difficult to postulate that the patient had a rare degenerative disorder of the central nervous system, an unexplained defect of calcium metabolism, and a mysterious conjunctivitis.

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¹ Smith, M J, and Hey, G B, *Postgraduate Medical Journal*, 1976, **52**, 86.

² Berlyne, G M, and Shaw, A B, *Lancet*, 1967, **1**, 4.

An unusual case of cerebrovascular disease

SIR,—I would like to raise a few points in connection with the recent clinicopathological conference (17 March, p 727).

The first patient presented with amaurosis fugax, in which it is generally accepted that embolism plays some part. The carotid angiogram showed an irregularity which could have been a source of platelet emboli. It is suggested that the stereotyped nature of the attacks makes embolism less likely, but experimental evidence¹ has shown that emboli may repeatedly go to the same site, owing perhaps to streaming of blood flow. The report mentions the blood pressure inequality between the arms and raises the possibility of subclavian stenosis and "steal," but this is most unlikely with a pressure difference of only 10 mm Hg and no bruits.

Surprise is expressed at the patient's remission while taking only aspirin, but this has well-known antiplatelet effects and is standard treatment for a patient with presumed platelet embolisation. Emboli from an atheromatous plaque may range from microemboli to large pieces and it is possible, in view of the fact that the vertebral arteries were occluded, that one of these caused death by obstructing the blood flow to the brain stem. It would be interesting to have necropsy information about the circle of Willis and associated arteries. This is a situation in which surgery to the carotid bifurcation could have been potentially life saving, as the risk of major embolic complications of such lesions is well known.

In addition, since we do not know whether antiplatelet drugs protect against stroke in patients who have had transient ischaemic attacks, it seems sensible to maintain them on these relatively safe drugs until trials have shown whether or not they are of value.

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¹ Wylie, E J, and Ehrenfeld, W K, *Extracranial Occlusive Cerebrovascular Disease*, ch 3. Philadelphia, W B Saunders, 1970.

Cardioselective beta-blockade and renal function

SIR,—We would like to confirm the observation by Dr R Wilkinson that atenolol has less effect on renal function than non-selective beta-blockers (3 March, p 617).

In a crossover study (n=27) of atenolol and three non-selective beta-blockers in hypertension¹ it was found that at doses producing equal reduction in systolic blood pressure serum creatinine level during atenolol treatment—92 $\mu\text{mol/l}$ (1.04 mg/100 ml)—was a little, but significantly ($P<0.01$), lower than during non-selective beta-blockade with

oxprenolol, propranolol, or pindolol—98 μmol (1.11 mg/100 ml).

A double-blind randomised crossover study of atenolol and identical placebo tablets in eight subjects with mild essential hypertension and normal serum creatinine levels has now been completed. Renal function was assessed during the eighth week of each treatment period by a double-isotope, single-injection technique using ⁵¹Cr-EDTA clearance for the estimation of glomerular filtration rate² and ¹²⁵I-iothalamate clearance for the estimation of renal blood flow.³ Glomerular filtration rate and effective renal plasma flow were below the normal range during placebo treatment (1.18 ml/s and 7.40 ml/s respectively) but did not diminish further to any significant extent on atenolol (1.22 ml/s and 7.06 ml/s). Serum urea was significantly higher on atenolol—6.7 mmol/l (40.36 mg/100 ml)—than on placebo—5.6 mmol/l (33.73 mg/100 ml)—but serum creatinine did not change.

Thus treatment with atenolol would appear not to cause significant reduction of renal function.

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¹ Waal-Manning, H J, *Clinical Pharmacology and Therapeutics*, 1979, **25**, 8.

² Bailey, R R, et al, *Australasian Annals of Medicine*, 1970, **3**, 255.

³ Blaurox, M D, et al, *Nephron*, 1966, **3**, 274.

Peripheral skin necrosis complicating beta-blockade

SIR,—I was interested in the report by Dr R Gokal and his colleagues (17 March, p 721) of peripheral skin necrosis complicating beta-blocker therapy. I have seen two such patients who, like Dr Gokal's patients, had no evidence of large artery disease.

The first, a 54-year-old man, presented in January 1975, having developed painful red toes within days of starting propranolol, 40 mg thrice daily, for hypertension. After three weeks' treatment he was noted to have an ulcerated little toe and bounding foot pulses suggestive of small vessel disease. His toe healed and his vascular symptoms disappeared on his stopping propranolol, and have not recurred.

The second patient, a 66-year-old woman on propranolol, 10 mg thrice daily, for angina, developed peripheral ulceration of a toe some weeks after increasing the dose marginally, to 20 mg twice daily, in February 1977. Although her feet felt cold the foot pulses were strong. The propranolol was stopped and the toe healed. However, the patient restarted propranolol of her own accord two months later as her angina deteriorated, and she has taken as much as 40 mg twice a day up to the present without further skin necrosis.

It thus appears that the absence of clinical peripheral arterial disease provides no guarantee against beta-blocker-induced skin necrosis and that the development of necrosis is not an absolute contraindication against further use of a beta-blocker.

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Drug-induced peripheral neuropathies

SIR,—Dr Z Argov and Professor F L Mastaglia (10 March, p 663), in their useful review "Drug-induced peripheral neuropathies," refer

to hydralazine as an agent responsible for "mild or subclinical" sensory neuropathy in as many as 15% of cases. In this context it is important to mention that side effects of this type (including systemic lupus erythematosus) were reported some 20 to 25 years ago, when hydralazine in high dosage was used, often as the sole agent, in the treatment of hypertension.

More recently, in the United States, hydralazine has been used in doses of up to 200 mg daily, in combination with other agents such as reserpine and diuretics, with very few toxicity problems. Perry reviewed the literature comprehensively in 1973,¹ pointing out that the evidence that late hydralazine therapy might represent a deficiency state was rather meagre.

Now that hydralazine and other vasodilating drugs are being used successfully with β -adrenergic blockers in the management of moderate-to-severe hypertension, it would be a pity if clinicians were misled by data from a previous era. It is the experience of clinicians today that peripheral neuropathy occurs rarely, if at all, when doses of hydralazine in the range of 100-200 mg daily are used. Indeed, no reports of neurological reactions appear in the Committee on the Safety of Medicines register of adverse drug reactions for the period July 1963 to June 1976.

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¹ Perry, H M, *American Journal of Medicine*, 1973, **54**, 58.

Accidental hypothermia and low-reading thermometers

SIR,—This winter has been the coldest since 1963. It is not unreasonable to suppose that there should have been an increase in the number of patients suffering from accidental hypothermia. The condition is common, as was shown in one survey during the relatively mild winter of 1975, when the incidence among the elderly admitted to hospital was 3.6%.¹

In spite of considerable national and local publicity, few cases have been noticed in the new Royal Liverpool Hospital. During the first five days of this year no cases were recorded in the casualty and admissions department. A possible reason for this was the absence of low-reading thermometers in the department. When commissioned, the hospital had an issue of low-reading thermometers but at the beginning of the year none was available on the wards—except in the geriatric department—or in the hospital stores. After discussion with the senior nursing staff the old thermometers are to be phased out and replaced by low-reading thermometers, without additional expense.

It would be interesting to know how many other hospitals do not use low-reading thermometers as a matter of routine. Admittedly, a low-reading thermometer does not guarantee that the mercury will be shaken down, but it may help to detect this lethal condition when the patient is first seen. Those patients suffering from accidental hypothermia do not complain of feeling cold, and the general use of low-reading thermometers in both hospitals and general practice may