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. Invalided 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-catarrhal 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

broth cultures of pneumococci and "mouse pathogenic green streptococci" were used because in animal experiments it had been found that they were more effective in producing immunity than saline suspensions, and experiments with human volunteers showed that the use of serum broth did not result in unduly severe reactions.

SOURCE OF CASES

I obtained the co-operation of a number of Leeds general practitioners, who sent cases suffering from unusually frequent and severe attacks of coryza. A clinical history was obtained from each patient, and an examination of his upper respiratory flora was made by the methods described previously (Hoyle, 1932). An autogenous vaccine was prepared as set out above, and a course of three injections given at weekly intervals—0.25 c.cm. for the first and second doses, and a third and final dose of 1 c.cm. Six months later a record of progress was obtained, and any patient desiring a further course of vaccine was examined again and a fresh vaccine prepared and administered.

BACTERIOLOGY AND RESULTS

As was expected, these individuals showed unusually large numbers of pathogenic bacteria in the upper respiratory tract. Out of ninety-four cases examined, in only one case were no pathogenic bacteria detected. Pneumococci were isolated in 59 per cent. of the cases, *B. influenzae* in 52 per cent., "mouse pathogenic green streptococci" in 72 per cent., haemolytic streptococci in 32 per cent., and Friedländer's bacillus in 11 per cent.

It was only possible to obtain satisfactory records in sixty-seven cases, and the results in these cases were as follows: twenty-eight cases derived no benefit whatever; in twenty-three cases the incidence of acute coryza was not affected, but the severity of the attacks was reduced; sixteen cases showed a definite reduction in both the frequency and the severity of the attacks. These results indicate that autogenous anti-catarhal vaccines, like stock vaccines, do not appreciably affect the incidence of attacks of acute coryza, and although some cases showed a reduction in the severity of attacks, this was not, in my opinion, sufficient to justify any very extensive use of such vaccines. It has been suggested that the failure of anti-catarhal vaccines is due to the causal agent of coryza being absent from the vaccine; but as the immunity conferred by an attack of coryza is negligible, there appears to be no reason for supposing that any greater degree of immunity is to be expected from vaccine therapy, and it is probable that a reduction in severity of the attacks is the most that can be expected.

SUMMARY

Sixty-seven individuals suffering from very frequent and severe attacks of coryza have been treated by autogenous vaccine therapy. The results show that the vaccine exerts no influence on the incidence of attacks. The suggestion has been made by previous workers that, while stock anti-catarhal vaccines have no effect on the incidence of acute coryza, they tend to diminish the frequency of severe complications such as pneumonia, and this suggestion has been supported by a small number of cases treated by autogenous vaccines.

I should like to express my indebtedness to a number of Leeds general practitioners who have assisted me in this investigation, to the Medical Research Council from whom I am in receipt of grants, and to Professor J. W. McLeod for some helpful criticism.

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ACETYLCHOLINE IN THE TREATMENT OF EPILEPSY

BY

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Since Hughlings Jackson,¹ in 1870, pointed out the possibility of the epileptic seizure being determined by contraction of the cerebral arteries, the role of "vascular spasm" in this disorder has been a subject of clinical and experimental interest. Vascular spasm is a mechanism now accepted by many clinicians as explaining a number of cases of transitory aphasias, hemianopias, and migraine. The sudden blanching of the extremities as a result of vaso-constriction is well illustrated in Raynaud's disease. The association of Raynaud's disease with cerebral vascular disturbances has been recorded by Norman,² and by Carp.³ Russell⁴ has noted the similarity between the stages of the epileptic convulsion and the symptoms accompanying heart-block in Stokes-Adams's disease. Many observations of the exposed cortex during epileptic attacks have been made. Foerster⁵ describes the sequence of events repeatedly seen by him on the operating table. Sudden pallor of the cortex and arrest of cerebral pulsation is immediately followed by extreme hyperaemia, venous engorgement, and bulging of the brain. Horsley,⁶ Leriche,⁷ and Kennedy and Hartwell⁸ have observed practically similar changes. Corroborative evidence is to be found in the observations of the fundus oculi during an attack. Jackson⁹ long ago noticed that the fundus was pale before a seizure; during the convulsion the veins became large and dark. Experimental evidence has recently been brought forward to show that the cerebral vessels contract after stimulation of the cervical sympathetic and dilate in response to vagus stimulation (Schiff,¹⁰ Forbes and Wolff¹¹). The effect of these observations has been to bring again to the foreground the hypothesis that fits are precipitated by cerebral vaso-constriction. But although it is now generally acknowledged that the cerebral arteries are under vasomotor control, a causal relationship between cerebral vaso-constriction and the epileptic attack is by no means accepted (Notkin *et al.*,¹² Wilson¹³). On the assumption that seizures are due to vaso-constriction of the cerebral arteries various operations on the cervical sympathetic chain have been performed in epileptic patients (Alexander,¹⁴ Bojovitch,¹⁵ Tinel,¹⁶ Zavialoff,¹⁷ Lauwers¹⁸). The results of cervical sympathectomy have on the whole been disappointing. Favourable results in certain subjects are reported recently by Lauwers¹⁹ following the removal of the carotid body.

Attempts to influence epileptic attacks by the administration of vaso-dilator substances have been made. Popea and Eustaziou²⁰ in 1927 recorded beneficial results following the inhalation of amyl nitrite at the onset of attacks. In 1929 Villaret and Justin-Besançon²¹ demonstrated the therapeutic value of injections of acetylcholine in Raynaud's disease, arteritis, and similar complaints. The beneficial effects of acetylcholine in Raynaud's disease appeared to lend support to the vaso-constriction theory of epilepsy. In 1931 Étienne²² and his co-workers at Nancy investigated the action of this substance in a group of seven epileptics. In two cases a notable reduction in the fit incidence was recorded. Later, de Gennes²³ reported that injections of acetylcholine arrested the seizures in two cases of status epilepticus. Similar results were described by Pagniez, Plichet, and Decourt.²⁴ Dino Bolsi²⁵ in 1932 reported a dramatic reduction in the number of seizures in five of his eight cases. In some of the group investigated the beneficial effect persisted for several days after the injections of acetylcholine.