every sign that the malady was gaining the mastery. He appeared to be quite demented, and physically he was but a pitiable shadow of his former robust self. To-day he is to all outward appearance in excellent physical health. His habits are tidy; his speech movements, which were formerly almost wholly disorganized, are now well co-ordinated; and his vitality is not now drained by bouts of severe seizures as it previously was. Admitting, as one must do, that it is difficult owing to his taciturnity to assess the degree of mental enfeeblement which remains, yet one cannot but be struck by the general transformation. The other case is described above as No. iv. Here the conspicuous change is in the patient's mental state, though his physical health is also improved. To those who knew him in his former phase he now appears a new creature, a different personality altogether. In the remaining cases lesser, though often substantial, changes are common, but it is now generally recognized that many of these changes (for example, in the character of the pupillary reaction) may develop in the ordinary course of the disease. The average duration of the disease in the twelve cases was two years, and in every case the greatest care in the diagnosis was taken, all the usual serological tests being applied. At the moment these are again being investigated and so far as this has been done Wagner von Jauregg's conclusion that the condition of the blood serum and cerebro-spinal fluid is not materially altered by the malarial infection has been confirmed.

To the extent, at least, that none of the patients are any the worse for their experience, the experiment has been justified. Time alone will show whether any further justification will be forthcoming. Assuming that the results eventually turn out to be more favourable than they seem at the moment, how is the phenomenon to be explained? As long ago as 1883 Clouston described two cases in which mental disorders had been arrested by incidental sepsis, originating in one instance in the parotid gland and in the other in the hand. This led him to prophesy that "some day we shall hit upon a mode of producing a local inflammation or manageable septic blood poisoning, by which we shall cut short and cure attacks of mania"—the type of disorder from which his two patients suffered. The hypothesis underlying Wagner von Jauregg's work is virtually identical with that which Clouston here adumbrates, though it is applied to a very different form of mental disorder. Their common quest is for an infection which, while not of itself endangering the patient's life, will either stimulate the common bodily defences against the original disease or else will facilitate the operation of remedial agents. With this end in view some experimental work has been done with tuberculin and vaccines of different strains of staphylococcus. Apart from the risks involved in the use of these, the results from a therapeutic point of view have not been encouraging. Later still, attempts have been made to produce a more active bodily defence along some particular line without evoking the risks and discomfort of a general febrile disturbance. In this connexion some work has recently been done in Morningside with substances—for example, phlogestan—which produce a leucocytosis without the other accompaniments of fever. Here again, though a definite leucocytosis could be maintained for a prolonged period, the results of such treatment in cases of general paralysis were negligible. Whether the method of treatment with malaria will prove more efficacious time and a large field of experiment will be necessary to show. And even if the claims made for the treatment are in the long run substantiated there will remain to be answered many questions: Is the high temperature which can be produced incompatible with the well-being of the spirochaete? Has the infection with malaria any influence on the permeability to salvarsan of the choroid plexus? If the success of the method does not depend on such more or less mechanical effects, what subtle chemical changes occur? That these cannot be answered at the moment is enough to invest the further progress of the experiment with engrossing interest.

Conclusions.

1. Of the nine cases in whom the treatment was completed two are conspicuously improved; in one case the

emphasis is on the mental, in the other on the physical improvement.

2. Besides these, four other cases show some improvement, although not so marked.

3. In the remaining three cases no distinct change has occurred. It is noteworthy, however, that in none of these cases has there been any progressive deterioration. This is specially true of the only early case—No. vii.

THE TREATMENT OF GENERAL PARALYSIS BY MALARIA.

BY

A. R. GRANT, M.B., CH.B. ABERD.,
DEPUTY MEDICAL SUPERINTENDENT, COUNTY MENTAL HOSPITAL,
WHITTINGHAM.

WAGNER VON JAUREGG'S¹ malaria treatment of general paresis, and the excellent results published by himself, Gertsman,² Weygandt,³ Kirschbaum, Delgado,⁷ and others, first attracted our attention in the early months of 1922, and through the kindness of Professor Stephens of the Liverpool School of Tropical Medicine, who inoculated the first cases for us, we were able to commence this treatment in July, 1922.

Mosquitos are common at Whittingham, and recognizing the possibility of spreading malaria we had, prior to commencing treatment, examined many mosquitos caught within a mile of the hospital building, and felt satisfied that only varieties of *Culex* were present. In September of this year, however (fourteen months later), a further hunt for mosquitos revealed the presence of *Anopheles plumbeus*.

