Dialysance of Molecules of Different Size

SIR,—We read with interest the paper of Dr. P. Kramer and others (6 May, p. 320) and while we agree that the decrease in efficiency with re-use may be the result of "blood deposits on the membrane surface inhibiting exchange," we feel there are two points which must be made.

Firstly, the authors say that of the dialysers studied, the Ab-Gambro dialyser had the greatest blood loss due to "blood pooling and clotting on the surface of the membrane" and yet they found the mean blood loss in this dialyser to be only 6.86 ml. This was compared with blood losses of 3.65 ml and 3.48 ml for the Rhône-Poulenc and the Kiil dialysers respectively. Surely an increase of blood loss by some 3 ml cannot interfere with dialyser performance? We feel that this discrepancy is explained by the fact that Dr. Kramer and his colleagues measured the blood losses by the technique of haemoglobinometry on a saline "wash-through" (although they do not give any details of their methodology). This technique is subject to considerable inaccuracies,¹ and, furthermore, it will underestimate blood loss should blood be retained on the membrane surface as adherent thrombus. We have studied in detail these and other dialysers, and have found that thrombus formation takes place upon the membranes of the Ab-Gambro dialyser in spite of adequate heparinization. This, in turn, will cause a high blood loss; using an accurate technique, involving ⁵¹Cr labelled red blood cells, we have found this to be 36 ml $\pm$ 4 (M $\pm$ S.D.) (unpublished data).

The second point to be made is that the Ab-Gambro dialyser in question was the Gambro-Alwall which we have found to have characteristics which encourage the in vivo formation of thrombus (unpublished data). We are currently engaged in assessing the new Gambro-Lundia dialyser, and can report that this does not have such characteristics and its use is associated with a very low blood loss (4.0 ± 1.7 ml). It is unlikely, therefore, that blood deposits will affect the efficiency of this dialyser.—We are, etc.,

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¹ Will, G., Lawson, D. H., King, P., Boddy, K., and Linton, A. L., *Nephron*, 1970, 7, 331.

Neuritis and Ultrafiltration Dialysis

SIR,—We would like to comment on certain features of the interesting paper by Dr. A. Meyrier and colleagues (29 April, p. 252). They suggest that high rates of ultrafiltration might have been responsible for the neuropathic defects observed. It may be relevant that we have been repeatedly subjecting six patients on maintenance haemodialysis to high rates of ultrafiltration for the past seven months, and at no time have we seen neuropathic effects such as described. Moreover, five patients were recently subjected to intensive progressive weight reduction using Travenol Ultra-flo 145 coils, such that mean pre-dialysis (and post-dialysis) weights were finally reduced by a total of between 4 and 6 kg during two weeks. Again no symptoms of neuropathy

were seen. Nerve conduction velocities, measured in the common peroneal nerve one month later, varied in these patients between 33.3 and 39.9 m/sec, results which were unchanged or improved, compared with previous measured velocities.

The lack of acute neuropathic involvement could arguably be related to the fact that our patients are all dialysed against a low magnesium¹—high sodium dialysate (magnesium— <0.2 mEq/l. derived from the non-deionized tap water; sodium—145 mEq/l). Unfortunately, Dr. Meyrier and colleagues do not mention the concentrations of these ions in their dialysis fluid, but we would surmise that the sodium concentration in their dialysate was nearer the customary 130 mEq/l. The incidence of cramps (which they mention in connexion with Case 3) is considerably greater using dialysis fluid of 132 mEq/l. of sodium, compared with 145 mEq/l.² Admittedly our five patients, although they showed no comparable neuropathic upset, all had some cramps during the two weeks of progressive weight reduction, despite the high sodium concentration of the dialysate used.

We would suggest that the neuropathy of the patients described by Dr. Meyrier and colleagues is not attributable solely to vasoconstriction or the accompanying plasma volume change. The neuropathy may possibly be a consequence of the cationic composition of their particular dialysis fluid. The cellular "overhydration" which probably accompanies dialysis with low sodium concentrations, as shown experimentally by Pappius and colleagues,³ could be a contributory factor. Cellular overhydration is virtually absent during high sodium strength dialysis.

Dr. Meyrier and colleagues do not mention how many of their patients, subjected to similar rates of ultrafiltration, have not developed neuropathy. The possible occurrence of some unrecognized transient or intercurrent process in the patients described cannot be ruled out. For example, it has been recently shown (12 February, p. 409) that inactive hepatitis occurring in patients on maintenance haemodialysis can cause a temporary reduction in nerve conduction velocities.—We are, etc.,

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- 1 Stewart, W. K., and Fleming, L. W., *Lancet*, 1969, 2, 1190.
- 2 Stewart, W. K., Fleming, L. W., and Manuel, M. A., *Lancet*, 1972, 1, 1049.
- 3 Pappius, H. M., Oh, J. H., and Dosseter, J. B., *Canadian Journal of Physiology and Pharmacology*, 1967, 45, 129.

