cases only. When they were not found it might mean that they had never been present or had been present and removed. The question was hardly a fair one. Dr. Nicol also spoke on the question of blood or mosquito inoculation. He (Dr. Nicol) preferred mosquito inoculation and gave his reasons. After listening carefully to what he had said one could at any rate be sure that he had made his statement after very considerable experience, and undoubtedly had reason for what he said. On the other hand, the question whether mosquito inoculation caused relapse or not was brought up later.

Dr. Walk stated that at the present time too much stress was *not* laid on laboratory findings. Unfortunately, a number of up-to-date men to-day were found who did lay too much stress upon such findings. Dr. Walk disagreed with Dr. Brander on the subject of the separation of cerebro-spinal syphilis from general paralysis, and he had interested the speaker very much by his statement that the late Sir Frederick Mott had referred to certain cases of general paralysis which exhibited tertiary lesions of syphilis. He (Prof. Shaw Bolton) remembered having disputes with Sir Frederick Mott on this subject, and when he had tried to say that a case was tertiary syphilis and general paralysis, Sir Frederick Mott had said that he must state one or the other—he could not have both. Sir Frederick Mott must have considerably modified his views in that respect. Dr. Walk then referred to certain foreign views, particularly to views held in France, and afterwards spoke of the treatment of early syphilis in Norway. He thought some reference to that would be found in the discussion of last November.

Dr. Rice had referred to the use of tryparsamide in small institutions, stating that it was not easy to employ malarial treatment in a small institution without proper laboratory facilities, and that tryparsamide offered an alternative. He seemed to have got

sufficiently good results to justify him in carrying on with the method. Of course, any sensible individual would be disposed, in view of the large number of methods of treatment of general paralysis now available, to agree that it would be better for individuals to employ the methods they thought best, rather than to try to make everybody treat cases on a pattern, whether correct or not.

Dr. Rudolf had disputed certain statements made by Dr. Nicol, but he need hardly refer to this. One point in Dr. Rudolf's remarks might be mentioned, namely, his reference to Dr. Nicol's method of counting the number of parasites in order to control infection. This seemed to indicate that there might be a certain amount of truth in what Dr. Rice had stated about the difficulty of applying treatment of the kind far away from large hospitals.

Dr. Duncan referred to the very careful examinations, serological and other, which had been made on every male patient admitted, to the number of eighty. He stated that at least 30% of these could not be diagnosed, but were certainly not general paralytics, and of the remaining 70% a considerable number exhibited intermediate symptoms, and it was not easy to state whether they were general paralytics or not. Dr. Duncan thought the term "general paralysis" or any similar term rather hampered the matter by tying one down to some particular treatment, instead of allowing individual cases to be treated, so to speak, on their merits without any label. He wished to make it perfectly clear that this was a syphilis of the nervous system.

Dr. McRae made one or two remarks about the views held by young men thirty or forty years ago. The majority of young men to-day had either forgotten or had never been aware of what was known to their fathers and grandfathers. Of course, to suggest that a case was general paralysis because it died and another case was cerebral syphilis because it recovered did not carry one very far. Dr. McRae had made an interesting remark on the question of whether a strain of mosquitoes could be kept going for years without any alteration of pathogenicity. This was a matter about which the present speaker knew nothing, but from his general knowledge of bacteriology, he would say that it was very likely that transmission from individual to individual, unless one transmitted periodically through the mosquitoes themselves, would result in a decreased value of the strain from the point of view of pathogenicity. On general pathological lines, a strain of the malarial parasite should, before it had been used more than three or four times, be passed through mosquitoes again. Dr. McRae then referred to the important point that general paralysis could not be diagnosed until a certain amount of harm had been

done to the central nervous system, and he asked whether that damage could be made good. He also referred to a remark made by Dr. Nicol that certain cases which had been treated by malaria and which some months afterwards had died were found to have no granulations in the floor of the fourth ventricle and no opacity on the surface of the brain. If Dr. Nicol meant that that was an indication that malaria had removed the opacity and the granulations he would feel exactly as Dr. McRae felt.

Finally Dr. Ross kindly made certain corrections in the summary of his previous remarks, and also drew attention to the fact that although Dr. Rice thought that malarial treatment could not be carried out in remote places, this in fact had successfully been done.

So much for the discussion which had taken place that afternoon. He wished now to consider rather more generally the trend of the discussion, both now and last November. The most important questions which had arisen in the discussion on the two occasions had been, firstly, the diagnosis of the disease, and, secondly, its treatment. Naturally, the question of diagnosis must be paramount. From the point of view of diagnosis there were three separate things to consider. The first of these was the physical signs on which general paralysis was frequently diagnosed. He thought that when they spoke of physical signs they should mean physical signs pure and simple. These signs were of very great importance from the point of view of diagnosis, but they were very frequently confused with mental signs. The second point was as regards the mental signs. In an ordinary early case, which might or might not be general paralysis, one came across exaltation, euphoria, and all sorts of erratic conduct, but these signs, so far as he personally was concerned, were not definite evidence of general paralysis. The only definite mental evidence was the existence of a certain degree of confusion of a particular type—a type which, he thought, was familiar to everyone. Cases which exhibited this type of confusion went on to an inevitable end. Cases without this type of confusion frequently remitted, and remitted under various forms of treatment. If the question of diagnosis was to be taken on the mental symptoms alone, he was afraid it would require a great deal of thought before any of them could set down those mental symptoms specifically, and state that general paralysis could be based upon them. It took quite an effort to separate out the true mental symptoms of general paralysis. The third type of evidence was the serological evidence. There were, he was quite certain, a number of cases of general paralysis which could certainly be diagnosed as such on the basis of physical and mental symptoms, which gave negative serological signs. This

