discipline may evoke animosity towards the department, it is effective.

Dr J D Wigdahl's point (2 September, p 707) about urgent general practitioner requests is taken. We now accept such requests if the urgent circumstances are outlined. The report copy and the letter are reviewed by the district medical committee to ensure that the facility is not regularly abused. I certainly do not wish GPs or anyone else to adopt a laissez faire attitude to disease. I hope no one else wants radiologists to develop a Lea Thomas attitude to organ-imaging.

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Dopamine and dobutamine

SIR,—I was distressed to read the letter from Mr Alan Yates (17 June, p 1622) in which he grossly misquotes my paper.¹ Mr Yates writes that "dopamine is dependent for its effect on the release of myocardial noradrenaline,¹ while dobutamine is not." In the paper to which he refers I wrote, "Dopamine increases myocardial contractility and heart rate by direct action on β -adrenergic receptors. It also releases norepinephrine from myocardial catecholamine storage sites."

The primary difference in the haemodynamic action of dobutamine and dopamine, in my opinion, is not because of difference in direct or indirect action on the heart but because of difference in their vascular actions.² In lower doses dopamine reduces blood pressure and total peripheral resistance, in part because of direct action on specific receptors which cause vasodilatation in the renal and mesenteric vascular beds. With slightly higher doses β -adrenergic receptors are activated to increase cardiac contractility and cardiac output. In this dose range dopamine has been used successfully for the treatment of refractory congestive heart failure.¹⁻⁵ When the dose of dopamine is increased further α -adrenergic vasoconstriction could occur which would be undesirable for treatment of congestive heart failure. On the other hand patients in shock may require the vasoconstricting action of dopamine to maintain adequate blood pressure. Recent studies have shown that vasodilators such as nitroprusside may be used in combination with dopamine to decrease vasoconstriction in patients with congestive heart failure.^{2,6}

Dobutamine acts on β_1 -adrenergic receptors and exerts relatively minor effects on α - and β_2 -adrenergic receptors. Accordingly it can increase cardiac output and decrease total peripheral resistance over a wider dosage range than dopamine. In the official package insert dobutamine is recommended "for inotropic support in the treatment of heart failure. . . ." Unlike dopamine it is not recommended for treatment of shock. Because dobutamine does not have the ability to increase peripheral resistance it could cause myocardial ischaemia if the heart were stimulated at a time when blood pressure was too low to maintain coronary blood flow.

Finally, Mr Yates states that "there are strong reasons to support the experimental evidence that the inotropic action of dobutamine does not produce expansion of myocardial ischaemia following infarction." In my opinion there are inadequate data to support

this suggestion without a special precaution included in the package insert: "Particular care should be exercised when Dobutrex (dobutamine) is used in patients with acute myocardial infarction, especially with widespread coronary artery disease. . . ." Dobutamine, dopamine, and all other sympathomimetic amines acting on the heart can increase the oxygen consumption of the myocardium with resultant arrhythmias or extension of the infarction unless myocardial oxygen consumption is simultaneously decreased by another mechanism such as reduction in heart size.⁷ We do not have sufficient knowledge to predict the effects of dobutamine on myocardial oxygen consumption in an individual patient with myocardial infarction.

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* * * We sent a copy of this letter to Mr Yates, whose reply is printed below—Ed, *BMJ*.

SIR,—In reply to Dr Goldberg's letter I really feel it is not necessary to discuss the differences of opinion between us regarding the modes of action of dopamine and dobutamine, as the primary reason for my original communication was the confusion arising from the similarity between the names of these drugs. Dr Goldberg's letter underlines the fact that there are definite pharmacological differences between them. Furthermore, I certainly agree with Dr Goldberg that we do not yet have sufficient knowledge to predict or confidently define the exact modes of action of these two drugs. Their differing effects on the peripheral vascular resistance is, of course, an important point, and as cogent an argument can be made for reducing the peripheral resistance as raising it in conditions of low cardiac output. Certainly raising the peripheral vascular resistance is of great importance when it represents a risk of peripheral ischaemia and gangrene.

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Alpha-fetoprotein levels in cirrhosis and cancer of the liver

SIR,—We have read with interest the report by Dr P J Johnson and others (2 September, p 661), though we think their results are rather surprisingly in contrast to those of other workers¹⁻³ and our own findings.

In patients with cirrhosis of the liver without evidence of malignancy we found raised serum levels (>20 mg/ml) of α -fetoprotein (AFP) in 80 out of 325 cases (26%), although the levels were never higher than 300 ng/ml. In 23 cases of primary liver cell cancer (PLC) arising in cirrhotic patients the concentration was higher than normal in 22 cases (95%)

(median 18 567 ng/ml). In 11 patients with PLC arising in normal liver AFP levels were abnormal in 10 (90%) (median 35 235). Of the 22 cases of secondary liver tumours AFP concentrations were higher than 20 ng/ml in 10 (45.4%) (median 1650 ng/ml).

