residual fragments at two months and 14% at 12 months; of those with multiple stones, 70% still had fragments at two months and 22% at 12 months.

We have to date treated 15 patients by percutaneous cholecystolithotomy, with complete success in 13—not a bad initial learning curve. Our last patient left hospital completely free of stones and tubes in 24 hours without any need for long term chemolysis.

We maintain that a direct endoscopic approach to the treatment of gall stones in a functioning gall bladder has much to commend it when compared with lithotripsy and long term chemolysis.

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Nifedipine for epilepsy?

SIR,—The study by Dr John Larkin and his colleagues (20 February, p 530) draws attention to the potential use of calcium channel blockers in the treatment of epilepsy. The absence of a control group, however, makes it very difficult to form any real conclusions about the efficacy of nifedipine.

The moderate reduction in the frequency of seizures could be explained by the placebo effect of a new medication and by the widely recognised reduction in frequency of seizures that accompanies admission to hospital. Moreover, the penetration of nifedipine into the central nervous system is likely to be limited. Although there are few formal studies available nifedipine is almost completely protein bound and animal studies suggest that very little of it crosses the blood brain barrier.¹ It is uncertain, therefore, whether the drug can achieve sufficient concentrations in the brain to produce a therapeutic effect.

A considerable number of patients with seizures remain symptomatic despite maximal pharmacological treatment, and there is a need for new therapeutic agents. Calcium channel blockers may have such a potential role since the influx of calcium ions into neurones is thought to be an important feature of epileptogenesis.^{2,3} Animal studies⁴ and limited clinical trials⁵ have also suggested that calcium channel blockers may be potentially useful in epilepsy. It is likely, however, that calcium channel blockers which have better central nervous system penetration—for example, nimodipine^{4,5}—would be more suitable agents for use in future controlled trials in the treatment of epilepsy.

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Hypnotic drug use among the elderly

SIR,—The papers by Dr Kevin Morgan and colleagues and Dr E K Rodrigo and others (27 February, p 601) on benzodiazepine users suggest, without openly stating, that the introduction of these drugs to elderly patients is by general practitioners. During 1975-9 I kept careful records of tranquillisers given to old patients. Much time was spent in weaning them off these drugs and occasionally in using placebo (vitamin C 50 mg). From 1970 onwards nitrazepam was heavily used in hospital at a time when open wards were in vogue. Visits paid to the ward sister indicated that she was at liberty to prescribe nitrazepam to keep the ward quiet at night.

Our practice was the south London practice studied by Cooper *et al* in their studies of depression rates in general practice and of how general practitioners' diagnoses corresponded with psychiatrists'.¹ During some of these discussions it became clear that depression is a dynamic state, often preceded by anxiety and stress. There seems little doubt that prolonged stress stimulates hypothalamic activity, leading to a rise in blood cortisol concentrations. This in turn activates tryptophan pyrrolase, leading to reduced synthesis of serotonin, inhibition of the amygdala, and activation of the hypothalamus. As a result, a vicious circle is formed which aggravates depression.²

The general practitioner encounters the patient at the beginning of this cycle and seeks to reduce exposure to stress, which may lead to depression. The widespread use of tranquillisers in the treatment of "depressed" people in the community is connected with the evidence that long term users of benzodiazepines report high levels of emotional distress. There is now widespread teaching of general practice trainees that the use of diazepam drugs must be short term but also that ability to cope with emotional stress is reduced, rather than enhanced, by these drugs.

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Procedures in dermatology

SIR,—May we sound a note of caution regarding the technique of curettage for superficial or small nodulocystic basal carcinomas referred to by Dr D W S Harris (12 March, p 769) in his article describing procedures which "can easily be used in general practice."

Though subject to controversy,¹ curettage and electrocautery has retained a place in the treatment of basal cell carcinomas because it is quick and simple and in expert hands recurrence rates (for carefully selected minor lesions) are similar to those with other treatments such as surgical excision or radiotherapy.^{2,4} There are, however, three important reasons why surgically minded general practitioners would serve their patients better with a scalpel than with a curette.

Firstly, the key to cure of a basal cell carcinoma lies in identifying its margins, and only careful histological examination of an excised specimen will show that this has been accurate. The distorted specimen obtained by curettage and electrocautery cannot yield such information.

Secondly, clinical diagnosis of skin lesions can be difficult even for experts (and should always be confirmed histologically if the lesion is removed,

though this step was omitted from the procedure for curettage given by Dr Harris). Simple excision with macroscopic clearance of 2-3 mm can be defended as satisfactory initial treatment for any small skin malignancy but the same cannot be said of curettage and electrocautery. To take an obvious and serious example, in assessing prognosis and the need for further treatment of a malignant melanoma (which can be mistaken for a basal cell carcinoma) the absolute thickness of the lesion and its depth of invasion are crucial. These histological features are ruined by curettage and electrocautery.

Thirdly, sutured excision wounds heal quickly by first intention whereas the open burnt wounds left by curettage and electrocautery heal slowly by second intention. Not surprisingly, the cosmetic results of excision are usually better⁵—an important consideration since most basal cell carcinomas occur on the face.

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Physical exercise and mental health

SIR,—In reviewing the possible association between physical exercise and improved mental health Dr E Szabadi (5 March, p 659) omits any discussion of the possible physiological mechanisms. For example, analogies have been drawn between the effects of exercise and opiate drugs.¹ Exercise has reward value, and like these drugs can induce positive moods so that "runner's high" has been described.² Exercise may also raise the pain threshold: Dale found unusually high concentrations of β endorphin in half marathon runners who collapsed.³ The opiate antagonist naloxone inhibits these effects of exercise on mood and pain perception.^{4,5} Similarly, withdrawal from regular exercise may lead to dysphoria.⁶

Any dependence on regular exercise may be regarded as a "positive addiction," compared with "negative addictions"—for example, to alcohol or drugs.⁷ Although both types of addiction may be mediated through opiates there appear to be important differences. With negative addictions the pleasurable effects tend to be more immediate with longer term disadvantages, whereas with positive addictions individuals gain beneficial results only after perseverance, often with some initial discomfort.

If exercise raises the concentrations of circulating endorphins which act on the same opiate receptors as exogenous opiates such as heroin this would support the notion of substituting drug dependence with a positive addiction such as exercise. There are also implications for the detoxification of opiate users, in whom exercise might be expected to facilitate this often difficult process.

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