

atebrin alone in order to test fully the value of that drug without quinine.

In a progress report issued locally in November, 1932, R. Green<sup>3</sup> states that both benign tertian and quartan parasites, including gametocytes, disappear from the blood more quickly with atebrin than with quinine. In subtertian malaria the rings disappear either with quinine or with atebrin in about three days. The febrile period in all types is slightly shorter with atebrin than with quinine, but, pending the cessation of febrile symptoms, the temperature among some of the subtertian cases seems to remain on the whole somewhat higher, and the patient to be more prostrate, than with quinine. The subtertian infection varies from the very mild case to the fulminating case, attended with fatal results whatever the form of therapy. In the small but certain proportion of subtertian cases which show alarming symptoms, Green regards it as at present advisable to administer quinine for two or three days as a preliminary to atebrin.

*Green's Relapse Rates*

Among forty-three patients who had 30 grains of quinine bihydrochloride a day for seven days, and were under observation for a maximum of forty-six days, Green's record is:

	Total cases	Relapses
Benign tertian ... ..	12	6
Subtertian ... ..	13	5
Quartan ... ..	18	5

Among forty-eight cases receiving a six-days' course of atebrin, and kept under observation for a maximum of eighty days (seventeen being benign tertian, twenty-three subtertian, and eight quartan), Green observed one relapse—a benign tertian case on the thirty-second day after treatment.

ATEBRIN IN SPLENOMEGALY WITHOUT MALARIA SYMPTOMS

On the presumption that an enlarged spleen indicates a latent malaria infection, it has been usual to give a course of quinine to all newly engaged local coolies with enlarged spleens, and to all coolies and dependants found in a similar state at periodic examinations of labour forces. Towards the end of 1932 I gave instead a five days' course of atebrin to forty-nine such cases; the first twenty-five were admitted to hospital, the other twenty-four were treated in the field. None of these has since developed malaria.

During the present year I am prescribing for the majority of patients with enlarged spleens a course of atebrin in the lines without taking them off work: one tablet is administered in the morning and two in the afternoon. A careful record is being kept: no further atebrin and no quinine will be administered to these cases—even if the spleen continues enlarged—unless an attack of malaria occurs.

CONCLUSION

The treatment of malaria with atebrin is short, simple, and economical. Most sufferers appear to be cured within a week. The consistent use of this drug should effect a great and permanent diminution of malaria among labour forces by sterilizing most of the reservoirs of infection.

I am grateful to Dr. Green for valuable information, and to my colleagues for their records.

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<sup>2</sup> Hoops, A. L.: The Treatment of Malaria with Atebrin in Estate Practice, *Trans. Roy. Soc. Trop. Med. and Hyg.*, November, 1932, xxvi, No. 3, 289.  
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TREATMENT OF MALARIA BY PLASMOQUINE AND QUININE

BY  
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 TRINIDAD

A remedy that will invariably cure malaria after a single course of treatment has yet to be found, unless the new preparation, atebrin, which is still on its trial, proves superior in this respect to the drugs at present in use. In the Tropics the assessment of the value of anti-malarial treatment is generally rendered difficult owing to the frequent presence of other diseases, the often poor living conditions of the patient, the difficulty of giving a prolonged course of treatment, and the liability to re-infection. In temperate climates patients are often lost sight of after treatment owing to their return to the Tropics, and in the event of a relapse they may fail to return to the prescriber of the original course of treatment. Control over any lengthy period is therefore the exception, while most of the cases treated must inevitably be cases of relapse. It therefore appeared to me that a high percentage of "cures" obtained with a standardized course of treatment under unusually well-controlled conditions might be of some general interest.

