glands are cholinergic and show muscarinic characteristics. They are therefore blocked by muscarinic antagonists such as atropine but are quite unaffected by alpha blockers.

The second point arises from the statement that noradrenaline is without direct effect on the myocardium. Although the spectrum of agonist activity of noradrenaline is predominantly alpha it does exhibit some beta activity, and therefore it is false to imagine the myocardium immune from the actions of noradrenaline.—I am, etc.,

A. V. P. MACKAY

Department of Pharmacology,
University of Cambridge,
Addenbrooke's New Site,
Cambridge

Asystole after Verapamil

SIR,—There may well be merit in the implication in Dr. M. E. Benaim's letter (15 April, p. 169) that the combination of intravenous practolol and verapamil may be dangerous. We have heard of isolated adverse reactions under these or similar circumstances. When confronted with an ill patient with paroxysmal tachycardia one is tempted to try a succession of measures, even though we know little of the possible interactions that may result. The anti-arrhythmic action of beta-adrenergic blockers and verapamil may, in part, be similar in mechanism and site, albeit for different reasons. We are at present recording intracardiac electrograms wherever possible to define the mode of termination of arrhythmias by various measures. Other agents may prove unsafe when used in combination and this requires clarification. Apart from digitalis, verapamil was the sole anti-arrhythmic agent used in the trial by Dr. L. Schamroth and others (11 March, p. 660), in which tolerance proved good.—We are, etc.,

DENNIS KRIKLER

Prince of Wales's Hospital,
London N.15

ROWORTH SPURRELL

Guy's Hospital,
London S.E.1

Azathioprine in Connective Tissue Disorders

SIR,—We were interested to read your leading article on "Azathioprine in Connective Tissue Disorders" (11 March, p. 645) following the review by Currey[1] on immunosuppressive agents in the treatment of rheumatoid arthritis. We should like to report details of a patient with rheumatoid arthritis who developed severe anaemia while taking azathioprine.

A 48-year-old man was started on azathioprine 50 mg eight-hourly in April 1971 for severe rheumatoid arthritis. At that time he was taking soluble aspirin and oral prednisone 10 mg daily. Within one month of starting azathioprine he felt much improved and by August 1971 we had been able to reduce the prednisone to 7 mg daily. It was noticed that his haemoglobin concentration, which was 13·1 g/100 ml in June 1971, had dropped to 7·8 g/100 ml in August, and the mean corpuscular volume (M.C.V.) had risen respectively from 91μ^3 to 98μ^3. By September 1971 the haemoglobin had fallen to 4·7 g/100 ml and the M.C.V. had risen to 115μ^3. The total white cell count at this time was 3.000/μl and the platelet count 141,000/μl—these estimations had previously been normal. He was admitted to hospital, azathioprine was stopped, and prednisone 7 mg daily continued. Occult blood in faeces was not detected, and a direct Coombs test was negative. Sternal marrow examination showed a small number of hypocellular fragments with disturbed erythropoiesis and some megaloblastic change. The serum folate level was 3·7 ng/ml (normal) and the serum vitamin B_{12} level was 150 pg/ml (lower limit of normal). The serum iron was 275μg/100 ml and total iron binding capacity 310 μg/100 ml. He was treated with blood transfusions, oral folic acid, and vitamin C, and intramuscular vitamin B_{12}. His haemoglobin gradually rose and is now 12·4 g/100 ml. The M.C.V. remained mildly elevated for four months, but is now 93μ^3. The total white cell and platelet counts are normal.

Fortunately this man's bone marrow appears to have recovered, but serves as a warning that regular blood counts must be carried out on patients being treated with azathioprine at all stages of treatment. At the time the haemoglobin had fallen to 4·7 g/100 ml, the patient had received a total of over 21 grammes of azathioprine. In a recent report[2] neutropenia developed in a patient for the first time after 24 months' treatment with the drug. The implications of a macrocytic blood picture and megaloblastic change are not clear. This has been noticed by other workers[3] using azathioprine, and is reversible on stopping the drug. Macrocytosis, as such, may warn of impending toxic effects. The severe haematological changes in this patient are the most marked that Currey (personal communication, 1971) has seen in his experience with azathioprine in rheumatoid arthritis.

