practitioners know that today's wonder sedation is often tomorrow's fiasco. I do not know how many doctors require night sedation because of problems such as Dr Grant's, but I wonder how such doctors ever do any night work.

I was surprised that following an acute illness involving coronary care admission Dr Grant was allowed to travel to Malaysia three days later. I am not surprised that a few days later after landing in Malaysia he "fainted" and was again admitted to coronary care.

Dr Grant writes: "We, as doctors, are not doing nearly enough to relieve the psychological distress—the fear of death indeed—which all intelligent patients with angina pectoris and coronary thrombosis are often allowed to suffer in a conspiracy of silence." Patients do not have to be intelligent to suffer such distress, and all general practitioners know this and deal with it all the time. Cardiac neurosis is a serious illness, and particularly so if patients are afraid to travel far, in case they go too far, by their way of thinking, from coronary care. There is much more to coronary thrombosis than coronary care, and sound advice and medical common sense are vital. I suggest that what Dr Grant requires is a general practitioner in every sense of the word, and he would be well advised to get one, seek his advice, and take it.

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Photocoagulation and diabetic retinopathy

SIR,—Absence overseas has prevented our commenting earlier on the excellent review article of Mr Hung Cheng (10 February, p 365) on "Photocoagulation and diabetic retinopathy." Proliferative change at the optic disc portends the worst possible prognosis, and yet initially often appears to remain in a quiescent state for years.¹ Reluctance to institute treatment at this stage is a consequence of the false sense of security created by the apparent natural history of this phase in the disease. This "wait for progression" philosophy superficially appears to be vindicated by the degree of success (quoted by Mr Cheng) that we have demonstrated in photocoagulation during new-vessel progression, when the glial-tissue component of the proliferative complex is increasingly predominant.²

Proliferative retinopathy is, however, a relentless, destructive process, constantly evolving, and involving a bipartite system of retinovitreal neovascularisation and vitreo-retinal connective-tissue deposition which terminates in blindness, glaucoma, and retinal detachment. A misleadingly arbitrary subdivision into distinct phases is routinely made in clinical practice. This is an inevitable consequence of undue emphasis being laid on the rapidly advancing component of the proliferative process, which requires little subtle monitoring and lasts six to nine months.

Thus the generally accepted situation belies the true evolutionary characteristics of the retinopathy. A rigid adherence to a classification of (a) initial quiescence, (b) active, florid deterioration, (c) terminal cicatricial quiescence highlights the effects of the short intermediate phase of intense activity and omits the more subtle changes that do not manifest themselves as an obvious increase in the fibrovascular retinal pathology.

In our trial of therapeutic response to photocoagulation² those eyes which showed early peripapillary and epipapillary new vessels were subdivided into "active" and "quiescent" groups. Mr Cheng was correct in ascribing significantly better retention of vision in one of these subgroups (treated eyes). However, the "quiescent" group showed no difference up to three years. The group demonstrated the latency of onset of rapid deterioration and remained unchanged before treatment. Therapeutic benefits in such circumstances are slow in becoming evident, as the tendency to a fall in visual acuity is usually slower. However, a significantly beneficial response was clearly conferred on treated eyes when more subtle changes were monitored. In control eyes there were significantly more nerve-fibre bundle defects and greater deterioration in colour appreciation in the blue-green than in treated eyes.

It appears that early photocoagulation produces benefits in several ways. Firstly, it confers these benefits during an unobserved progression of the early "quiescent" phase of retinal neovascularisation. Secondly, several weeks may be required in which to complete treatment, and if the disease is active there is a potentially blinding condition which is increasing through the period of photocoagulation. Any prevarication and delay until observed "activity" presents inevitably leads to treatment benefits being conferred too late, or else vitreous haemorrhage makes photocoagulation impossible at the vital time. Finally, in the rationale of "early" versus "wait for progression" photocoagulation the quintessence of treatment benefit is to be found as much in the attitude of mind of those who embrace a change to prompt and early treatment as in the modalities and techniques they adopt.

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¹ Larsen, H W C, *Acta Ophthalmologica*, 1960, suppl No 60, p 42.

² Hercules, B L, et al, *British Journal of Ophthalmology*, 1977, 61, 555.

Diagnosis of cholestasis

SIR,—We would like to comment on your recent leading article (12 May, p 1232). Your editorial took exception to our published statement¹ that it may be unnecessary to confirm (by preoperative cholangiography) that jaundice is caused by gall stones when ultrasonography shows only stones in the gall bladder.