Whilst recognizing the impossibility of the restoration of degenerated cells and fibres we hoped for destruction of spirochaetes and complete and permanent arrest of degeneration. Authorities explain the influence of malaria upon the course of general paralysis in different ways. One is the destructive influence of high temperature as such on spirochaetes, as shown by Jahnel and Weichbrocht;⁴ it is conceivable that waves of high temperature, as in malaria, may be more efficacious than continuous temperatures. Muehlens and Kirschbaum⁵ believe that following inoculation there is a marked impoverishment of the blood, followed by a rapid regeneration of blood, which leads to a non-specific reactivation of the immunity processes. This theory would be supported by the views of Hauptmann. If these theories be correct, then high temperature and impoverishment of the blood should be aimed at.

It seems possible that different strains of *Plasmodium vivax* give different clinical types of malaria. Some authorities recognize only three species of malarial parasites, while others count double this number; it would appear that Muehlens and Kirschbaum were using a strain of *P. vivax* giving a different clinical type of malaria from ours, for in their experience of 76 cases of artificial malaria jaundice occurred in 12 cases, whilst in our 40 only one case of jaundice has been observed.

It was with these considerations before us that, after inoculating cases with quartan, malignant tertian, and two strains of benign tertian, we decided to allow all strains to die out except the second strain of benign tertian, which we named "W." This strain from the first gave a reasonably high temperature and a marked degree of anaemia. It has produced no untoward effects, no local disturbance at the seat of injection, and no very marked enlargement of the spleen. All cases have at once responded to quinine, and there have so far been no relapses. This strain has already passed through fifteen hosts and is at present in use in other hospitals. It seems advisable to name the strain so that it may be traced, for many points, such as increase or weakening of the virulence of the parasite, and various other questions which arise, will be more easily answered when the strain has passed through many more hosts than at present.

It has been said that life in the invertebrate host increased whilst life in the vertebrate host decreased the virulence of the parasite, and again that the absence of true sexual reproduction would weaken the parasite, but we are of the opinion that the virulence of "W" strain is increasing. Temperatures now tend to higher levels than they did a year ago.

In our cases the blood for inoculation has, as a rule, been withdrawn from the host after allowing as many rigors as possible, often after ten rigors, our object being to use blood with as many parasites present as possible, and thus diminish the chances of the inoculation being unsuccessful. The parasites may become more attenuated the longer they are in the body, but on the other hand they may become more virulent owing to the fact that possibly only the fittest may survive.

In one case (No. 5) spontaneous recovery took place. In our experience the most noteworthy features of inoculated malaria are (1) entire absence of relapses, and (2) the promptitude with which the temperature subsides and parasites disappear from the blood on the administration of quinine. These features were pointed out by Wagner-Jauregg; in explanation he suggests that the parasites which reproduce themselves only in the asexual way are less capable of resistance.

In the first patient to be inoculated with the "W" strain, the blood was withdrawn from a patient in the Liverpool School of Tropical Medicine, and after being citrated was placed in a thermos flask which was kept as far as possible at body temperature. The time that elapsed between the taking of the blood and injecting it into the patient in this hospital was two and a half hours. The inoculation was successful. In another case citrated blood was sent from here to Liverpool, and patients were successfully inoculated. Ten days ago we sent some blood to Aberdeen, but at the time of writing the patient does not seem to have developed malaria.

The cases under review in this article were not specially selected; they were at very different stages of the disease, ranging from early to advanced, and showing psychoses of the most varied types. The ages ranged from 21 to 56 years, the former being a case of juvenile general paresis which exhibited some unusual features.⁶ In all cases diagnosis was confirmed by the serological findings. Wassermann tests were made on the blood, and on the cerebro-spinal fluids Wassermann, Lange gold, and colloidal gamboge tests were made; in each case the cerebro-spinal fluid was examined for protein and a cell count was made. There has been no difficulty in obtaining the consent of relatives to this method of treatment.