was probably due to the fact that they contained no spirochætes in the cortex, or probably in the body, and had not contained any for a long time, but still showed these mental and physical signs.

The important question which arose here was whether general paralysis must only be diagnosed when the physical, mental and serological signs agreed. If so, the field within which the term "general paralysis" was used was a very limited one. If it was necessary to accept all these three varieties of signs before general paralysis could be diagnosed, cases with negative serological signs must be excluded, even though they gave positive physical and mental signs. Was it necessary to have this trinity of evidence? Could not physical and mental signs be evidence of syphilitic disease of the nervous system, marked serological signs being taken as probably indicating obvious and definite active syphilis, while the absence of such signs might mean either a very early stage of the disease, or possibly a condition in which no active syphilis or syphilis of importance was present, although the secondary results were very marked? At any rate, if it was specifically stated what was meant in the diagnosis, then they knew where they were. If they knew what they meant by general paralysis, they could then go on to the question of what exact physical, mental and serological signs were necessary to establish diagnosis. That, again, was a question which required some consideration. It was only this which had to be done, but the word "only" in this connection was a longer word than "Mesopotamia"!

He did not want to throw any doubt upon the claim for 90% correctness in the diagnosis of average cases of general paralysis. He was merely drawing attention to the various stumbling-blocks which could be found if it was desired to state precisely what was meant by general paralysis, or to indicate precisely how to diagnose with certainty any and every case presented. This was a much more important matter than appeared at first sight. Recent methods of treatment appeared, as a rule, either only to have given good results, or to have been employed, in cases where the diagnosis was, to say the least of it, uncertain. Every effort had been made to apply the treatment to what were called early cases, to cases where a certain degree of uncertainty existed, because these cases were regarded as the most favourable for cure. It was clear that classical progressive general paralysis was a fulminating cerebral dissolution, and not merely a spirochætosis. What could a spirochæticide do in such a case as that? Further, had malaria ever been proved even to be a murderer of spirochætes?

He came now to the question of treatment, and here he desired to refer in some detail to a most remarkable paper by Dr. Richard

B. Wilson, which was published in the last number of *Brain*. Dr. Wilson referred to thirty-eight cases of general paralysis. He did not state that they were fairly early cases. They had run a clinical course fairly typical of paresis. Then he classified them not according to the type or duration of case, the type of general paralysis, or anything of that sort, but solely according to the length of time after malarial treatment at which they died. Some died during treatment, some a fortnight afterwards, some three to six weeks afterwards, some three to five months afterwards, some six to nine months afterwards, some one to two years afterwards, and some three to five years afterwards. Dr. Wilson made some astounding statements with regard to these cases, and he produced some of the most beautiful microphotographs of the cortex that the speaker had ever come across. These were very fine examples of the cortex indeed. The first of his figures gave a most acute, strong, and diffuse infiltration of the cortex, the blood-vessels, etc., which occurred in a case of general paralysis dying during treatment. If he (the speaker) had examined that cortex, he would have said that it signified an extremely advanced general paralysis. When one went through these various photographs one found later on that the cases, as one might expect, if they were not acute, fulminating cases, showed less marked signs in the cortex, and in a couple of years they showed practically no signs of general paralysis. But the astounding thing to the speaker was that in these cases Dr. Wilson should speak of a *restoration* of the architecture of the cortex. He seemed to be satisfied that malarial treatment had removed from the cerebral cortex all those gross physical signs which had been produced by the severe action of syphilis. His paper was simply astounding from that point of view. If it were really established that malaria could cure those neuroglia changes one could almost believe anything, for it was known that these were due to a general action of the syphilis, not to a local attack of spirochætosis. If it were really possible to remove such conditions as Dr. Wilson showed in his earlier pictures, the speaker could not understand why any of them need ever die! All they had to do was to be infected with the malarial parasite, and they would be cured from all the secondary reactions of repair from which the body suffered. If credulity could be pushed thus far, it was not surprising that malaria had been credited by many with more influence than any other systemic irritant or constitutional disturbant. The speaker had seen many cases of general paralysis remit after pneumonia, and even after accident, and constantly after good nursing and fresh air. He would never suggest for a moment that any of the forms of pyrexial treatment or other treatment were of

no effect, but they could not be regarded from the purely specific point of view. It was quite inconceivable that the ordinary euphoric and grossly confused cases which died so suddenly or rapidly, and whose brains contained no spirochætes, could be cured by malaria; besides, such cases never remitted. On the other hand cases which did not exhibit the same marked vicious circle as was exhibited in these fulminating cases might be treated, for they did not run such an inevitable course.