Of course, this recommendation is made only when there are no clinical or ultrasonographic features to suggest an alternative cause for jaundice, and further extensive experience has not changed our opinion. However, it is true that most jaundiced patients do need invasive cholangiography even after expert ultrasonography. The relative merits of percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiopancreatography (ERCP) have been well rehearsed, but we wish to emphasise two points.

Firstly, the results and risks of both techniques are highly dependent on the experience of the operator. In the learning phase both methods carry a significant failure rate and

complication rate.^{2,3} Our success rate for endoscopic cholangiography is now well over 90% and we have not seen a complication in the last 1000 diagnostic ERCP examinations.

Secondly, the choice of cholangiography route is increasingly being influenced by the therapeutic applications. Thus we may well choose PTC to confirm a clinical and ultrasonographic diagnosis of malignant obstructive jaundice, in order to insert a drainage tube or endoprosthesis at the same time; we choose ERCP in many patients who probably have stones because it allows us at the same time to remove any duct stones by endoscopic sphincterotomy.

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¹ Vallon, A G, Lees, W R, and Cotton, P B, *Gut*, 1979, 20, 51.

² Juler, G L, Conroy, R M, and Fuelleman, R W, *Archives of Surgery*, 1977, 112, 954.

³ Bilbao, M K, et al, *Gastroenterology*, 1976, 70, 314.

Operative cholangiography

SIR,—At this hospital operative cholangiography is routine during cholecystectomy. The operating table can be tilted and it has a fixed grid incorporated within it. However, the films have often been technically disappointing. The problem was the difficulty in striking a balance between the need to tilt the table in order to display the common bile duct clear of the spine and tilting too much so that grid "cut-off" gave rise to uneven exposure and poor definition.

The grid lines were at that time aligned along the long axis of the operating table. We have solved the problem quite simply by removing the grid and rotating it through 90° so that the grid lines are now aligned across the table. When the table is tilted obliquely grid cut-off cannot now occur. In addition, we routinely use a cone on the tube head in order to reduce scatter and this also improves radiographic definition.

These changes have transformed the quality of our operative radiography and are recommended to any theatre with a similar table where similar difficulties have occurred.

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Tap water for electrocardiographic recording

SIR,—It was with great interest that I read the article (17 February, p 454) from the Charitable Infirmary, Dublin, on substituting tap-water for electrode jelly. It is most laudable that this attempt to reduce expenses has been made.

I would like to note that the use of surgical spirit BPC is just as good as water. I have personally used this method since I learnt about its use from Professor A Nadas at the Children's Medical Centre, Cardiac Clinic, Boston, in 1961. The ECG recordings are as

good as those obtained with any jelly and the method is far less messy and much cleaner. One does not even need to use a towel to dry the patient off afterwards as the surgical spirit evaporates.

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officialdom, on present-day trends there will be a vast number of the population available for study who have submitted themselves to this form of therapy at their own hands.

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¹ McGibbon, D H, and Briffa, D, *Clinical and Experimental Dermatology*, 1978, 3, 371.

Saxophonist's diverticulosis

SIR,—Further to Dr L D Gardner's letter (26 May, p 1428) drawing attention to the extravagant claim for oral pressure made by the saxophonist with diverticulosis (5 May, p 1217), I am at a loss to understand the pathogenic mechanism proposed for saxophonist's diverticulosis, even if the oral pressures generated had been more physiological.

The incomplete Valsalva manoeuvre performed by the blowing saxophonist would be expected to increase intra-abdominal pressure equally on both sides of the colonic wall. I would find more acceptable a description of saxophonist's hernia, piles, varicose veins, or even periphonic petomania.

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PUVA and solariums

SIR,—While the DHSS continue to bombard dermatologists using PUVA therapy for skin diseases with warnings of potential long-term hazards, of which most of us are aware, it might perhaps be more appropriate for them to direct their warnings to the ever-increasing number of the normal population who are attending commercially run solariums or have their own private units and are receiving doses of ultraviolet A in excess of those given by us to our patients.

I recently examined two commercially available solarium units and measured the UVA output with a Waldmann black ray meter, which is used to calibrate our departmental SAS unit. Both "health lamps" had an emission of approximately 15 mW at nine inches, whereas our own unit gives approximately 10 mW at the same distance. Once the customer acquires a tan he or she is encouraged to attend weekly for half-hourly "treatment" to maintain the tan. On my calculations this involves a dose of approximately 30 joules UVA a week.

The DHSS is also right to draw our attention to the possible side effects of the psoralens themselves, but it is also possible to obtain a therapeutic dose of psoralens from the diet. I saw one patient, a tailor's cutter, who developed friction blisters on the first three digits of the right hand where his scissors caused pressure. He had recently bought a UVA health lamp and was also a food faddist in that he ate large quantities of celery, parsnip, and fresh citrus fruits, all of which contain psoralen. Friction blisters in patients undergoing PUVA therapy have been described.¹ This patient's blisters subsided when he abandoned his UVA lamp.