Controlled Drinking for Alcoholism

SIR,—Until recently, total abstinence was the unquestioned aim of all types of therapy for alcoholism. Abstinence may well be a reasonable aim for numerous alcoholics and for a variety of treatment approaches. However, if the goal of abstinence is replaced by that of achieving a pattern of moderate, controlled drinking, then we may be able to provide valuable assistance to many alcoholics whose prospects of achieving total abstinence for prolonged periods is precisely nil. A return to controlled drinking is a more realistic form of behaviour than abstinence in our

alcoholic society in which most of the adult population drink with regularity. If our goal is controlled drinking an occasional bout of excessive drinking need no longer be conceived of as a self-evident failure or "relapse" but rather as a temporary loss of control. Consequently, the despair and humiliation presently engendered by repeated "relapses" may be attenuated.

In part, consideration of these possibilities arose from clinical observations of Davies¹ and others that some alcoholics are capable of returning to a life of controlled drinking, constructive activity, and satisfaction. Some of these possibilities are being explored by research groups in Baltimore and elsewhere and their early findings are of considerable interest.^{2,3}

At present, disulfiram is used to induce severe reactions as soon as a single alcoholic drink is ingested. The aim is to ensure total abstinence. However, if we wish to achieve moderate drinking instead, then disulfiram could be replaced by a drug which begins to act only when a certain (moderate) blood alcohol level is reached. This critical level can be varied according to the needs and reactions of individual patients by varying the amount and breakdown rate of the nausea-inducing drug. Moreover, the nausea (or other distasteful or discomforting reactions) should ideally increase with increments in blood-alcohol level instead of reaching their climax when the critical level is reached. In this way the patient will receive continuous and increasing feedback signals of discomfort or distress if he persists in drinking once the critical level is reached.

The first requirement of the present proposal is the development of a suitable drug. Once we have a safe and reliable drug, which can produce steadily increasing degrees of nausea or distress once activated by a pre-determined blood-alcohol level, its efficacy will need to be assessed on a group of patients with damaging and unyielding patterns of excessive drinking. A drug with the properties described may also find minor uses in helping to control the drinking of moderate drinkers who have to remain sober for driving or other purposes.—I am, etc.,

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- 1 Davies, D. L., *Quarterly Journal of Studies on Alcoholism*, 1962, 23, 94.
- 2 Cohen, M., Liebson, I., and Faillace, L., *Behaviour Research and Therapy*, 1971, 9, 375.
- 3 Mills, K., Sobell, M., and Schaeffer, H., *Behaviour Therapy*, 1971, 2, 18.

The Electronic Pencil

SIR,—A survey of the advertisements in the weekend papers will show that there are current additions to the existing British market of pencil-like devices for the removal of superfluous hair, particularly from the face. It seems standard practice to advertise these as being "safe, easy, and permanent" though in no instance does it seem that these claims be substantiated and one wonders if the Trade Descriptions Act is not being routinely breached.

With these battery-operated gadgets the purchaser is advised, without demonstration, to insert a tiny needle deep into any offending pilo-sebaceous follicle and for ten painful seconds to apply this direct galvanic current

to the hair root to destroy it before lifting out the hair. While it might be possible to gain some practice on a clearly visible site on the leg, the sheer physical impossibility of probing, on the face and neck, into a tiny follicle which may point in any direction and, in a situation where the operative hand must prevent vision of the site in the prerequisite mirror, must deny any claim to ease or safety. The things likely to have permanence will be the multiple pitted scars due to extra follicular burning and infection and, of course, the hirsutism which the gadgets are claimed to cure.

As with the many unskilled purveyors of short-wave faradic electrolysis, these manufacturers can safely bank on the fact that distressed, embarrassed, and scarred women and girls will never face the possibility of litigation. What is worse, perhaps, from the aspect of medical responsibility, or lack of it, is that these firms may be able to produce a sheaf of certificates signed by doctors, largely in general practice, if, as commonly happens, completion of such a certificate is required by them prior to their effecting a sale to a young person.

The B.M.A. Dermatologists Group Committee condemns these articles as unsafe, even in trained hands, and begs its medical colleagues neither to recommend them nor tacitly to encourage their sale to young girls by signing any required certificates.—I am, etc.,

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Propranolol-induced Hypoglycaemia and Myocardial Infarction

SIR,—The blood glucose is usually normal or increased following myocardial infarction. A case of myocardial infarction with hypoglycaemia is described.

The patient, a 71-year-old man, was admitted to the coronary care unit of Hammersmith Hospital on 29 December 1971 with a two-day history of an upper respiratory tract infection and increasing angina. In 1967 because of troublesome angina propranolol 40 mg q.d.s. was started with good effect. During the day of admission 80 mg propranolol had been taken. Food intake was normal, but fluid intake had been reduced on 29 December. There was no past history of diabetes mellitus.

