scopy a small percentage of patients showed *Giardia lamblia* or *Entamoeba histolytica* infections and were treated with metronidazole (or other anti-amoebic agent). However, it was found that in patients with a similar chronic history but who had not had *E. histolytica* identified in the stool a course of metronidazole produced the same dramatic subjective improvement in about 24 hours, with stool improvement within a few days. Most cases that presented with this clinical picture were therefore regarded as having gastrointestinal amoebiasis even in the absence of positive identification in the stool.

Tetracycline was more effective than the sulphonamides in treatment but was inferior to metronidazole, and it was assumed that tetracycline, as a weak anti-amoebic agent, was suppressing even if not eradicating the amoebae whereas the sulphonamides were treating only a superimposed upset in bacterial flora. After treatment with metronidazole patients felt cured rather than improved, but "relapses" are difficult to interpret when the patient remains in the area of possible reinfection. Is finding two stools and one specimen of jejunal aspirate negative for amoebae sufficient to exclude amoebiasis? Even if they did not have amoebiasis might these patients in London respond to metronidazole in the same way as the patients in Katmandu? I would also be interested to know whether any of the authors' series had received metronidazole treatment, without lasting benefit, before their referral to the Hospital for Tropical Diseases.—I am, etc.,

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Myopathies and Malignant Hyperpyrexia

SIR,—Muscle from individuals who are susceptible to malignant hyperpyrexia is very sensitive in vitro to a variety of physical and chemical stimuli, including general anaesthetics.[1] Halothane, succinylcholine, and potassium chloride all produce an abnormal contracture in this muscle and the caffeine-induced contracture is greater than normal. These contractures all result from a rapid and abnormally large release of calcium into the muscle cell.

As hyperpyrexia during anaesthesia has been described in two patients with myotonia congenita[2,3] the question arises whether myopathies in which myotonia is a feature also predispose to malignant hyperpyrexia. In order to examine this possibility we have used in-vitro pharmacological techniques to study muscle from two patients with myotonia congenita (one of whom was the patient described by Morley *et al.*),[3] three patients with dystrophia myotonica, and one patient with hypokalaemic periodic paralysis. Muscle from two of these patients, one of whom was the myotonia congenita patient who had developed hyperpyrexia, and the other had dystrophia myotonica, gave a small contracture on exposure to halothane, but this was not greater than occasionally seen in normal human muscle.[4] In no other way did muscle from any of these patients show evidence of the increased pharmacological sensitivity which we have shown to be the characteristic feature of malignant hyperpyrexia muscle.

The only abnormalities that could be demonstrated pharmacologically in any of these patients were a large contracture produced in both samples of myotonia congenita muscle when the bath temperature was suddenly lowered in the presence of 4 mM caffeine, and a large, short, non-sustained contracture produced in two of the three samples of dystrophia myotonica muscle by succinylcholine (0·13 mg/ml).

These negative results throw doubt on an association between myotonia congenita and malignant hyperpyrexia. In considering the case described by Saidman *et al.*[2] it is uncertain whether the patient really had myotonia congenita, as no clinical details were given, and in the patient described by Morley *et al.*[3] the temperature rose only to 38°C. It is perhaps possible that in myotonia congenita the development of malignant hyperpyrexia is mediated by a mechanism other than a rapid and excessive release of calcium into the muscle cell, but it seems more likely that none of the myotonic disorders that we have studied, and indeed probably none of the previously well recognized myopathies, do in fact predispose to malignant hyperpyrexia.—We are, etc.,

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Beta-adrenergic Blocking Agents in Renal Failure

SIR,—We are disturbed by the suggestion of Dr. D. J. Warren and others (27 April, p. 193) that beta-adrenergic blocking agents should not be used in patients with impaired renal function. Two years ago at the International Society of Hypertension meeting we reported our experience with large doses of propranolol in patients with impaired renal function. We showed that though when the blood pressure is first controlled renal function may deteriorate it subsequently improves and remains stable.[1] The beta-adrenergic blocking agents do not differ from other hypotensive drugs in this regard. If renal function is impaired lowering the blood pressure by any method may cause a fall in glomerular filtration rate and hence a further decline in renal function.[2] Experience with different hypotensive agents over 20 years has shown that when there is an initial decline in renal function it is usually followed by stabilization, and renal function subsequently improves in many patients.

Our records show that we have used propranolol in doses exceeding 400 mg/day in 400 patients attending our hypertension, renal, and pyelonephritis clinics. Since the report by Dr. Warren and his colleagues appeared we have reviewed records of 25 patients with marked impairment of renal function in whom the serum creatinine level exceeded 3 mg/100 ml. The mean maximum dose of propranolol for these patients was 824 mg/day and the period of treatment ranged from one month to four years. In 16 patients serum creatinine levels after treatment with propranolol did not change by more than 0·5 mg/100 ml above the pre-treatment level. Five patients showed an improvement in renal function and a significant fall in serum creatinine levels during treatment with maximum doses of propranolol. In four patients, all of whom had active glomerulonephritis, there was a steady decline in renal function, but this did not appear to be influenced by the addition of propranolol to other hypotensive agents.

The blood pressure is often refractory to treatment in patients with impaired renal function, and such heroic procedures as bilateral nephrectomy have been suggested for control of the blood pressure in such patients.[3] We have not found this necessary but regard beta-adrenergic blocking agents as one of the most important groups of hypotensive agents necessary for the control of severe hypertension. It is almost always necessary to combine several different hypotensive agents for control of the blood pressure in such patients, with the possible exception of oral diazoxide which may be effective on its own.[4] The combination of a beta-adrenergic blocking agent and a vasodilator such as prazosin[1] or hydrallazine is the commonest regimen which we use for the control of severe hypertension.[5] It would be a great pity if experience in the three patients reported by Dr. Warren and his colleagues persuaded doctors that they should not use beta-adrenergic blocking agents in patients with impaired renal function. Our experience in patients with more severely impaired renal function than those reported by Dr. Warren and his colleagues fails to substantiate their findings.—We are, etc.,

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Drug-induced Gynaecomastia

SIR,—Though numerous drugs have been implicated as a cause of gynaecomastia in many instances adequate biochemical investigations which could demonstrate a mechanism for this association have not been undertaken. Four cases of gynaecomastia caused by two types of drugs and produced by different mechanisms are described.

Case 1.—A man aged 25 years had been taking diethylpropion (Tenuate Dospan) for four weeks when he noticed that both breasts had become swollen and tender. There was no loss of libido. Apart from the well-marked gynaecomastia there were no abnormal physical signs. Investigations, including full blood count, sedimentation rate, blood urea and electrolytes, liver function tests, thyroid function tests, chest *x*-ray and *x*-ray examination of the pituitary fossa, were all normal. The results (see table) showed an increased excretion of all the hormones studied and their return to normal after stopping the drug. The breasts returned to normal after one month.

Case 2.—This was a man aged 60 years who had been a diabetic for 24 years. He was controlled with insulin and had been taking diethylpropion