Another interesting feature is that this patient had a severe reaction to intramuscular gold in 1969. Following a test dose of 10 mg (Myocrisin), he developed mild pyrexia, severe aching in all joints, a sore throat, an itching rash, and albuminuria. He made a complete recovery, and has had no further gold injections. One of our colleagues (B. E. W. Mace) recollects a similar case where a patient who had a severe gold reaction subsequently had a severe haematological reaction to azathioprine. It would be interesting to know whether there have been other instances of similar hypersensitivity reactions. As far as we know there is no cross-reactivity between gold and azathioprine.—We are, etc.,

ANTHONY J. RICHARDS
D. R. SWINSON
ERIC B. D. HAMILTON

Department of Physical Medicine and Rheumatology,
King's College Hospital,
London S.E.5

1 Currey, H. L. F., *Prescriber's Journal*, 1971, **11**, 134.
2 Harris, J., Jessop, J. D., and Chaput De Saintonge, D. M., *British Medical Journal*, 1971, **4**, 463.
3 Mason, M., Currey, H. L. F., Barnes, C. G., Dunne, J. F., Hazleman, B. L., and Stickland, I. D., *British Medical Journal*, 1969, **1**, 420.

Diabetics and Motorway Crashes

SIR.—Dr. J. A. Frais raised a pertinent point (1 April, p. 49) regarding hypoglycaemia and multiple crashes on motorways. In an article on driving and medical disabilities[1] we include an example of such an accident on a road which is virtually a motorway.

In June 1966, a man was driving north in a four-ton van with power steering. He crossed the central reserve and collided head-on with other vehicles travelling south. Four people died and others were injured. The driver of the van sustained only minor injuries to the legs. A charge of dangerous driving was dropped when it became known that he was a diabetic and that the accident was attributed to hypoglycaemia. The man was taking 88 units of insulin lente and 12 units of insulin semilente daily at the time of the accident.

His licence was revoked as he was considered to be an unstable diabetic and liable to sudden attacks of disabling giddiness or fainting. In September 1969 he re-applied for his driving licence. His insulin requirement was now 40 units of soluble insulin and 28 units of protamine zinc insulin daily. However, a series of blood sugars on two separate occasions showed the following results:

	Blood Sugar in mg/100 ml	
Fasting	170	52
noon	34	30
3 p.m.	15	30
6 p.m.	90	66
10.30 p.m.	50	198

At no time did he lose consciousness or complain of symptoms of hypoglycaemia, though it is almost certain that there would have been some transient cerebral impairment. His licence was not granted. It later became known that this man often took his wife along with him in his van to stop him if he began to behave oddly.

Diabetics need not disclose on their application form their disability, except if they suffer from disabling attacks of giddiness or fainting.

In the experience of the County Medical Officer, who acts as adviser to the driving licensing department, the majority of diabetics become known to the licensing department only after an accident, and over the past nine years in the West Riding diabetics were involved in more reported accidents than epileptics.—We are, etc.,

G. E. LEYSHON
R. W. ELLIOTT
J. LYONS
H. W. S. FRANCIS

Health Department,
County Council of the West Riding of Yorkshire,
Wakefield, Yorks

1 Leyshon, G. E., Elliott, R. W., Lyons, J., and Francis, H. W. S., *Community Medicine*, 1972, 127, No. 15, 201.

Total Body Potassium and Chronic Renal Failure

SIR,—I was interested to read the paper by Dr. Keith Boddy and others (25 March, p. 771). However, there are certain points that deserve comment. While appreciating that in patients with chronic renal failure equilibration between administered radioactive potassium and native potassium takes 72 hours, it would have been difficult to apply this method in my patients who were undergoing dialysis every second or third day using a Kiil exchanger. My study[1] was done on the basis of the statement by Veall and Vetter[2]—"the 24-hour exchangeable K probably represents all the exchangeable potassium in normal subjects and about 90-95% in those diseased patients where equilibrium is delayed. . . . The agreement is better if 48 hours are allowed for equilibration, but this is not only necessitates a fourfold increase in the tracer dose owing to the short radioactive half life, but it also