On examination he was pale, sweating, cyanosed, and had cold upper and lower limbs. Though initially responding to command he later responded only to Achilles tendon pressure. The pulse was regular 76/min; blood pressure 180/120, falling to 80/40 after 5 mg diamorphine was given intravenously, and on auscultation a left ventricular third and atrial heart sounds were heard. Widespread inspiratory and expiratory rhonchi were present in both lung fields. No limb reflexes or plantar response could be elicited. Serial E.C.G.s from the time of admission showed the pattern of a developing anterior myocardial infarction (confirmed) and in addition electrical alternans. Chest x-ray showed a normal sized heart and prominence of the upper lobe veins. The blood sugar was 38 mg/100 ml; venous serum insulin 3.7 μ units/ml (normal < 10 μ units/ml); no ketones were detected

in the urine; blood urea was 80 mg/100 ml; K 6.9 mN, and P.C.V. 45%, subsequently falling to 39%. The urinary adrenaline was high during the first 36 hours.

Intravenous glucose (25 g) produced a dramatic improvement in his mental state and he talked rationally. Over the next few hours limb temperature, which had been falling, returned to normal; the left ventricular third heart sound and electrical alternans disappeared. Acute bronchitis and left heart failure were treated in the usual manner and propranolol discontinued. Three weeks after admission a 48-hour fast while receiving propranolol resulted in a blood sugar of 32 mg/100 ml without symptoms at 36 hours. The serum insulin was low throughout the fast.

Propranolol-induced hypoglycaemia is well described in insulin dependent diabetic patients.¹ However, the combination of physical findings due to propranolol-induced hypoglycaemia and myocardial infarction appears to be unrecorded. This treatable condition, which presents in many respects like progressive cardiogenic shock, should be excluded in patients taking propranolol who sustain a myocardial infarction.—We are, etc.,

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¹ Kotler, M. N., Berman, L., and Rubenstein, A. H., *Lancet*, 2, 1966, 1389.

Radiation Menopause

SIR,—Your leading article on "Radiation Menopause" (13 May, p. 365) deserves comment because of failure to distinguish between the menopause induced by radium and that induced by x-ray therapy. The following observations are based on a series of over 1,000 menopausal irradiations using x rays compared with a smaller series treated by intrauterine radium. The series started in 1950 and throughout the whole period dosage has been consistent, giving a central pelvic dose of 200r, 300r, or 400r to the over-50s, the 45 to 50, and the under 45 years of age respectively, using 250 kV x rays. Those treated by radium received a 50 mg intrauterine tube for 48 hours. In all cases in both groups a D. and C. showing non-malignant endometrium was obtained prior to treatment.

The first distinction to be drawn between the groups is in the level of dose received by the endometrium. The x-ray dose may be regarded as the maximum received for no allowance has been made for bone absorption in the pelvis. In 48 hours from radium the dose which could be received by the endometrium ranges from over 10,000r to under 2,000. Since somatic mutation is under consideration the differing overall times of treatment have no significance, and thus the radium-treated cases received dosage ranging from 5 to 50 times greater than those treated by x rays.

The second distinction is drawn from an analysis made in collaboration with the Birmingham Cancer Registry. With a virtually complete register of endometrial and cervical malignancy, it has only been possible to find a single instance of gynaecological malignancy arising after menopausal irradiation by x rays, whereas six cases in

the smaller series are known to have developed the disease. This analysis is to be published shortly. Meanwhile one can only recommend x-ray methods where a radiation menopause is advisable in the certain knowledge that the overall risks are very much smaller, and condemn radium techniques as inducing a significant risk of subsequent pelvic malignancy.—I am, etc.,

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SIR,—Your leading article "Radiation Menopause" (13 May, p. 365) is ambiguous in that at no time does it distinguish between induction of a menopause by intracavitary radium and that by external irradiation using modern megavoltage equipment.

We would agree that hysterectomy is the treatment of choice for dysfunctional bleeding, but if for any reason surgery is not feasible external irradiation is simple, reliable, and safe. The side effects and sequelae described by Bamford and Wagman¹ from this hospital relate only to the insertion of intracavitary radium. Although Bamford and Wagman do not mention it in their article the radiotherapy department here abandoned this procedure for this purpose 10 years ago, and we would join them in condemning it.

Preliminary examination under anaesthesia and curettage remain essential. The theoretical convenience described of radium insertion at the same time is nullified by the need to await negative histology on the curettings. We agree with the need for careful follow up after radiation menopause by either method.—We are, etc.,

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¹ Bamford, D. S., and Wagman, H., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, 79, 82.

SIR,—Your leading article "Radiation Menopause" (13 May, p. 365) rightly concludes that hysterectomy is to be preferred to irradiation for intractable dysfunctional uterine haemorrhage. In discussing the incidence of genital tract malignancy following irradiation, however, no distinction is drawn between those treated with radium and those subjected to external radiotherapy.

Recently, two independent surveys of the long-term effects of radiation menopause were published. In the first¹ 2,054 patients who had received external radiotherapy were followed up for 24 years; in the second² 1,817 patients treated by radium insertions had been followed up to 40 years afterwards. In the analysis of these two series of cases the only significant findings were in the differing incidence of subsequent uterine cancer, seven deaths occurring in those treated by x-ray therapy against an expected 5.46, whereas 61 died of this disease when radium had been used to control the haemorrhage, the expected incidence being approximately 11 deaths.

The cases reported by Bamford and Wagman, whose paper³ formed the basis of