It is surprising how seldom, in adults, worms are seen in the faeces. One patient of mine, a medical man, looked at every motion passed during a period of several weeks. Although nocturnal pruritus was constantly present, only a single worm was seen, and this in a motion resulting from a sharp purge given as part of his treatment.

TREATMENT

Prolonged infestation always results from auto-infection by the mouth, and until this source of supply has been cut off no treatment can be effective. The ova are deposited in enormous numbers in and around the anal region. They may reach the mouth either directly by the hands or they may be smeared over the body and clothing, and the hands reinfected later from these sources. Crushing of worms either in scratching or otherwise liberates eggs in large numbers. I have recovered several dozen eggs from a single finger-nail, and Professor D. B. Blacklock tells me that he has found ova in washings made from garments as low down as the knee. From this it is obvious that the washing of the hands before food and after defaecation, as often directed, is totally inadequate. The hands must be washed thoroughly every time that the surface of the body, or an undergarment, is touched, for there is no certainty that eggs have not been picked up. For example, on waking, the hands must be washed before the morning cigarette and cup of tea. Suppose the patient next rises and removes a vest, then another washing is necessary before he shaves, or cleans his teeth. In dressing, further contamination is likely, therefore the hands must be washed again before breakfast, and so on throughout the day. Laxness in this respect will be followed by vexatious reinfections. Even with scrupulous care, occasional disappointments will be experienced. Nature is unceasing in the attempt to complete the life-cycle of the parasites, and if auto-infection is prevented the infestation will die out of itself.

Treatment proper falls under two heads: first, the removal by lavage of the adult female worms which have migrated to the rectum, and second, attempts to destroy the developing stages in the caecum, appendix, and neighbouring parts of the intestine. For the first-mentioned purpose nothing is superior to salt and water in a strength of 2 table-spoonfuls to the pint. If this should cause griping, reduce the salt by half, and increase later if possible. Four ounces of the solution is sufficient for an injection, which can be given most readily by means of an infant's 2-oz. enema bulb, the patient remaining recumbent, with the hips raised, during the operation. Probably he will be unable to retain the solution for more than one or two minutes, and when it is ejected the itching is found to have ceased completely, and is not felt again during the night. It is essential that the patient should administer this treatment for himself, because it is useless if given at any time that pruritus is not felt. A preliminary simple enema, more elaborate apparatus, and larger quantities of fluid, are unnecessary complications. When a sufferer who has been wakened nightly for months or years finds that a simple procedure completed within a very few minutes will protect him from the tortures of pruritus, at once his whole outlook on life is altered.

The second part of treatment is the administration of anthelmintic drugs in the hope of destroying the parasites before they migrate to the lower portions of the large intestine. It is difficult to assess their respective values, for most of the preparations recommended are either given with some laxative or themselves act as purgatives, and a sharp action of bowels due to any cause may give a temporary relief from pruritus; for this reason sufferers from undiagnosed enterobiasis sometimes attribute their troubles to constipation. I do not know of any drug so efficacious

as to do away with the necessity for rectal irrigations. Indeed, it is difficult to see how anthelmintics can reach worms lurking in the appendix and caecal pouches, and so long as even two or three are left they may suffice to drive the host into a state of frenzy. On the whole, my experience has been that when a patient finds that a rectal injection gives instant relief from his sufferings, he prefers not to be inconvenienced by purgative drugs, even though his course of treatment might be shortened thereby. Of the preparations usually recommended, I have found 2 grains of santonin combined with $\frac{1}{2}$ a grain of calomel distinctly helpful. Stovarsol had no appreciable effect. Carbon tetrachloride is reported to be very efficacious, but its employment is hardly justifiable in simple enterobiasis which can be cured with certainty in other ways. Oil of chenopodium and butolan I have not tried.

Treatment, especially lavage, may affect the remarkable periodicity of *Enterobius*, the commonest change being an earlier descent of the egg-laying females, so that pruritus may be troublesome before bed-time. But whenever it may appear, a rectal irrigation with salt and water will stop it at once. Rectal irrigations, given as advocated, do away altogether with the necessity for application of mercurial ointments and the like.

I do not know to what extent pruritus ani is met with in general practice, nor can I say what proportion of these cases is due to enterobiasis. My submission is that enterobiasis should be considered as a possible cause in every case of pruritus ani in adults.