Malaria in Trinidad is the largest single cause of death. In 1931 this disease was responsible for 734 deaths out of a total of 5,374 (Registrar-General's Report for Trinidad and Tobago, 1931), and it must accordingly be assumed that the disease here is of a moderately severe type. All the cases in the accompanying table are those of members of the staff (including dependants) of an oil company operating in Trinidad. These form only a small percentage of the total cases of malaria treated, the disease being far more common among the labourers; but, for reasons stated above, the latter are unsuitable for the purpose of this paper. The total number of staff and dependants in this company is approximately 200, living in several widely scattered "fields" in the south of the island. All cases of illness occurring on these "fields" are bound to be reported to me, and thus no case of relapse could fail to come to my notice. The living conditions of these people are good. Comfortable mosquito-proof bungalows are provided, none of which is situated in a malarial area, and infection with this disease is therefore only accidental. Other tropical conditions are rarely found among them, and the general health is excellent. While all three varieties of malaria parasite are found in Trinidad, quartan infection is in my experience unusual, while benign and subtertian are almost equally common, though each predominates in its respective areas.

In the cases shown in Table I the attacks have generally been severe, with maximum temperatures of 103° to 105° F., the fever lasting three to four days. In no case has the fever persisted longer than the fifth day of treatment or risen again subsequently. I have for long been of the opinion that fever which did not respond to suitable treatment within five days was due to some cause other than malaria, providing the drugs administered were being absorbed. In nearly all cases the fever was of a remittent type, the regular intermittent fever frequently associated with relapses being notably absent. This was to be expected in a series where most of the cases were primary. In no case was an injection of quinine found necessary. I limit such injections entirely to cases in which administration of drugs by mouth is impossible owing to intractable vomiting, delirium, or coma. The treatment prescribed has been in use for over three years, and is the outcome of a trial of a number of different combinations of quinine, plasmoquine, and arsenic. No case of

intolerance to plasmoquine has occurred, nor is it expected to occur with the dosage prescribed; and none of the toxic symptoms occasionally seen with that drug (for example, cyanosis, abdominal pains) has been noted. The treat-

TABLE I.—Cases Shown in Tabular Form

Case	Date First Seen	Previous Malarial History	Type of Infection	Relapse	Under Observation to	Remarks
E. C....	12/29	Two previous attacks	Benign and subtertian	None	4/33	Mixed infection contracted in Venezuela five months previously. Contracted in Ceylon eighteen months previously. Had a "cure" in European tropical hospital in July, 1929. No further attack
H. P....	1/30	Many attacks	Benign	12/30	7/31	
G. M....	3/20	None	Benign	None	4/33	
Mrs. F.	6.30	None	"	None	4/33	
L. S....	7/30	None	Subtertian	None	4/33	
H. S....	7/30	None	"	None	4/33	
Mrs. T.	8/30	None	"	None	4/33	
G. C....	9/30	None	Benign	None	12/31	
Miss W.	5/31	None	Subtertian	None	10/32	
S. L....	7/31	None	"	None	4/33	
Miss L.	10/31	None	Benign	None	4/33	
Miss U.	11/31	None	"	3/32	4/33	Child aged 10. Treatment of first attack delayed ten days owing to absence from home
Miss B.	12/31	Many attacks	"	None	4/33	
Mrs. F.	12/31	None	"	6/32	4/33	No further attack after relapse
R. G....	12/31	Two attacks	"	None	4/33	Contracted in Venezuela fifteen months previously. Invalidated for malaria
Mrs. W.	1.32	None	"	None	4/33	
G. H....	2/32	Many attacks	"	None	4/33	
Mrs. E.	2/32	None	"	None	4/33	
Mrs. N.	3/32	None	"	None	4/33	
Mrs. B.	5/32	None	"	None	4/33	

ment pamphlet, together with the requisite drugs, is supplied to the patient as soon as convalescence sets in, and he is instructed to report any symptoms of ill-health which may arise.

TABLE II.—Standard Five Weeks' Antimalaria Course

Preliminary calomel and Epsom salts. Constipation must be avoided while this course is being taken.

*1st week: 1st to 3rd day (inclusive).—*Quinine grains x + one plasmoquine tablet morning and night. Quinine grains x midday.

