[A summary of the clinical form in use at Parkside Mental Hospital, Macclesfield, in regard to ultra-violet treatment is added by kind permission of Dr. Dove Cormac:

Name Sex Age
Date Height Mental condition
Blood-pressure (3 lines—left): (1) at commencement, (2) at end of 4th week, (3) at end of 8th week.
Basal metabolic rate (same 3 lines—right): (1) at commencement, (2) at end of 4th week, (3) at end of 8th week.
Bodily disease (1 line).
General condition (2 lines).
Blood-count (6 lines—left). Weight (right), 1st, 2nd, 3rd and 4th weeks.

Date.	Period of exposure.	Date.	Period of exposure.	Weekly notes on— Condition. (20 lines.)	Pigmentation.	Mental state.

Blood-count at end of 4th week (6 lines).—EDS.]

The Care and Management of Induced Malaria. By W. D. NICOL, M.R.C.S., L.R.C.P., D.P.M. Assistant Medical Officer, Horton Mental Hospital.

FOR the treatment of general paralysis of the insane by induced malaria, the Board of Control, in consultation with the Ministry of Health, decided, at the end of 1924, to make an official arrangement by which a pure strain of the benign tertian malaria parasite would be cultivated in mosquitoes, and would be made available for inoculation by mosquito-bites instead of by the direct inoculation of blood from other patients. In consultation with the Mental Hospitals Department of the London County Council, the Horton Mental Hospital was selected for the work of preparing and maintaining the strain of malaria in mosquitoes, and Col. J. R. Lord, *C.B.E.*, Medical Superintendent of the Hospital, undertook the necessary arrangements in collaboration with Col. S. P. James, of the Medical Staff of the Ministry of Health. An isolated villa in the hospital grounds was selected as a treatment-block and laboratory; the Horton Mental Hospital authorities caused it to be mosquito-proofed and furnished, and the Ministry of Health supplied the scientific equipment of the laboratory. The Ministry also arranged that the routine laboratory work should be done by one of their laboratory assistants, Mr. P. G. Shute, under Col. James's supervision. I undertook the selection of cases suitable for treatment and their clinical care and management. The arrangements were completed in April, 1925, and since that month 33 batches of infected mosquitoes have been prepared and utilized for the inoculation of more than 300 patients in 69 hospitals in England, Wales and Scotland.

In 1926 the treatment block and laboratory were visited by

professors and doctors from France, Italy, Germany and Holland, and by post-graduate students from the London School of Hygiene and Tropical Medicine, as well as, on two occasions, by members of the Royal Medico-Psychological Association. During these visits various details relative to the selection and management of patients were discussed.

In this paper I propose to describe the procedure at Horton relative to those items of the therapeutic measure, supplemented in some respects from notes kindly placed at my disposal by Col. James from his experience of the treatment in other hospitals.

The Selection of Cases.

At Horton the attack of malaria is invariably induced in the natural way by the bites of infected mosquitoes instead of by the direct inoculation of blood from other patients. Though not essential to obtain evidence of antecedent syphilitic infection in the patients to be treated, nevertheless every case is confirmed to be a general paralytic by serological examination of the blood and cerebro-spinal fluid. The matter which is considered to be of most importance in the selection of cases is the patient's physical condition from the point of view of his ability to stand the strain of the malarial course. It is held that the prolonged and severe attack of malaria which is essential for the success of the treatment is a serious illness which, even with the greatest care, involves a risk to life. The relatives of the patients are always informed of this risk. In a series of 310 cases inoculated successfully by mosquitoes supplied from Horton to different hospitals in England and Wales, the fatality-rate during or immediately following the malarial course has been approximately 6%. The period of the course at which there appears to be most risk of a fatal issue is during the first twelve hours after quinine has been begun.

The earlier the diagnosis, the better the prospect of recovery, but the treatment is not reserved for early cases only; advanced cases are also given the benefit of it, provided that their physical health appears from thorough clinical examination (particularly of the circulatory and renal systems) to warrant that they will stand the course. On more than one occasion a fairly advanced case, after open-air treatment and special nursing and management, has recovered sufficiently in physical health to justify being given a malaria course, and the final result has been discharge from the hospital as cured.