TREATMENT OF GENERAL PARALYSIS OF THE INSANE BY INDUCED MALARIA

NOTE ON FIFTY CASES

BY

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Since the introduction on a large scale of malarial treatment of general paralysis of the insane by Wagner von Jauregg in 1917, great interest has been aroused in the subject, and this therapeutic measure has been extensively practised by numerous workers. The literature is already considerable; it has been fully summarized by G. de M. Rudolf,¹ by Surgeon Rear-Admiral Meagher,² and by J. Gerstmann.³

This communication is intended as a preliminary note on a series of fifty cases which have been treated in Edinburgh under the auspices of the Corporation venereal diseases clinic. The majority of the cases have been treated in the wards of Edinburgh Royal Infirmary, the remainder in Corporation hospitals. This series differs from most others reported in that, without exception, the cases were first seen in the out-patient department of a venereal diseases clinic or in consultation in the medical wards of a general hospital. None of the patients was certified as insane; many of them were at the earliest stage at which the disease may be recognized; only a few were at an advanced stage, at which they might have been certified insane. The series includes a relatively high proportion of cases of juvenile general paralysis of the insane (28 per cent.). In practically all the cases under review, treatment by therapeutic malaria has been followed by the administration over a prolonged period of antiluetic drugs.

In treating these patients our aim was to secure lasting remission of the mental symptoms and restoration of physical vigour; as a result of the combined treatment success has been achieved in a gratifying proportion of cases. Accordingly, we have extended the use of this method of treatment since we started our work in 1927.

THE SCOPE OF THE REVIEW

Fifty cases are reviewed, and are classified as follows:

General paralysis of the insane (adult)...	28 cases
General paralysis of the insane (juvenile)...	14 "
Tubo-paresis ...	6 "
Paresis sine paresi ...	2 "

The age periods of the patients were:

Up to 30 years ...	14 cases
30 to 40 years ...	12 "
40 to 50 years ...	14 "
Over 50 years ...	10 "

Of the adult cases 29 were males and 7 were females.
Of the juvenile cases 9 were males and 5 were females.

DIAGNOSIS

Every patient had definite symptoms and signs of general paralysis of the insane, and the diagnosis was always confirmed by an examination of the blood and of the cerebro-spinal fluid. The Wassermann test was strongly positive in both blood and cerebro-spinal fluid in every case. In the majority, the cerebro-spinal fluid showed a pathological increase of cells and globulin, and Lange's gold solution test gave a paretic or strong luetic reaction.

SELECTION OF CASES

The cases selected for malarial therapy included:

1. Cases showing pronounced mental symptoms, and in which the disease was advancing rapidly.
2. Cases of general paralysis of the insane which had received prolonged treatment with anti-syphilitic drugs, but had not responded favourably.
3. Cases already advanced when first seen.

Several patients in whom the disease was advanced, or who were seriously ill from other maladies, were included, even though the gravity of the prognosis was recognized. It was considered that malarial therapy offered the only reasonable hope of improvement. The patient in Case 32, for example, had a large aortic aneurysm; Case 44 suffered from severe diabetes mellitus; Case 40 showed marked dementia, incontinence, and bed-sores.

PROCEDURE ADOPTED

In every case a full neurological examination was made, and the blood and cerebro-spinal fluid were examined. A detailed physical examination of the patient was conducted, particular attention being paid to the circulatory system. Blood films from a known case of benign tertian malaria were examined to ascertain the activity of the infection. If malaria parasites were present in fairly large numbers, 3 to 5 c.cm. of blood were withdrawn by vein puncture and inoculated into the patient with general paralysis of the insane. The most favourable time to withdraw blood is prior to the onset of the rigor, or during a rigor. The blood may be inoculated immediately into the recipient, either intravenously or subcutaneously in the interscapular region; on the other hand, the blood may be citrated, kept on ice, and inoculated into a patient at any time within twenty-four hours. Every patient was confined to bed after inoculation, and a four-hourly record of the temperature and pulse was kept. After the first rise of temperature above 100° F. the temperature was recorded every two hours, and hourly during rigors. If the patient was debilitated, or if there was any evidence of cardio-vascular disease, appropriate tonics and cardiac stimulants were administered from the time of inoculation. Iron was given in all cases to counteract the anaemia. Very careful nursing was required.

INOCULATION

Benign tertian malaria was used in all cases except one (Case 31), in which quartan malaria was inoculated. Several different strains of benign tertian malaria were employed. These strains had been used for the treatment

of general paralysis of the insane for a considerable period. The patients were inoculated either subcutaneously or intravenously, according to whether a long or a short incubation period was desired. By the subcutaneous route the average incubation period from inoculation to the first rigor was fourteen days, with extremes of five and twenty-two days; by the intravenous route the average incubation period was eight days, with extremes of two and fifteen days.