The method of inoculation is as follows: From a vein of a patient who has received a malarial infection an amount of blood varying from 2 to 4 c.cm. was drawn, and about 2 c.cm. injected subcutaneously in the region of the shoulder-blade of the patient to be treated, the needle being moved about a little to cause a slight haemorrhage. In two cases blood was injected intravenously. If the patient to be inoculated could be brought into the same ward the blood was injected as it had been drawn. If this were not possible it was citrated. Blood films were examined in all cases at least once daily, in some others twice daily, and in others every two hours from rigor to rigor. These films have been preserved and may be further inquired into at any time. It has been our experience that once the parasites appeared they were present at all times and increased in number daily until the fever was controlled by quinine in the third week. In several of the cases the blood was taken during an interval free from fever, and from a practical point of view it seems immaterial whether the blood for injection is taken during a paroxysm or not. Where blood was citrated inoculation was as successful as where blood was injected as it was withdrawn.

As there was in our minds some doubt as to the effects of malaria on an already weakened constitution, and as we had not had previous experience of the prompt and permanent control of malaria by quinine in these cases, we selected four cases to ascertain if we could modify malaria in any way by giving quinine prophylactically. We gave quinine sulphate gr. x once daily for four days before inoculation

and for four days after. In all four cases the patients failed to develop malaria.

Of 34 cases successfully inoculated with benign tertian it was noted that the first rise of temperature above normal took place on an average between the ninth and tenth days after inoculation. Parasites appeared between the twelfth and thirteenth days on an average. The earliest day on which parasites were found for the first time was the fifth day, and the latest on which parasites were found for the first time was the twentieth day.

The length of time we allowed to elapse between the finding of the parasites and the giving of quinine was largely determined by the physical state of the patient. General paralytics seem to stand malaria well. The high temperature does not seem to inconvenience them to the extent that might be expected. The number of paroxysms allowed was usually from eight to twelve, but the latter number has been exceeded on certain occasions.

It has already been said that one of the features is the promptitude with which the temperature subsides and the parasites disappear on the administration of quinine; there is usually no fever after the first dose, and in the majority of cases parasites are not found after the second or third day. During the past year we have not had a single relapse. This is contrary to what has been experienced in the treatment of malaria in the ordinary way, where the disease can be controlled but relapses are frequent. The absence of relapses may be accounted for by the absence of the intermediate host and consequently the absence of true sexual reproduction, or by the fact that the parasites may in some way acquire properties, or lose some of those they already had, during the time they are in the blood of a general paralytic.

While the cases inoculated with quartan malaria showed a fairly typical temperature chart, those inoculated with tertian malaria showed for the most part atypical charts; the general tendency in these tertian cases seems to be that while during the first few days of fever the charts may be fairly typical, in the later stages they become quotidian or irregular.

To cut short the malaria Wagner-Jauregg advises quinine bisulphate in doses of 0.5 gram twice daily for three days in succession and then 0.5 gram once daily for fourteen days—a total of 10 grams. Our first few cases were given quinine in total amounts varying from 32 to 48 grams, and in these cases the administration of quinine was continued for about two months, although the parasites disappeared from the blood in a day or two after treatment by quinine was begun. From Case ix onwards, however, we have found that a total of 2 grams of quinine sulphate daily for three days produces an equally good result.

In one case instead of quinine we gave 0.15 gram novarsenobenzol, and next day an examination of blood films did not reveal any parasites, although a few hours before the giving of the neosalvarsan there were on an average 51 per 100 microscope fields (1/12 inch). Concurrently with the quinine treatment weekly doses of novarsenobenzol, novarsenobillon, or silbersalvarsan have been given in 17 of the cases. Six doses have usually been given—0.3 gram, 0.4 gram, and four of 0.6 gram.

The following cases present features of unusual interest:

CASE I.

E. M., male, aged 37. Admitted July 11th, 1922.

History.—Patient served in the army during the war, and was discharged as unfit in November, 1916, after having been wounded in the head by a fragment of shell. He subsequently resumed civil employment and was able to work until May 9th, 1922, when he attracted the attention of his fellow workmen by an "emotional outburst." On admission he was mentally confused and unable to give a satisfactory account of himself. He was disorientated for time and place, and at times became lacrymose for no apparent reason.

On examination he was seen to be poorly nourished; weight 8 st. 12 lb. The cardio-vascular, respiratory, and genito-urinary systems were all normal. The right pupil was small and slightly irregular; consensual reflex present. Reaction to light brisk. The left pupil was dilated and irregular; consensual reflex sluggish; reaction to light very sluggish. Knee-jerks slightly increased and equal; plantars flexor; no sign of Rombergism. Superficial reflexes apparently normal. The blood gave a positive Wassermann reaction (1 in 5). The cerebro-spinal also gave a positive Wassermann reaction; the Lange gold test gave zone 1 curve; cell count 196; gamboge test precipitation in all five tubes; protein test positive.