Infecting the patient.—To infect the patient four or five infective mosquitoes are transferred to a small glass jar, the mouth of which

is closed with mosquito netting. The mouth of the jar is placed against the patient's thigh while he lies in bed. The mosquitoes bite through the netting which covers the mouth of the jar. The skin should be thoroughly cleaned before the mosquitoes are applied. After the mosquitoes have bitten, the marks are painted with iodine (which allays the irritation) and bandaged to prevent the patient from scratching them.

The incubation period.—The period that elapses between the date of inoculation and the first malarial rise of temperature is usually 12 days, but it is often only 10 days, or it may be as long as 24 days. At Horton, patients receive special nursing and attention from the date of infection. As a rule they are not allowed up during the incubation period. The reasons are: (1) Warmth favours the development of the infection; (2) rest in bed prevents to some extent the irregular non-specific rises of temperature observed in many cases of general paralysis; (3) as the onset of malaria in a person infected by mosquitoes cannot be prevented by quinine or other known means, it is important that no untoward event should happen during the incubation period. On one occasion at Horton a female patient during the incubation period had an accident resulting in a severe fracture, which made it advisable to endeavour to prevent or to postpone the expected malarial attack. With that object she was given 30 gr. of quinine (10 gr. *t.d.s.*) on two following days, namely, on the fourth and fifth days after having been infected. It had no effect in preventing or postponing the attack. Other modes of quinine administration during the incubation period, as well as other drugs have been tried without success on other patients in whom it has been considered advisable to prevent the onset of the attack.

In order that the initial febrile manifestations of the attack may not be missed, all patients are put on a four-hourly temperature chart from the seventh day after infection. Routine daily blood examination is commenced from the day on which the first febrile temperature is noted.

The Attack.

From the day of the first rise of temperature the instructions for taking temperatures are as follows: (1) Note the hour of the day or night at which the rise of temperature occurred on the first day. (2) On the next day, about an hour before that time, begin to take temperatures every half-hour. (3) As soon as a rise above normal is observed, take the temperature every fifteen minutes, and continue to do so throughout the febrile paroxysm until it has fallen to normal. (4) Then resume the four-hourly rule until the

next rise. This is the only plan by which a correct chart of temperatures during the attack can be obtained, and by which "anticipation" or "retardation" of the daily paroxysms can be accurately ascertained and recorded.

In a primary attack of benign tertian malaria three stages are recognized—the initial stage, the developed stage and the terminal stage. The initial stage begins as a gradually increasing fever which at first is sub-continuous or irregularly remittent. On the third or fourth day it becomes intermittent, and the termination of this stage is often indicated by an intermission lasting twenty-four or forty-eight hours. The following is an example of a usual chart during this stage:

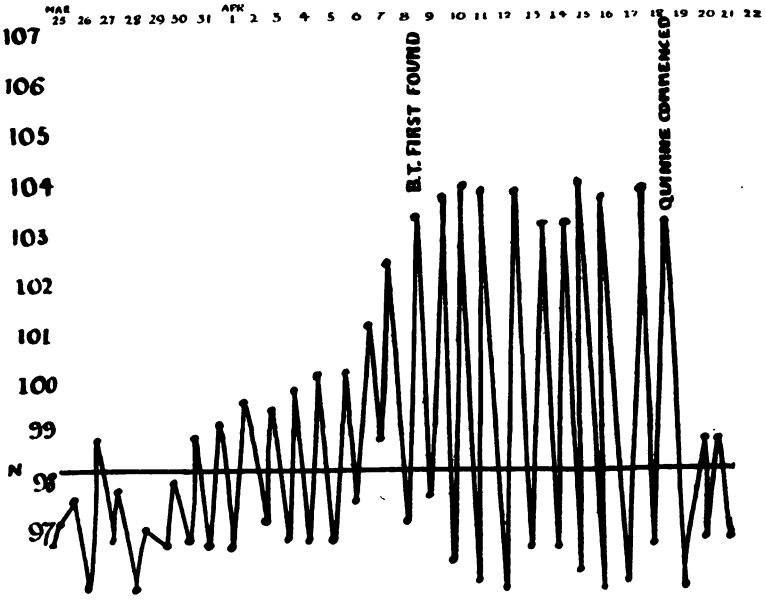

CHART I.