INCUBATION

The incubation period did not vary with the volume of blood injected, but a heavily infected inoculum appeared to give a shortened incubation period. Malarial parasites may be found in small numbers in the peripheral blood for several days before the first rigor. Within twenty-four or thirty-six hours of intravenous inoculation there was in many cases a rise of temperature to 100° or 101°, lasting for about twelve hours. This initial pyrexia was not seen in patients inoculated subcutaneously. It has been suggested that such initial rises are due to haemolysis in incompatible blood groups, but this did not appear to be the case in our series. Further study of blood grouping in relation to inoculation by malaria is being made. Patients who have suffered from a natural malaria infection in the Tropics can be inoculated successfully, and the disease seems to run the usual course. Four of our cases had suffered previously from malaria, and one had had an attack of blackwater fever. Some degree of immunity seems to be acquired after induced malaria; four of our cases, however, have been successfully re-inoculated after an interval of a year.

OBSERVATIONS DURING THE COURSE OF INDUCED
MALARIA

Type of Fever.—In many cases the malaria did not run a true "tertian" course; often it assumed the quotidian type, or became quite irregular. Quotidian pyrexia is very exhausting to the patient. The tertian type is said to be commoner when the bloods of donor and recipient are incompatible. Jauregg considers that the quotidian type of fever in induced malaria is due to particularly favourable conditions for the growth of the malarial parasites afforded by cases of general paralysis of the insane.

Hyperpyrexia.—When the temperature exceeded 105° tepid sponging usually prevented further rise, and stimulants assisted the patient. Quinine in small doses has been recommended as a means of controlling the fever; we have found that even a single dose of 1½ grains of quinine bi-hydrochloride arrests the malaria. In five cases in which this amount was given to control pyrexia, or to secure a longer interval between rigors, no further rise of temperature occurred.

Symptoms.—Mental symptoms were aggravated in some cases during the rigors, and tabetic pains and crises were increased in severity. Not infrequently the excited and exalted patient became subdued and depressed.

Complications.—Albuminuria and gastro-intestinal disturbances were not a prominent feature in our cases. Herpes labialis was common. Cardiac failure is the greatest risk of this treatment. Enfeebled patients are very susceptible to broncho-pneumonia. In most cases, at the end of the febrile period, the patient was exhausted, and hypodermic injections of stimulants were required. A slight icterus was noticed late in the course of the fever in most cases, and the liver and spleen were increased in size in every case. In two cases severe jaundice developed, and the malaria had to be terminated. It is significant that both these patients had suffered from natural malaria in the Tropics, and one had had blackwater fever. One of these patients was successfully

reinoculated one year later, and did not develop jaundice. The patients recovered rapidly from the jaundice as soon as the malaria was stopped, and they have been treated subsequently by tryparsamide without intolerance. The malaria parasites live on and feed at the expense of the red blood corpuscles, and the degree of anaemia is proportional to the severity and duration of the malaria. All our patients showed a marked anaemia, but recovered rapidly after the fever was terminated. Retention of urine was occasionally troublesome.

Termination of Fever.—Most patients were allowed to have twelve rigors, unless there were signs of cardiac failure or of other severe complication. In several cases the fever was spontaneously arrested after six to ten rigors, but even in such cases quinine or plasmoquine compound was administered to prevent subsequent relapses. The largest number of rigors allowed in any case was sixteen, while the average was 10.6. Quinine bi-hydrochloride orally or plasmoquine compound tablets (Bayer) were effective in curing the malaria. No malaria relapses have come to our notice. Our observations suggest that better results were obtained in cases having at least eight rigors. The absence of relapses after treatment of inoculated malaria confirms the observations of other observers (James⁴). On the other hand, malarial therapy induced by the bites of mosquitos is followed by a relapse in 50 per cent. of the cases after treatment. This is a very striking difference, and has important bearings on the epidemiology of malaria.⁴

Convalescence from Malaria.—Convalescence was generally very rapid, and with iron tonics, sunshine, and fresh air the patient was able to go about in three weeks in almost every case.

Immediate Effects of Malaria.—Clinically most cases showed a marked amelioration of symptoms, and their physical state was greatly benefited; two patients developed acute maniacal symptoms on terminating the malaria, but both subsequently made an excellent mental recovery. The influence of malaria on the serological changes was indefinite. In several of our cases the blood and cerebro-spinal fluid were examined a few days after stopping the malaria, and in all cases both blood and fluid were examined within a month of terminating the fever. The Wassermann test of the blood showed little alteration; the cerebro-spinal fluid changes were very variable, and did not correspond to the clinical condition. The pleocytosis, globulin content, and gold sol test were more favourably affected than the Wassermann test. Serological improvement has been observed to appear at a much later date than the clinical improvement.