It is probable that the only way of determining the long-term effects of PUVA therapy will be to administer it to a large number of patients carefully followed over many years, but, should our attempts to give PUVA to a select group be thwarted by

Amitriptyline plasma concentrations and clinical response

SIR,—We agree with Dr T R Norman and others in their letter (31 March, p 894) that investigations of the relation between plasma antidepressant concentrations and clinical response should be conducted in those groups of patients who are most likely to benefit from tricyclic antidepressant therapy. With this in mind, we included in our study (27 January, p 230) only hospital patients with a diagnosis of endogenous depression, as defined by recognised scales, who did not respond during a placebo treatment period. Unfortunately, the concise presentation of our report has led Dr Norman to misunderstand some of our results.

The mean response rate, measured by a decrease on the Hamilton rating scale (HRS), of patients who developed plasma concentrations inside our proposed therapeutic range of 80-200 µg/l amitriptyline plus nortriptyline was not 58%, as stated by Dr Norman, but a satisfactory 72% improvement. In contrast, the mean response rate of those patients with plasma concentrations outside this range was only 42%. The difference in response between these two groups was highly significant irrespective of whether final HRS score, amelioration score, or percentage change in HRS score was used ($P < 0.001$). Furthermore, non-parametric statistical analysis produced similar results.

Reanalysing our data along the lines suggested by Dr Norman, we have compared the clinical response of those patients with plasma concentrations inside and outside the suggested therapeutic range. The criterion for clinical response was set, as in our earlier study,¹ at a final HRS score of 8 or less. Twenty-nine of the 38 patients with plasma concentrations within the 80-200 µg/l range responded (76%), compared with only 10 out of 27 patients (37%) with plasma concentrations outside this range ($\chi^2 = 10.2$, $P < 0.005$). Measurement of drug plasma concentrations was carried out by gas chromatography,² which has been shown by external quality control tests to be extremely reliable, with a variation index of only 0.25.³ The figure shows the mean percentage change on the HRS with increasing plasma concentrations of amitriptyline plus nortriptyline for the 65 patients completing our study. The seven patients whose plasma concentrations were below 80 µg/l had a poor mean response (38%). There was no apparent difference in response for the three groups of patients with plasma concentrations of 80-120, 120-160, and 160-200 µg/l; while the 20 patients with plasma concentrations in excess of 200 µg/l showed a successively poorer response with increasing plasma concentrations.

Where previous studies have included only small numbers of patients there is an increased chance that the plasma drug concentrations

Mean percentage change in HRS ($\pm$ SE of mean) according to plasma concentrations of amitriptyline plus nortriptyline.

observed will form a cluster. Such an occurrence at low concentrations may well produce a positive linear correlation between plasma drug concentration and clinical response,^{4,5} while a preponderance of high concentrations could produce a seemingly negative one.^{1,6} This phenomenon may produce results from different trials which appear to be contradictory but are in fact complementary. When a large, well-conducted study such as ours is completed these apparent contradictions are largely reconciled, and the true curvilinear relation between plasma concentrations of amitriptyline and clinical response is revealed.

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¹ Montgomery, S A, et al, *Clinical Pharmacology and Therapeutics*, 1978, 23, 309.

² Dawling, S, and Braithwaite, R A, *Journal of Chromatography*, 1978, 146, 449.

³ Jones, S, and Turner, P, *British Medical Journal*, 1979, 2, 1217.

⁴ Braithwaite, R A, et al, *Lancet*, 1972, 1, 1297.

⁵ Ziegler, V E, et al, *Archives of General Psychiatry*, 1977, 34, 607.

⁶ Kragh-Sorensen, P, et al, *Lancet*, 1973, 1, 113.

Historical fats

SIR,—Your journal (2 June, p iv) carried an advertisement from the Butter Information Council which could be misleading. The heading of the advertisement states, "If you were convinced that the population is not eating any more animal fat than it was in 1909—would it make you stop and think?" If we accept the truth of the statement, it is still misleading, because the quality of animal fat in 1909 was almost certainly different from the quality of animal fat at the present time. The animal feeding was completely different—for example, the soft fat pig was considered of good quality, whereas today the bacon factories want only hard fat pigs. Also the dripping sold in 1909 contained unsaturated fatty acids as opposed to the present hard cooking fats and lards, which contain only saturated fats.

The point I am making is that within the total amount of animal fat consumed in 1909