The symptoms during the initial stage resemble somewhat those of a commencing attack of typhoid fever, but the spiky nature of the temperature is more apparent. There is seldom or never a obvious "rigor" during this stage, though the patient may complain of feeling "chilly." It is a period of the malaria course which is liable to be entirely unobserved if it is the practice to take temperatures only morning and evening, or to watch only for the occurrence of the first "shivering." Parasites can seldom be found even by the "thick-drop" method until the second or third day of the initial stage.

In the developed stage the temperature becomes definitely

intermittent. There is nearly always an attack of fever every day —not every other day, as is often expected. The height of the temperature reached in each paroxysm rises daily during the first three or four days and the duration of each febrile paroxysm lengthens. Parasites can now be easily found in thin films of blood, and their number increases from day to day during the first two or three days of this stage. Then a balance is established between the infection and the patient's resisting power, and usually the parasites remain moderate in number and the fever moderate in degree. It often happens during this stage that the maximum temperatures reached during the paroxysms are equal on alternate days, and that they are lower on the first, third, fifth, etc., days than on the second, fourth, sixth, etc. This indicates that the fever in the developed stage of a primary attack is of "double tertian" type, but it is seldom easy to correlate the course of the temperature with the stages of growth of the parasites. The temperature chart shows two separate febrile attacks, each of them occurring on its own day, but blood examination shows parasites in nearly all stages of development.

In the management of the case during the developed stage two points are of particular importance, namely, (1) the temperature, while the paroxysm lasts, must be taken every fifteen minutes in order that the nursing staff may adopt appropriate measures to prevent hyperpyrexia; (2) blood examination must be made at least once a day in order to ascertain that the number of parasites is not increasing beyond a safe limit. On the first point the practice at Horton is to begin cold-sponging when the temperature reaches 105° F., and to repeat it as often as may be necessary to keep it at or below 105° while the paroxysm lasts. This is illustrated in Chart 2, which shows the duration of the paroxysm (usually about ten to twelve hours), and the importance of taking temperatures frequently during the paroxysm.

As regards the second point, a thin blood-film stained with Leishman's stain is examined daily, the parasites being counted in relation to the leucocytes or to a stated number of fields of the microscope. Using a $\frac{1}{12}$-inch oil-immersion objective and No. 2 eye-piece twenty-five fields are usually passed in review. If thirty-five or more parasites are found at this examination (*i.e.*, more than one parasite in every field), it is considered an indication that the fever should be stopped. Account is also taken of the clinical condition of the patient, the duration of the paroxysms, the maximum temperature reached, and whether there is a paroxysm every day or every other day. Persistent vomiting, faintness or collapse during the paroxysm, cyanosis, seizures, undue restlessness,

TEMPERATURES DURING THE MALARIAL PAROXYSM.
DURATION 14 HOURS.

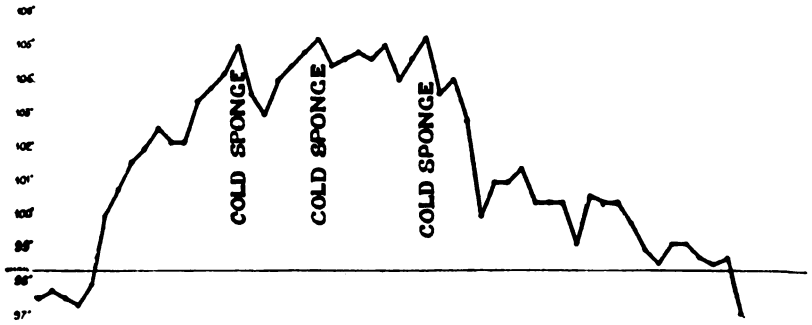

CHART 2.

albuminuria and the earliest suggestion of jaundice are regarded as signals that the course should be terminated.