ANTILUETIC TREATMENT

It has been shown—and our cases substantiate this view—that malaria does not cure the syphilitic infection, and that most cases of general paralysis of the insane have a progressive systemic infection and a pathological cerebro-spinal fluid even after malaria. Accordingly, we have tried to stabilize the improvement due to malaria by starting antiluetic treatment as soon as the patient is convalescent from malaria. In many cases the serological findings have shown progressive improvement during this subsequent treatment, and concomitantly the mental and physical state has been maintained or has steadily improved. Tryparsamide has proved effective in the treatment of neuro-syphilis, but is less potent in systemic syphilis. In view of this we have adopted a combined treatment with tryparsamide and bismuth simultaneously. Iodides are also given, and occasionally mercury, although, in our experience, mercury is more toxic and less efficacious than bismuth. The "914" compounds have not given good results in this type of case. The average amount of treatment in a period of six months has been

50 grams of tryparsamide intravenously, and 6 or 8 grams of metallic bismuth intramuscularly. The patient attends once weekly as an out-patient, and at each visit receives 3 grams of tryparsamide intravenously and 0.2 to 0.4 grams of bismuth intramuscularly. A course consists of ten weekly injections, and an interval of four weeks elapses between each course. During the interval iodides are given orally, and tonics may be required. This routine may be continued with advantage over a very long period; persistence is, in our opinion, the essence of the treatment, and our earliest patients have received very large amounts of these drugs—for example:

Case 1: Tryparsamide 361 grams, bismuth 44.4 grams, in five years.

Case 4: Tryparsamide 305 grams, bismuth 38.1 grams, in four and a half years.

Case 41: Tryparsamide 211 grams, bismuth 31 grams, in three years.

Both drugs have been tolerated well, and we have had no cases of toxic amblyopia or of optic atrophy following tryparsamide injections in general paralysis of the insane. Tryparsamide in moderate doses has a marked tonic effect after malaria.

RESULTS OF TREATMENT

It has been necessary to adopt a standard by which to estimate results. The following classification has been used for our cases:

A. *Complete Recovery*: There are no mental symptoms present, and the patient is able to resume his usual occupation.

B. *Partial Recovery*: The patient is free from mental symptoms, but is not able, from physical causes, to resume his normal occupation—for example, is incapacitated by ataxia.

C. *Improved*: Slight mental symptoms or physical signs present; patient is unable to work, but does not require institutional care.

D. *No Improvement*: Mentally and physically impaired, and institutional care required.

Grades A and B are considered satisfactory results, C and D poor results. In the following table all patients now dead are included, irrespective of the cause of death.

TABLE I

	Satisfactory (A and B)	Poor (C and D)	Deaths
	Per cent.	Per cent.	Per cent.
Whole series ...	28.0	54.0	18.0
Adults only ...	30.6	50.0	19.4
Juveniles only ...	21.4	64.3	14.3

CONSIDERATION OF SUCCESSFUL CASES

Of the series, 14 patients (28 per cent.) showed complete remission of their mental symptoms and have returned to work. Four patients were not able to resume fully their normal occupation, owing in three instances to tabetic symptoms such as ataxia. Of the 14 successful cases, 11 were males and 3 were females; 8 were adult and 3 were juvenile cases of general paralysis of the insane, while 3 suffered from tabo-paresis. Their ages, which ranged from 20 to 60 years, did not appear to influence the result. The average duration of the syphilitic infection in these cases was seventeen years. The average number of malaria rigors was eleven, and the average period of observation of the successful cases following malaria therapy was twenty-two months.

The changes in the cerebro-spinal fluid as an immediate result of malaria were estimated as: marked improvement 3, slight improvement 3, no change 7, worse 1. Accordingly the immediate changes in the cerebro-spinal fluid were not a reliable guide to prognosis. All these success-

ful cases have had subsequent anti-syphilitic treatment. The present results as regards serological tests are seen below.

TABLE II.—*Serological Results in Successful Cases*

	C.S.F.	Blood	Both Blood and C.S.F.
Negative	7	5	2
Positive	7	9	5

In five cases the blood Wassermann test is now negative, but the cerebro-spinal fluid remains positive. In no case has the cerebro-spinal fluid become negative while the blood has remained positive.