He was inoculated with benign tertian on September 8th, 1922. During the attack of malaria and for some weeks afterwards his mental condition underwent a change. From being apathetic and lacrymose he developed well marked auditory and visual hallucinations, and also delusions of persecution, which for a time made him very troublesome with his food. Gertsman refers to similar cases and seeks to explain the presence of the auditory hallucinations by the greater infiltration of the temporal lobes. The patient, however, made a good recovery and was discharged. He has since written a letter to his medical officer which shows that he has at present remarkably good insight.

On his discharge (June 30th, 1923) the following notes were made:
Nervous System.—Pupils: right, slightly irregular, reactions (direct and consensual) to light sluggish; left, dilated, oval reactions to light, direct sluggish, consensual absent. All superficial reflexes equal and present; tongue, no tremors; speech, no impediment. Right knee-jerk diminished; left knee-jerk diminished; sensations normal, gait normal; Rombergism absent. Plantars flexor; sphincters normal. In good bodily condition. Cerebro-spinal fluid: Lange gold test, zone 2 curve; gamboge, precipitation in all five tubes; cell count 61; Wassermann test positive. Blood: Wassermann test positive 1 in 5.

CASE II.

J. A., male, aged 36. Admitted October 11th, 1922.

History.—Patient is unmarried. He is stated to have had ordinary health prior to being wounded in the head during the late war. He was, however, in the army until September, 1919, and was able to follow his employment until July, 1922, when he complained of severe headaches. No history of his having contracted syphilis has been given. On admission he was rambling and incoherent in conversation, disorientated, wet and dirty in habits. He usually lay in bed with his legs drawn up, and his face partially or wholly covered with blankets. He was in poor bodily health; unable to walk; his weight was 9 st. 4 lb.

On examination, the cardio-vascular and respiratory systems were normal. The pupils were small, unequal, irregular, and sluggish; tongue and lips tremulous; speech slurring; knee-jerks positive; plantars both flexor; showed intention tremors in hands. The blood and cerebro-spinal fluid both gave a positive Wassermann reaction; Lange gold test, zone 1 curve; gamboge test, precipitation in all five tubes; protein tests, positive; cell count 24.

He was inoculated with benign tertian on January 25th. At the end of March he was noted to have improved a little mentally—he was not so apathetic; there was also a slight improvement in his physical condition and he was just able to walk. In another month his condition improved both mentally and physically; he still remained wet and dirty in habits, but was able to walk a great deal better. By the end of June he was no longer wet and dirty in habits. His weight had increased by 2 st. and he was able to walk fairly well. At the time of writing he is in good bodily health, is able to walk fairly well, takes an interest in his surroundings, but his memory is very defective for recent and remote events.

CASE III.

J. W. B., male, aged 52. This patient contracted syphilis in 1906; he was diagnosed as a case of general paralysis in 1915 in another mental hospital, and was discharged presumably in a state of remission. He was admitted here in December, 1921. From the date of his admission until May, 1922, the disease did not seem to be making much progress so it was decided not to inoculate him with malaria. In the beginning of May, 1923, however, he had several seizures and his condition began to deteriorate rapidly. He became wet and dirty in habits, and eventually a bed sore developed. It was then decided to inoculate him with malaria. This was done on June 9th, and on June 20th he was put on quinine. Since that date he has improved steadily. He is up and able to walk about, the bed sore is practically healed, and his mental condition has improved a great deal.

CASE IV.

J. B., male, aged 54. On admission the patient was simple and childish; was completely disorientated for time and place. He was in feeble physical condition. Since March of this year he had been confined to bed and he was unable to walk. He had marked tremors of his hands and was unable to do anything for himself. He was inoculated on June 5th. He continued to improve rapidly after inoculation and is now able to walk about. He still has tremors of the right hand, but is able to work in the ward. His mental condition is much better; he is now orientated for time and place. The rapid amelioration of his mental and physical condition was commented on by his relatives.

CASE V.

R. B., male, aged 44. This patient made a spontaneous recovery from his attack of malaria. Parasites appeared in his blood nine days after inoculation; they remained in the blood for thirty-nine days, and then disappeared. He has had no rise of temperature since, nor have any parasites been found in his blood. A period of over three months has now elapsed.

Of the 40 cases under treatment during the past fourteen months, 6 have died. Three patients have been discharged to their homes and are now following their usual occupations. Three patients formerly wet and dirty in habits have ceased to be so. Two of the cases formerly confined to bed have regained their strength to a considerable degree and are able to be up and about.