Temporary interruption of the course.—In some of the above conditions it is our practice, where the patient has not completed a sufficient number of febrile attacks, to abort the malaria attack instead of curing it outright. This is effected by giving the patient only one dose of 5 gr. of quinine. The result usually is cessation of fever and almost complete disappearance of parasites from the peripheral blood, to be followed in from ten to twenty days by a recrudescence. During this interval of temporary recovery the patient's physical condition improves and some degree of resistance to the malarial toxin is developed, the result being that the recrudescence is usually of tertian instead of quotidian type, and less severe than the original attack. The following chart illustrates this procedure:

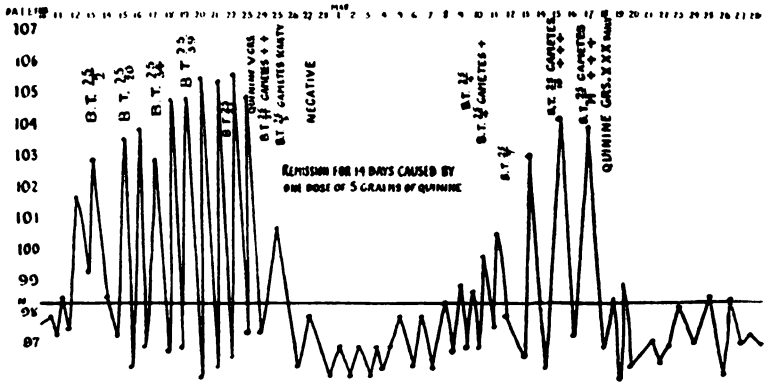

CHART 3.

The terminal stage, in patients who are allowed to continue the course uninterruptedly, is characterized by the fever changing from quotidian to tertian type, and by a gradually diminishing severity of the fever attacks. In some cases the attacks get milder day by day until they fail to recur (so-called "spontaneous recovery"), but in these cases parasites usually persist in the peripheral blood for some time after the cessation of fever.

Management during the paroxysms.—The time of day at which the paroxysm begins is known, and care is therefore taken that the patient is comfortable in a warm blanket-bed before the actual attack of shivering begins. Hot-water bottles are put into the bed in good time, and a cup of hot broth or tea is given as soon as the patient begins to feel cold. The instructions regarding taking the temperature every fifteen minutes from that time have already been mentioned, and the necessity of cold-sponging when the temperature rises above 105°. During the hot stage the patient should be allowed to drink as much fluid as he will—preferably barley-water, soda-water or other alkaline drinks. For nausea or vomiting a full dose of gentian with soda, repeated at intervals, is sometimes useful. Nothing should be done which may delay the onset of the sweating stage, in which the patient gets almost immediate relief. Shortly after the onset of this stage the patient's wet clothing is changed and a stimulant drink is given.

Management between the paroxysms.—Care is taken to maintain the patient's strength as much as possible by nourishing diet and to keep the digestive functions in good order. Constipation is the rule, and usually has to be corrected by a daily enema. In addition a dose of aperient water may be required each morning throughout the course. The urine is examined daily. Albuminuria is often only temporary, but is regarded as a serious complication, necessitating abandonment of the course. A careful watch is kept on the working of the heart, and the patient's strength is supported by heart stimulants when necessary. Tenderness of the spleen is not often noted, and no useful object is served by endeavouring to detect enlargement of that organ by deep palpation. *Herpes labialis* is fairly common and sometimes severe.

Treatment to stop the attack.—Two plans of quinine treatment for stopping the attack are practised at Horton, namely (1) 10 gr. of quinine three times a day for five days, or (2) 5 gr. of quinine three times a day for ten days. The quinine is given in solution by the mouth. With either treatment the fever invariably ceases within forty-eight hours, and the parasites usually disappear by the third day. As regards their immediate effect, either plan is equally good.