CLINICAL RESULTS IN OTHER CASES

In the patients who made an incomplete recovery there was in every case considerable physical improvement and some mental improvement. The patients, for example, were less excitable, became continent and clean in their habits, and were often able to go about in hospital. Tabetic pains were often relieved.

JUVENILE GENERAL PARALYSIS OF THE INSANE

Fourteen cases of juvenile general paralysis of the insane have been treated. It was to be expected that this group would be rather a barren field, but, as the figures show, quite a fair measure of success has been achieved. Some observers consider juvenile general paralysis of the insane as a contraindication to malaria therapy (Johnson and Jefferson*). The clinical picture was usually very definite—a young person who had become dull, stupid, backward, dirty in habits, careless, and unduly “childish.” The clinical recovery in 21.4 per cent. of these patients, with a mortality of 14.3 per cent., justified this method of treatment, as otherwise the prognosis in such cases is progressive dementia and early decease. All juvenile patients improved physically, almost all regained control of their organic reflexes, and returned to clean habits. Drug treatment alone has not produced such gratifying recovery.

TABLE III.—*Serological Results in Juvenile General Paralysis of the Insane*

	Strong Positive	Weak Positive	Negative
Blood	9	0	3
Cerebro-spinal fluid	8	1	3

TABLE IV.—*Serological Results in Whole Series*

	Strong Positive	Weak Positive	Negative
Blood	32	2	10
Cerebro-spinal fluid	29	11	4

MORTALITY

In our series nine patients (18 per cent.) are now dead. Of these deaths three were not directly attributable to malaria. In Case 7 the patient died nineteen months after malaria from dementia and cerebral seizures; in Case 35 the patient committed suicide; in Case 19 the patient improved sufficiently to attend as an out-patient, then went on holiday, and three months later was found dead, the cause being unknown. Malaria, or intercurrent disease occurring during or very soon after the pyrexia, was the cause of death in five cases (10 per cent.). One patient died in hyperpyrexia; this was a very enfeebled case of juvenile general paralysis of the insane that had been inoculated with quartan malaria. Three cases showed an advanced degree of mental enfeeblement and physical debility, so that malaria was considered a grave

risk; these patients developed cardiac failure and bronchopneumonia, and died shortly after terminating the rigors. One patient, aged 55, suffered from severe diabetes, and though he was carried through eight malarial rigors, he died three months later from diabetic coma.

As this series includes several advanced cases of general paralysis of the insane, and several cases of other serious disease, and as all deaths to date are included irrespective of cause, the mortality is not unduly high. When it is recalled that the death rate from untreated general paralysis of the insane is considerable, the treatment by induced malaria is not, in our opinion, an unduly dangerous procedure. This view is supported by results obtained by others, particularly in the clinic of von Jauregg in Vienna. Our observations have so far been in favour of this therapeutic measure, and we hope that by earlier diagnosis of general paralysis of the insane, and by applying this method to cases before marked mental changes are observed, even better results will be obtained. Further observation over a long period is essential before a final estimate of results is possible.

SUMMARY

1. Fifty cases treated (36 adults and 14 juveniles).
2. Successful result in 28 per cent. of cases (30.6 per cent. adults alone, 21.4 per cent. juveniles alone).
3. Mortality due to malaria is small (10 per cent.).
4. Induced benign tertian malaria is easily cured. No malaria relapses in this series.
5. Serological improvement in blood and cerebro-spinal fluid frequently observed.
6. Value of anti-syphilitic treatment following malaria. Both clinical and serological results often show progressive improvement.
7. Necessity for prolonged observation of all cases.

I am greatly indebted for permission to observe and report these cases to Mr. David Lees, and to the honorary physicians of Edinburgh Royal Infirmary, under whose care the patients have been: Colonel E. D. W. Greig, lecturer on tropical diseases, Edinburgh University, has observed nearly all the cases throughout the course of the malaria, and has given great assistance in the treatment, and very valuable help in the preparation of this report. Colonel S. P. James of the Ministry of Health has supplied us on several occasions with strains of malaria for use in this series.

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THE FUNCTION OF THE ISOLATION HOSPITAL IN MODERN PRACTICE*

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Isolation hospitals are designed to isolate, until no longer potential sources of danger, those suffering from certain of the acute specific infectious diseases, with a view to the control of those diseases in the community. Since most of those so isolated are also physically ill, treatment of the illness occasioned by the infection is a necessary corollary.

The primary functions, then, of the infectious diseases hospital are the isolation and treatment of the infectious sick. The fact that in this country most of those sick from

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