by an infected mosquito in the previous autumn.

In the great epidemic of malaria in Ceylon in 1934, in which both *P. falciparum* and *P. vivax* were involved, there was another wave of fever cases nine months later, but all were *P. vivax* infections. Based on our observations at Horton Hospital, the late Colonel S. P. James warned the Ceylon authorities to expect this wave and Dr. Briercliffe wrote to Colonel James saying that had he, Colonel James, not given this warning he would have thought that another epidemic had begun.—I am, etc.,

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1 James, S. P., Nicol, W. D., and Shute, P. G., *Proceedings of the Royal Society of Medicine*, 1935, 29, 879.

2 Shute, P. G., *Journal of Tropical Medicine and Hygiene*, 1939, 42, 201.

Neuromyopathy during Malaria Suppression with Chloroquine

SIR,—Neuromyopathy has been described as a rare side effect of chloroquine when used in arthritis and collagenosis¹⁻⁴ but not previously during malaria suppression, when usually 300 mg base weekly is used. We would therefore like to report a patient who, during malaria suppression, developed a neuromyopathy possibly due to accumulation of chloroquine. Since the World Health Organization has recently recommended the double dose of chloroquine in regions where malaria is strongly endemic,⁵ this side effect may be seen more often.

The patient was a young, healthy Swedish woman who in November 1971 moved to Kenya, fully vaccinated, including polio immunization. She was prescribed 300 mg chloroquine base weekly for malaria suppression, but for safety she took 600-900 mg weekly. In November 1972 she noticed a gradually increasing weakness in her legs, with difficulty in climbing stairs and rising from a chair. In December a physician in Mombasa found absent knee and ankle reflexes. Her erythrocyte sedimentation rate, white blood count, and cerebrospinal fluid were normal. She was transferred to Sweden, where in January 1973 examination revealed general good health, a moderate atrophy of her thighs, marked weakness on flexion at her hip joints, and slight weakness of the flexors and extensors of her knees. She could walk on toes and heels easily. Knee and ankle jerks were absent. Superficial and deep sensation was normal.

Routine laboratory investigations, including C.S.F., were normal. Electroencephalograms and electrocardiograms were normal. Motor conduction velocity in the right peroneal nerve was normal. An electromyogram from the left quadriceps muscle showed a moderate reduction of motor units at a fairly high repetition rate. The action potentials had normal duration and amplitude. There was normal insertion activity and no spontaneous activity. This pattern of abnormality is consistent with a peripheral nerve lesion (see fig.). Biopsy of the right quadriceps showed no abnormalities. Chloroquine was discontinued on 12 January and on 15 January the concentration of the drug in the blood was 37 µg/100 ml. On reexamination on 9 February muscle strength had improved and the ankle jerks had returned, but the knee jerks were still absent. She returned to Kenya at her own request and was prescribed 50 mg pyrimethamine weekly for suppression. In May 1973 normal muscle strength and knee jerks were reported.

This case of neuromyopathy is in good accordance with those earlier reported. A neurogenic component was indicated by absent jerks with moderate or no weakness

in the corresponding muscles and by the E.M.G. findings. The clinical picture was otherwise that of a myopathy. Polyradiculitis, polyneuritis, collagenosis, and metabolic disorders could be excluded. The patient did not drink alcohol and took no drugs except chloroquine. A daily dose of 300 mg chloroquine base has been reported to increase the plasma drug concentration to a plateau of 20-40 µg/100 ml after four weeks.⁶ A weekly dose of 316 mg base produced plasma levels of 10-20 µg/100 ml after six hours, decreasing to about 2 µg/100 ml 42 hours later.⁷ Our patient's chloroquine levels after 300 mg base on two occasions at an interval of 54 hours are shown in the table. Her blood

Concentration of chloroquine in blood (g/100 ml) after two separate oral doses of 300 mg base

Dose	Hours after administration					
	0	4	8	12	24	48
1	10	80	55	45	15?	50
2				60	80	50

levels were fairly high (up to 80 µg/100 ml) even considering that chloroquine concentration in the erythrocytes is up to twice that in plasma. This might indicate a tendency to accumulate chloroquine in spite of normal liver function. Together with her symptoms and signs this strongly suggests a chloroquine neuromyopathy.—We are, etc.,

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Cerebral Embolism and Oral Contraceptives

SIR,—I was most interested in the paper by Drs. Karin Enzell and Gunnar Lindemalm (1 December, p. 507) because ever since Dr. J. MacD. Holmes and I first wrote

about episodes of cerebral arterial insufficiency in the users of oral contraceptives¹ I have become increasingly convinced that embolism was a more common cause for proven arterial occlusions than thrombosis at that site, and that the passage of emboli might account for many of the more transient episodes. This is not based so much on the clinical presentation the authors quote, for this can be a very unreliable way of diagnosing embolism, but from the arteriographic appearances, which resemble those in other known causes of embolism, and from the normal state of the arterial wall repeatedly shown radiologically and also from records of necropsies, including one of our own series involving the vertebrobasilar system.² This applies at the site of the occlusion and elsewhere.

What then is the origin of such an embolus? In an experience of over 60 examples of cerebral ischaemic episodes in young women on the pill I had been very impressed that only one case had occurred in a nullipara. The present authors' series does not support this, but I had hypothesized that in a previous pregnancy a reservoir of venous thrombi might have formed in the legs or pelvis and that for reasons unknown, and by *per hunc modum* unknown, had been mobilized and gained access to the arterial side of the cerebral circulation. This was the crux of the problem because patent cardiac septal defects could account for only very few. Drs. Enzell and Lindemalm suggest an alternative reservoir in the pulmonary vascular bed. This is an attractive idea because it would solve many of the difficulties, and I hope that any necropsy studies that may have been, or will yet be, carried out will pay special attention to this possibility. The fact of an association between the pill and episodes of arterial cerebral insufficiency is now widely accepted—the explanation of that fact still eludes us.—I am, etc.,

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1 Bickerstaff, E. R., and Holmes, J. MacD., *British Medical Journal*, 1967, 1, 726.

2 Ehtishamuddin, M., *British Medical Journal*, 1965, 1, 921.

Oral Contraceptives and Myocardial Infarction

SIR,—Dr. G. Lloyd suggests in his letter (20 October, p. 167) that three patients in our series of young women who had myocardial infarction while using oral contraceptives (25 August, p. 428) may have been taking this form of contraception because they were already hypertensive and unable to accept other methods of birth control.

This is not so. Of the three women documented as being hypertensive, one had normal blood pressure readings during pregnancies in 1959, 1962, and 1964. She was then started on oral contraceptives, on the recommendation of a gynaecologist, for symptoms of menorrhagia, premenstrual tension, and backache. Her records subsequently showed elevated diastolic pressure readings in 1971 and her name was placed on the waiting list for a hysterectomy in February 1972, but before she was called for operation she had a myocardial infarction in May 1972. Another woman had been taking oral contraceptives for eight years. She was