when the patient was ill and taking drugs. These drugs may have included (for example) aspirin, which can be a potent cause of hyperuricaemia. Such a diagnosis would be acceptable only if urate crystals had been identified in the joint aspirate, a simple test which for some reason was neglected here. The information provided suggests that the patient actually had a pyogenic arthritis partly suppressed by antibiotics.

The second error was in management. Treating acute gout with a short course of allopurinol is not only useless but may actually be harmful by provoking a new attack.

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Serum creatine phosphokinase and malignant hyperpyrexia

SIR,—Professor M A Denborough's criticisms (15 November, p 408) of our findings (30 August, p 511) that serum CPK estimation is of little or no value in screening for malignant hyperpyrexia are invalid.

He states that 30% of muscle fibres taken from 54 normal individuals developed contracture with halothane. In a much larger series in our own laboratory we have found only one apparently normal muscle specimen which developed contracture with halothane. The reason for Professor Denborough's finding may be related to his choice of the rectus abdominis muscle for his study of normal controls. We consistently use the vastus medialis muscle and all our samples are taken across the motor point.

If false-positives were as numerous as he suggests this would be seen as a positive bias in our overall results (see table). Since the halothane-induced muscle contracture test was introduced in 1971[1] we have investigated 106 patients, of whom 48 (45%) developed halothane contracture. Even allowing for a number of patients being referred for this investigation who were found to have unrelated anaesthetic problems (for example, muscle spasm with suxamethonium without hyperpyrexia) this represents a positive result in 48 of 89 patients—that is, 54%. Thus our results are close to the 50% which could be anticipated for a condition inherited as a Mendelian dominant.

Muscle biopsy results for malignant hyperpyrexia

	1971	1972	1973	1974	1975 (up to 22.11)
Patients investigated ..	2	17	24	24	38
MHS+	2	7	13	11	15
MHS−	—	8	10	10	11
Unrelated conditions ..	—	2	3	3	9

MHS+ indicates halothane-induced contracture
MHS− indicates no halothane-induced contracture.

The slight positive bias in our results can be easily explained because among the 89 patients from malignant hyperpyrexia families 12 were "indexed" patients (that is, patients who had recovered from a clinically diagnosed episode of malignant hyperpyrexia). Even if Professor Denborough completely rejects the relevance of the halothane-induced muscle contracture as a satisfactory test for malignant hyperpyrexia susceptibility he surely cannot claim that serum CPK activity is of any value if 6 out of 12 indexed patients have consistently normal values (less than 60 U/l). It must be remembered that CPK estimations can often give falsely high values if the conditions for, and method of, venesection are not ideal. Blood should be taken without venous occlusion and the patient should not have exercised excessively for 48 hours before.

The more detailed in vitro tests quoted by Professor Denborough do not seem to be of any greater value or specificity than halothane-induced contracture. In our experience, if the latter is positive so are all the others.

Of much greater importance than the multiplicity of pharmacological tests used by Professor Denborough is the direct demonstration of myopathy by routine neurohistological techniques. All our patients have extensive histological and histochemical investigations and the excellent agreement between halothane-induced contracture and histological myopathy was shown in our paper. It is only in the light of these findings and their correlation that it is possible to demonstrate the inadequacy of serum CPK estimation as a screening test for malignant hyperpyrexia.

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[1] Ellis, F R, *et al*, *British Journal of Anaesthesia*, 1971, **43**, 721.

Phenformin and lactic acidosis

SIR,—In lactic acidosis associated with phenformin at therapeutic dosage Professor P H Wise and others (10 January, p 70) give good evidence for a combined aetiology, involving both phenformin itself and co-existent disease (which may act via reduced removal of the drug). How much the diabetes contributes, however, will necessarily remain in doubt until a therapeutic use of phenformin is found in unrelated diseases. The main evidence at hand for the production of lactic acidosis by phenformin in non-diabetics comes from a very few cases of self-poisoning, in most of which the patient did not both survive and demonstrate a normal glucose tolerance. In this context the following case may be of some interest, supporting the view that toxic levels of phenformin are the crucial factor.

A healthy 28-year-old woman was admitted having ingested 3 g of phenformin and six capsules of pentobarbitone. On admission she was comatose with a normal respiratory rate (14/min). After 5½ hours she developed hyperpnoea which continued at 35-60/min for three days (but which resembled the hyperpnoea of salicylate poisoning rather than acidotic respiration and did not correlate with arterial pH). Arterial pH estimations varied from 7·20 to 7·38 over the first 60 hours despite administration of 23 200 mmol of $NaHCO_3$. Blood lactate at 39 hours was 30·6 mmol/l (276 mg/100 ml). Blood glucose at 5½ hours was 6·2 mmol/l (111 mg/100 ml), but fell to 1·2 mmol/l (22 mg/100 ml) at 20 hours despite 75 g of intravenous glucose. A further 75 g of intravenous glucose was needed to maintain normal levels over the next four hours. Mild ketonuria persisted for 36 hours. ECG showed very peaked T waves after 24 hours despite normal serum potassium. Consciousness was regained after 48 hours. Blood pressure and temperature were normal throughout. There were no clinical or laboratory signs of cardiovascular or renal disease, and glucose tolerance was normal some weeks later. The patient made a full recovery.

These clinical and biochemical features are similar to those seen in previously reported cases of phenformin-induced lactic acidosis with the exception of rather profound hypoglycaemia, which clearly may relate to the non-diabetic state, and the time scale of the drug intoxication.

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Beta-blockers in the treatment of chronic simple glaucoma

SIR,—I was interested to read your excellent concise leading article on this subject (24 January, p 180). For the information of some of your readers, however, I would like to suggest that there is some recent good evidence that an important contribution to reduction in intraocular pressure in humans is made by β-adrenergic blockade alone, whether or not a membrane-stabilising or initial β-mimetic effect may also be involved; Tenormin (atenolol), which is a pure β-adrenergic blocker, has been found to reduce intraocular pressure when given by mouth[1 2] and it has quantitatively a very similar effect to that of propranolol.[2 3] Another supportive observation is that DL-propranolol (which has both membrane-stabilising and β-blocking properties) was more effective in reducing intraocular pressure than D-propranolol (which has an equal membrane-stabilising but a much weaker β-blocking effect); the difference was more clearcut in glaucoma patients than in rabbits.[4]

Also, two longer-term studies do suggest that the effect is not short-lived[5 6]

These drugs reduce intraocular pressure in chronic closed-angle glaucoma but of course early operation is very much the treatment of choice in almost all cases of angle-closure glaucoma and most cases of chronic closed-angle glaucoma.

The place of β-adrenergic blockers in the treatment of the glaucomas is still undecided, especially if systemic administration is required, as your article indicated. However, as you also mentioned, the efficacy of pindolol eye drops[7] is encouraging because it has the significant advantage of not producing topical anaesthesia, unlike guttae propranolol, which are also effective.[9] Unfortunately guttae practolol,[9] as potent as guttae propranolol,[8] and without the local anaesthetic effect, may well carry the risk of the oculo-muco-cutaneous reaction even if not given systemically. We are awaiting the opportunity to test the effect of guttae Tenormin (atenolol).

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