We are of opinion that this form of treatment is worthy of an extended trial, as, in our experience, benefit seems to be obtained in almost every case. In 296 cases Gertsman

claims to have obtained a complete remission in 38 per cent. So far, we are not in a position to make a similar claim. Our idea in this article has been to record preliminary observations on the 40 cases under treatment in the hope that we may be able to refer to them at a later date.

It has been suggested that better results might be got from subjecting the patient to relapsing fever, a spirochaetal infection which produces a continuous fever for three or four days instead of an intermittent fever for a longer period. It is hoped that the antibodies produced will have an effect on the *Spirochaeta pallida*. We have, again, through the kindness of Professors Stephens and Yorke, been able to inoculate with relapsing fever, and we hope to be able to refer to this form of treatment again.

REFERENCES.

- ¹ Wagner-Jauregg: *Ars Medici*, vol. i, No. 1, 1923; *Journ. of Nerv. and Mental Dis.*, vol. 55, No. 5, p. 369.
- ² Gertsman: *Zeit. f. d. ges. Neurol. und Psychiat.*, lxxiv, 1912.
- ³ Muehlens, Weygandt, and Kirschbaum: *Muench. med. Woch.*, 1920.
- ⁴ Jahnel and Weichbrocht: *Schenke, Zeit. f. d. ges. Neurol. u. Psychiat.*, 69, 220, July 30th, 1921.
- ⁵ F. Muehlens and W. Kirschbaum: *Zeit. f. Hyg. u. Infektionskr.*, 94, 1, October 12th, 1921.
- ⁶ Hauptmann: *Zeit. f. d. ges. Neurol. u. Psychiat.*, 70, 254, August 9th, 1921.
- ⁷ Delgado: *Journ. of Nerv. and Mental Dis.*, vol. 55, No. 5, p. 376.
- ⁸ Riddel and Stewart: *Journ. of Neurol. and Psychopath.*, vol. 3, No. 12, 1923.

THE CARE OF CHOREIC CHILDREN.

BY

A. DINGWALL FORDYCE, M.D., F.R.C.P. EDIN.,

HONORARY PHYSICIAN, ROYAL LIVERPOOL CHILDREN'S HOSPITAL.

THE overflowing nervous energy of healthy children exhibits itself in lively motor activity, which to the adult eye appears constant, and may be regarded as uncontrollable. The healthy child is nervous in the sense that his nervous system is comparatively unstable; but, granted moderate heredity and suitable hygiene and environment, he develops within the bounds of an ever-increasing power of control. Psychoanalysis and neurology must here be based on child-study and experience of children; knowledge of the characteristics of childhood is the essential basis for the interpretation of nervous phenomena. Much can be learned by close observation of emotional control, mental activity, and the neuromuscular condition, but it is important not to exaggerate the significance of nervous symptoms. A marked form of expression of nervous instability is muscular spasm, and this spasm in some form is a common symptom in most illnesses. Its form of expression ranges from general restlessness to twitching of individual muscles, from violent convulsion to faint tremor.

DIAGNOSIS.

The "nervous" child oversteps the limit of self-control. The mild initial symptoms of "nervousness" are excessive motor and mental activity. Later, it may be noticed that, while the mental activity remains excessive, it becomes increasingly associated with emotionalism, and a lack of sustained or reserve motor power. The child is easily tired, he is irritable, he cries readily, and jumps at sudden sounds, etc. There may be motor lethargy, unwillingness and inability to play strenuous games. With further development of the condition emotionalism becomes more strongly marked, lack of reserve mental power and even mental peculiarity supervenes, and motor spasms occur. The cause of such a "nervous" condition is usually complex. Neurotic heredity is common, and, when present, is usually supplemented by neurotic environment. An extreme sense of responsibility on the part of the parents or guardians, or their ignorance or fear, often develops the unsuitable environment.

Frequently, however, the nervous element, whether in heredity or environment, is not primarily at fault. The common basal error in these cases is digestive. Irregular, improper, or excessive diet deranges digestion, and manifold sequelae result—among them nervous instability, diminution in the power of control, spasm. Endocrine function is sometimes, but rarely, markedly affected.

This "nervous" child is, further, exposed to the common hazards of childhood. In outstanding degree he is liable to suffer shock from the onset of puberty, from arresting and violent physical stimuli, and from rheumatic infection;