He thought the balance of evidence, as brought out in this discussion, necessitated the reduction of malaria from the altitude of a specific for general paralysis to the mere position of a constitutional irritant. Tryparsamide, on the other hand, appeared to have partly justified its claim as a spirochæticide.

As a last word, he thought they could all say the discussion had been extremely valuable, and had clarified the ideas of many of those who had been present, though it would be unwise to credit it with having brought out any notable contribution to the knowledge of the subject of the diagnosis and treatment of general paralysis. That remained an open question for general future investigation.

Dr. J. L. BASKIN (Berks), whose ill-health prevented his attendance, wrote: "I am sorry I had not the privilege of hearing Dr. Brander's paper, especially as the disease receiving the nomenclature, tallies with the description by Dieulafoy, 'Quelques uns arrivent au terme de leur existence ayant conscience de leur decadence, leur intelligence est affaiblie mais ils n'ont pas d'alienation' (ninth edition, 1896). This disease, like the gout, shows itself in the very highest of our species—there is no poor man's general paralysis. For years my experience had led me to look behind the erudite opinion of the late Sir George Savage (that general paralysis was commonly found in the husband of the voluptuous type of woman), and on the arrival of the Wassermann reaction and the later Sigma test, I came to the same opinion as Dr. Nathan Raw, 'No syphilis, no G.P.' I may say, modestly, that I have seen an average amount of this disease in my work, first in the Mental Hospital, Belfast, then in the Devon Mental Hospital, but among the higher grade of patients seen in the large private asylum, where I was fortunate in having plenty of leisure to follow up the cases, I came across a good number, and most of them were unusually interesting.

"I remember well the visit of Dr. Mercier to see one case; he disagreed in his diagnosis with both my colleagues and myself, although I had paid attention to this case sufficiently to write a monograph

owing to the grandeur with which this patient expatiated on his 'fleet of yachts' and 'stables.' Now, without further digression, may I stress what (in my opinion) is of the most vital importance, *viz.* the view that treatment should be started at the earliest opportunity? I feel so strongly on this that before waiting for a Wassermann or Sigma I should, on the clinical signs alone, plus, of course, a provocatively corroborative history, start treatment on the patient's first visit to my clinic or study, to be followed later by the systematic and most approved methods of practice.

"I find that in this opinion I am in harmony with many who have had much experience in medicine, especially Sir Frederick Mott, Dr. Soutar, Dr. R. M. Stewart and others, but I have decided for instant action, on account of two very similar and important cases that I have seen during the last few years.

"One of these cases turned out not to be general paralysis, and the second seems likely, also, to be an unusual case; in it the physiological characteristics appeared to mask the restricted pathological findings (*i.e.*, Wassermann, Sigma). I will not take up time here by going deeply into the diagnosis of this case and its treatment, but when a healthy-looking man, equally active and athletic, develops a septicæmia followed by focal myelitis, as this case did, immediate treatment with salvarsan intravenously (avoiding the colloidal form—so productive of anaphylactic shock) is called for. This treatment can, of course, be reinforced by mercury inunction or vapour. But let me emphasize the avoidance of iodides (although the action of intramine may be enhanced by iodides as stressed in the Hunterian lectures of Mr. Macdonagh) from the baneful effects of iodides which I have seen in these cases, I recommend their avoidance.

"I have never seen fatal results from salvarsan in early cases without concluding that the dose had been insufficiently graded, too large a first dose or insufficient attention to blood-pressure (which is of great import), and lastly, the state of the kidneys and heart. I agree with Dr. Shaw that there is here one variety of spirochæte; but, like the bacillus of tuberculosis, long incarceration in nervous tissue with poor oxidation may in the course of years not only change its character in certain directions, but its toxic products acting on this environment may lead to apparent variation, acting in a vicious circle.

"I agree with Dr. Brander's remarks that the loss of expression, tremors, spasticity, etc., may be due to changes in the basal ganglia or substantia nigra. There is no doubt that many cases may have been carriers of the spirochæte, which, locked away in tissue, has started a period of recrudescence due to some trauma, toxæmia or other cause.

“May I say that I think a duty rests on the specialist to keep accurate registration of these cases, as advised by Lt.-Col. Lord.”

CLOSE OF THE DISCUSSION.

Dr. LORD said that the meeting would desire to express its great thanks to Prof. Shaw Bolton for having on two occasions summarized so ably their views on this subject. He had clarified the minds of all of them of many difficulties in regard to this subject.

Dr. MENZIES seconded the vote of thanks for the President's most able summary, but with regard to what he had said about malarial therapy, the old Biblical phrase occurred to him, “Had Zimri peace, who slew his master?”

The vote of thanks was accorded by acclamation, and the discussion then terminated.