Several preparations reputed to be effective remedies for malaria have been tried (including "Plasmoquin," "Harmine," "Harmaline" and "Toxotropin"), but none of them is the equal of quinine.

Treatment during convalescence.—At the end of the course patients are profoundly anæmic and much exhausted. Every endeavour is made to improve their general health as quickly as possible, chiefly by nourishing food, fresh air and medical comforts, including a moderate allowance of stout. Many patients during convalescence develop an abnormal appetite and quickly put on weight. Drugs which have a tonic action are not greatly relied upon, but it is a usual practice to give Fellows' syrup (℥ss *t.d.s.*) for a few weeks.

As an aid to the cure of general paralysis, an anti-syphilitic course of one of the organic arsenical compounds is prescribed after complete recovery from the malarial attack.

Malarial Relapses.

In about 50% of cases a relapse of the malarial attack occurs. It may happen either at a short interval (twenty days to six weeks) after cure of the attack or at a long interval (eight to ten months). No known method of quinine treatment either during or after the attack is effective in preventing these relapses, but they are very easily cured by 5 gr. of quinine three times a day for two or three days. All that is necessary is that the medical attendant of a patient discharged from hospital should be informed of the possibility of their occurrence, in order that the diagnosis may be confirmed and treatment be given at an early stage.

General Notes.

The importance of attending to the patient's physical health before the attack has already been mentioned. Septic foci in one part of the body or another are common in patients suffering from general paralysis, and they are dealt with as far as possible before the malarial course is begun. It is important to correct any disorder of the alimentary system, particularly constipation, and to ascertain that the patient's urine is normal and that there is no serious disorder of the circulatory or respiratory systems.

The number of febrile attacks allowed varies in each case with the patient's condition, but in most cases ten to twelve paroxysms are permitted. A second course has been given to several patients whose physical condition is good, but whose mental state has not improved within two or three months. A relapse has sometimes

served as a second course of treatment, and as a general rule it is mild in character, with a tendency to "spontaneous recovery."

From a limited number of results collected at Horton, it appears that the percentage of "cures" of general paralysis in cases inoculated by mosquito-bites is considerably higher than the percentage in cases infected by direct blood inoculation.

I wish to express my thanks to Col. Lord for his kind permission in allowing me to refer to cases and charts.

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*Tryparsamide Therapy in General Paralysis of the Insane.**

By T. M. DAVIE, *M.C.*, M.D., Assistant Physician, The Royal Hospital, Morningside, Edinburgh.

TRYPARSAMIDE, the sodium salt of N-phenylglycineanmid-p-arsonic acid, was first prepared by Jacobs and Heidelberger in 1915 in the laboratories of the Rockefeller Institute. Following on the excellent reports of its efficacy in the treatment of neuro-syphilis in America, it was distributed to various research centres in this country through the agency of the Medical Research Council prior to its liberation for general use.

Of the twelve cases to be described in which tryparsamide was administered, six were treated at the request of the Medical Research Council, to whom we were indebted for the supply of the drug. The results were sufficiently encouraging to lead us to pursue the same method of treatment subsequently in the other six cases.

The laboratory experiments of Brown and Pearce, and of others, on animals had shown the very definite effect of tryparsamide upon infections by the *Treponema pallidum*. It seemed that ordinarily the organisms were not destroyed by the drug, and that beneficial results were to be explained not by its treponemacidal action, but by its capacity of increasing the resistance of the tissues to the spirochæte.

Later, clinical experiments by Lorenz and others (1) gave particularly good results. These observers comment on the marked tonic effect of this drug as one of its characteristics.

SELECTION OF CASES.

The number of cases under tryparsamide treatment was twelve. The number might have been larger, but it was deemed advisable not to interfere with those cases of general paralysis which had been

(*) Read at a Scottish Divisional meeting held at Gartloch Mental Hospital, November 16, 1926.