In our experience, and in agreement with Mr Johnson and his colleagues, in most cases of PLC in cirrhotic patients the AFP level is high, but in contrast the level is also high in 90% of cases of PLC arising in normal livers and in a high proportion of cases of secondary liver deposits, while concentrations of AFP are raised in 26% of cirrhotics without evidence of malignancy, so that this finding does not permit the prediction of an ominous outcome. The work of Dr Johnson and his colleagues must be regarded with caution, at least in geographical areas other than Britain.

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Behçet's disease

SIR,—Although, as your leading article states (22 July, p 234), the exact aetiology of Behçet's disease remains unknown, it is clear that much of the diverse symptomatology is secondary to vasculitis.¹ In addition there is often a defect in fibrinolysis² with the development of venous thromboses and, as Dr R A C Graham-Brown has pointed out (19 August, p 570), treatment with ethyloestrenol and phenformin or with streptokinase has been shown to be of benefit. The anabolic steroid stanozolol has been shown to enhance fibrinolysis³ and to be of value in the treatment of both idiopathic recurrent thrombophlebitis⁴ and Raynaud's phenomenon.⁵ We should like to report the apparently successful use of this drug in a patient with Behçet's disease.

The patient, a 50-year-old Indian, was diagnosed as suffering from Behçet's disease in 1965 when oral and genital ulceration appeared. Subsequently he developed arthralgia and neurological symptoms and in June 1977 a deep-vein thrombosis in the left leg. Conventional therapy, including anticoagulation, did not prevent further extensive thrombotic episodes over the following six months. Investigations during this period revealed normal coagulation and platelet function studies but the resting fibrinolytic activity in his blood was reduced, as measured by a fibrin plate lysis area (FPLA) of between 25 and 40 mm² (normal 80 ± 40 mm²). In December 1977 treatment aimed at improving fibrinolysis with stanozolol 5 mg twice daily was started. Therapy has now been continuous for nine months and during that time he has had no further thrombotic episodes, although oral and genital ulceration has persisted. After six months the resting fibrinolytic activity was reassessed and the FPLA had increased to 169 mm².

The effectiveness of anabolic steroids in enhancing fibrinolysis is well recognised, though their action is often short-lived. Resistance soon develops to ethyloestrenol given alone, although when phenformin is also given a sustained action is achieved.⁶ We

consider, however, that the risks of lactic acidosis make the use of phenformin undesirable.⁷ Stanozolol on the other hand has been shown to be effective when given alone for periods up to 30 months and it is relatively free from side effects.⁸ We should like to suggest that stanozolol is effective in reversing the deficiency of fibrinolysis found in Behçet's disease and that it deserves further consideration as long-term therapy to prevent the development of potentially serious thrombotic episodes in patients with this condition.

We would like to thank Dr B Colvin for advice and Professor R D Cohen for permission to report this case.

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Eyesight standard for driving

SIR,—As an ophthalmologist I am regularly seeing middle-aged patients who come in to have their reading glasses strengthened but who, I find, have been driving with visual acuity below the legal standard. None of these had realised that the distance vision was not good, so that there was no question of writing to the Vehicle Licensing Centre. There was also a driving instructor who worked for three months with substandard vision following the loss of his spectacles.

I would agree that poor vision is not one of the main causes of road accidents. However, I think that the legal standard is reasonable. It should be enforced by having the police carry out spot checks with the number-plate test in laybys when they check the lights, brakes, and tyres. We seldom hear of a prosecution for driving with inadequate vision. There could also be more publicity on this subject.

All my patients became "legal" by my prescribing a distance corrector for their hypermetropia.

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Hypotensive effect of propranolol and phenoperidine in tetanus

SIR,—Dr N Buchanan and others (22 July, p 254) describe a patient with tetanus who developed profound hypotension after receiving propranolol. I have recently seen a similar phenomenon in which both propranolol and the synthetic narcotic phenoperidine appeared to be implicated.