*4th to 7th day (inclusive).—*Quinine grains x + two tonic pills morning and night. Quinine grains v midday.

*2nd week: 1st to 3rd day. —*Quinine grains x + one plasmoquine tablet morning and night. Quinine grains v midday.

*4th to 7th day. —*Quinine grains v + two tonic pills morning and night. Quinine grains x midday.

*3rd week: 1st to 3rd day. —*Quinine grains x + one plasmoquine tablet morning and night.

*4th to 7th day. —*Quinine grains v + two tonic pills morning and night. Quinine grains v midday.

*4th week. —*As for third.

*5th week: 1st to 3rd day. —*Quinine grains v + one plasmoquine tablet morning and night. Quinine grains v midday.

*4th to 7th day. —*Quinine grains v + two tonic pills morning and night.

The quinine used is generally quinine hydrochloride in capsule. Occasionally quinine is used in solution (where there is difficulty in swallowing capsule). The plasmoquine referred to is plasmoquine simplex. The tonic pills are the standard pills of B. W. and Co., containing quinine grain i, iron, arsenic, and strychnine.

In view of recent statements suggesting that delay in commencing treatment in malaria might be of benefit in permitting the acquisition of some natural immunity, and thus facilitate subsequent cure, I may state that all these cases commenced treatment as soon as the diagnosis was made, and my own experience indicates that where delay has occurred, owing to incorrect diagnosis or some other cause, the severity of the attack in primary cases has been very much aggravated, without any diminished liability to relapse. For the purpose of this paper I am assuming that all patients carried out their treatment according to instructions, and that any subsequent attack of malaria was in the nature of a relapse, and not a new infection.

## TREATMENT OF ACUTE CORYZA BY AUTOGENOUS VACCINES

BY

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Anti-catarhal vaccines of various types are widely used by clinicians, and stock vaccines are marketed by a large number of commercial houses. There is, however, very little evidence that such vaccines have any beneficial effects, and extensive investigations by von Sholly and Park (1921), Jordan and Sharp (1921), and Ferguson, Davey, and Topley (1927), showed that stock vaccines exerted no influence on the incidence of acute coryza. The object of this investigation has been to determine whether autogenous vaccines were of any greater value than stock vaccines.

In previous studies of the bacteriology of acute coryza (Hoyle, 1932) it had been found that individuals who suffered from unusually frequent and severe attacks of coryza harboured pneumococci, influenza bacilli, and "mouse pathogenic green streptococci" in large numbers in the upper respiratory tract, these organisms showing an increased incidence during infections. Similar observations have been recorded by Webster and Clow (1932). Haemolytic streptococci, while absent from the upper respiratory flora of the majority of normal individuals, were present in a small number of cases, and showed an increased incidence during infections. Friedländer's bacillus was observed in some cases of chronic catarrh. No other organism which could be cultivated on the media employed appeared to play any part in upper respiratory infection.

### TYPE OF VACCINE USED

In view of the above findings it was considered essential that all vaccines employed should contain pneumococci, *B. influenzae*, and "mouse pathogenic green streptococci," and, if an autogenous strain was not available, a stock strain was included. Haemolytic streptococci and Friedländer's bacillus were only included in the vaccine when autogenous strains were available. The composition of the vaccine was as follows:

1 c.cm. of an eighteen-hour culture of pneumococci in 5 per cent. rabbit's serum broth;

1 c.cm. of an eighteen-hour culture of "mouse pathogenic green streptococci" in 5 per cent. rabbit's serum broth;

8 c.cm. of saline.

*B. influenzae* from a chocolate agar slope was suspended in the above to a concentration of 1,000 millions per c.cm., and, if autogenous strains of haemolytic streptococci and Friedländer's bacillus were available, they were added in concentration of 500 millions per c.cm. and 1,000 millions per c.cm. respectively; 1 in 1,000 formaldehyde was used as antiseptic. Serum