A previously very fit 71-year-old man developed tetanus six days after sustaining a penetrating injury of the forearm while gardening. Artificial ventilation

was established, D-tubocurarine and diazepam being used as relaxants. Heart rate and intra-arterial recordings of blood pressure were monitored continuously. Phenoperidine 2 mg was given intravenously for sedation on five occasions during the first 24 h, during which period the heart rate and blood pressure remained stable. On the second day after admission the heart rate rose gradually to 150/min with a blood pressure of around 150/70 mm Hg. After a short burst of supraventricular tachycardia propranolol 2 mg was given intravenously over 5 min. The heart rate fell to around 120/min with no change in blood pressure. An hour later phenoperidine 2 mg was given intravenously and the systolic blood pressure immediately fell to 30 mm Hg at a heart rate of 100-120/min. There was no evidence of reflex vasoconstriction and the hypotension persisted for 5-10 min until it was rapidly and completely reversed by the narcotic antagonist naloxone 0.4 mg intravenously. The patient appears to have suffered no ill effects during this episode.

There is little doubt that phenoperidine was the immediate cause of the fall in blood pressure in view of the sequence of events and the prompt response to naloxone. However, previous doses of phenoperidine had not produced hypotension in this patient and it appears that prior β -blockade with propranolol was an important contributory factor.

The autonomic manifestations of tetanus are complex and unpredictable. When a β -blocking drug is considered essential to control sympathetic overactivity it would seem advisable to use the minimum effective dose and the possibility of a synergistic hypotensive effect with narcotics should be borne in mind.

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Body weight and endocrine function in anorexia nervosa

SIR,—Dr R D G Leslie and his colleagues (19 August, p 526), in their study on the influence of weight gain on hypothalamic-pituitary-thyroid (HPT) function in anorexia nervosa report that pituitary thyroid-stimulating hormone (TSH) reserve, as assessed by a standard thyrotrophin-releasing hormone (TRH) test, was reduced at low body weight. In a previous letter (20 August 1977, p 521) they reported a similar finding for prolactin. They suggest that these results are in accord with the theory that there is excessive dopaminergic activity at central receptors in anorexia nervosa.

We have recently completed a study of 20 patients with anorexia nervosa with particular emphasis on interrelationships between body weight and concentrations of gonadotrophins, prolactin, TSH, and thyroid hormones.¹ Our results in relation to the HPT axis are in substantial agreement with those of Dr Leslie and his colleagues, as were the findings of normal resting prolactin concentrations, but we were unable to demonstrate any correlation between body weight and the prolactin response to TRH. Beumont *et al*² were also unable to show any effect of weight on prolactin responses to TRH. In our own study and that of Beumont *et al*, however, TRH tests were performed on patients of low weight only after they had been in hospital for at least five days and had resumed an adequate diet. It is important to know whether Dr Leslie and his colleagues studied their patients initially in the starvation phase or after a period of refeeding,

as it is known that prolonged fasting results in a blunting of prolactin response to TRH.³

Many of the endocrine changes in anorexia nervosa occur as a consequence of malnutrition and quickly resolve with either the resumption of a normal diet or restoration of normal weight.⁴ It is clearly inappropriate to accord such endocrine changes and their central mechanisms any primary significance in the aetiology of the disorder. Many patients, despite weight gain, retain the characteristic psychopathological features of anorexia nervosa. In order to attach primary aetiological significance to changes in endocrine function it would have to be demonstrated that such changes are not merely the secondary effects of a low body weight. The clearest evidence so far of failure to resume normal endocrine function after resumption of body weight relates to the hypothalamic-pituitary-gonadal axis.⁵ Findings in this area, however, are not yet sufficiently advanced to permit aetiological hypotheses in terms of central neurotransmitter activity.

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Phenothiazine-induced dystonic reaction while swimming

SIR,—We wish to call attention to a rather unusual but potentially very serious situation in which a 24-year-old woman who had been admitted to hospital with a diagnosis of acute schizophrenia developed a dystonic reaction during a swim with other patients. Eight days previously she had experienced a dystonic reaction involving eye, neck, and lower extremity muscles approximately 26 h after she had received 20 mg of oral fluphenazine hydrochloride. The dystonia quickly subsided after 2 mg of intramuscular benztropine mesylate, which was continued orally at 1 mg twice daily. Oral fluphenazine hydrochloride was resumed at a dosage of 10 mg once daily at 9 pm.

Approximately 19 h after the patient had received her evening dose of fluphenazine and 7 h after her morning dose of benztropine mesylate she felt her legs "tighten up" while swimming in the deep end of the pool. She went under several times but managed to call out for help. She was pulled out almost immediately; one observer noted that her eyes "rolled back" several times, an apparent oculogyric crisis. She reported that after swimming 1½ lengths her legs had gone into spasm, making it impossible for her to stay afloat. After approximately 20 min these symptoms subsided completely.

We believe that this patient developed a phenothiazine-induced dystonic reaction of the lower extremities. We do not think that there is any association between swimming and dystonic reactions because many patients have participated in our swimming programme during the past four years without an incident