"gamble with the nation's health." Should this not be a time when the medical profession should clearly abandon its traditional role of keeping aloof from discussions of the "drink problem" and take a clear stand?

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¹ Glatt, M M, *British Journal of Addiction*, 1958, **55**, 51.

² Wilson, G B, *British Journal of Inebriety*, 1942, **39**, 76.

³ Glatt, M M, *Alcoholism a Social Disease*, London, English University Press, 1975.

⁴ De Lint, J, *British Journal of Addiction*, 1975, **70**, 3.

⁵ *Daily Telegraph*, 28 February, 1976, p 8.

SIR,—I am a medical student, but at present I am a patient in hospital. I have just been offered an alcoholic beverage as a non-medicinal nightcap supplied, presumably, on the NHS (I declined the offer.)

I would like to question whether this is in accordance with your recent leading article (14 February, p 359) which protested against the increasing availability of alcohol to the public and in which you suggested that "there should be a moratorium on all measures which make drink more available." Is a hospital ward now a place where alcohol consumption is to be encouraged?

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Beta-blockers in anxiety and stress

SIR,—Your recent leading article on beta-blockers in anxiety and stress (21 February, p 415) suggests there is little to choose between the various available compounds in this respect.

With regard to selectivity, it is known that the various beta-blockers differ in their pharmacology. The action of beta-blockers in relieving the somatic manifestations of anxiety may result from peripheral blockade of sympathetically mediated symptoms. The widespread distribution of such symptoms would suggest that the most appropriate and effective agent for this purpose would be the most non-selective compound available and that propranolol may then be the drug of choice.

In this context there may be a rational basis on which to choose between the available beta-blockers—a minor point of disagreement with your article.

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Diagnosis of intracranial haemorrhage

SIR,—Your leading article on this subject (28 February, p 483) touches on the management of head injuries, pointing out that "in those fortunate hospitals with a [computerised axial-tomography (CAT)] scanner the precise diagnosis may now be made on admission, and if necessary a patient may be in the operating theatre in about an hour." This is true, but what is of at least equal importance is that the patient with a closed head injury with no sign of intracranial haemorrhage could be put under curare-like relaxants and hyperventilation on admission and therefore given the best chance of survival with minimal morbidity, with no need to monitor him on clinical neurological findings, since repeated

CAT scanning will reveal the development of acute extradural haematoma or other surgically remediable lesion.

An open head injury can be safely treated by hyperventilation, as found with missile injuries in Belfast, but as the method of hyperventilation masks the clinical signs of progressive intracranial haemorrhage in a closed head injury, such as dilating pupil, development of hemiparesis, etc, the method is unsafe and the advantages are outweighed by the risks. We consider that the immediate accessibility of CAT is essential for any neuro-surgical unit and that for a busy head injury unit not to have immediate and continuous access to a scanner demonstrates failure to provide optimum treatment for patients.

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Pseudo-obstruction due to clonidine

SIR,—We read with interest the case report by Drs R Bear and K Steer (24 January, p 197) and would like to record a similar experience relating to a patient who was subjected to two laparotomies.

A 52-year old woman presented in September 1970 with visual failure due to malignant hypertension. Blood-pressure control with standard antihypertensive medication remained suboptimal until the addition in November 1971 of clonidine in a dose varying between 450 and 900 µg daily. Serum creatinine at that time was 203 µmol/l (2.3 mg/100 ml). She was readmitted in November 1972 complaining of abdominal pain and severe constipation of recent onset. Barium enema examination revealed a tender, spastic caecum but no other abnormality. Treatment for her abdominal symptoms was symptomatic. In October 1973 a laparotomy was performed with a provisional diagnosis of intestinal obstruction due to a polyp-induced intussusception. At operation a few adhesions and a dilated large bowel full of faeces were found but no evidence of organic obstruction.

During the next two years she had several readmissions to hospital because of progressive deterioration of renal function, serum creatinine rising to 636 µmol/l (7.2 mg/100 ml) and severe painful constipation. Her blood pressure was reasonably well controlled with clonidine, beta-adrenergic blocking drugs, and loop diuretics. In November 1975 emergency laparotomy was undertaken for suspected intestinal obstruction when she presented with severe abdominal pain, distension, and radiological fluid levels, though bowel sounds never disappeared. The findings at operation were identical with those of October 1973.

In January 1976 clonidine therapy was gradually withdrawn; bowel function returned to normal within three to five days but blood-pressure control was difficult in spite of the addition of the maximum tolerated doses of vasodilator drugs.

Experience with clonidine at the cardiovascular clinic and in the wards of this hospital extends to over 800 patients treated during the past eight years.¹ We regard clonidine as a very effective drug for the treatment of all grades of hypertension, from mild to malignant, including hypertension of pregnancy and the control of hypertensive emergencies. Side effects are usually minimal and well-tolerated, the commonest being drowsiness, dryness of the mouth, and insomnia. Rebound hypertension following the sudden cessation of clonidine therapy occurs in some subjects and can be promptly controlled provided the mechanism is recognised.

In the previous communication from this

hospital it was stated that "constipation occurred occasionally but ileus was not seen." Now that pseudo-obstruction due to clonidine has been recognised more attention will have to be given to this potentially lethal complication. The exact mechanism remains uncertain; alteration of central autonomic visceral control seems more likely than peripheral parasympathetic blockade similar to the now virtually forgotten mecamlamine ileus.

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¹ Raftos, J, et al, *Medical Journal of Australia*, 1973, **1**, 786.

Propranolol schedule before paradoxical hypertension

SIR,—It would be interesting to know the interval between the doses of propranolol and the increase in daily total dosage that preceded the unexpected rise in blood pressure observed by Dr I Blum and his colleagues (13 December, p 623) in eight psychotic patients who were given 600-5000 mg daily.

Transient hypertension occurred in our first case of schizophrenia treated with propranolol¹ when we followed the same regimen, giving propranolol every three hours around the clock² and increasing the dose by 400-800 mg daily. Toxic effects led us to modify this regimen. The drug was given twice daily because the biological effects of propranolol persist longer than the pharmacological half life of 2-3 hours.³ Further, we raised the dose by some 40-80 mg/day—that is, at about one-tenth of the rate of increase described by Dr Blum and his colleagues. In 55 patients with schizophrenia no further case of hypertension was seen, and other toxic effects became rarer and milder with the modified regimen.⁴

It would thus be valuable to know if Dr Blum and his colleagues found that the conditions that preceded paradoxical hypertension with high doses of propranolol also included giving it every few hours and raising the dose steeply. If so this rare complication of propranolol treatment may be not only treatable (with alpha-blockade) but also preventable.

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¹ Yorkston, N J, et al, *British Medical Journal*, 1974, **4**, 633.

² Steiner, M, et al, *Kupat Holim Yearbook*, 1972, **2**, 201.

³ Carruthers, S G, et al, *British Medical Journal*, 1973, **2**, 177.

⁴ Yorkston, N J, et al, *European Journal of Clinical Pharmacology*. In press.

Toxic effects of propranolol on the heart

SIR,—In relation to the extensive use of beta-adrenoceptor blocking agents the reported cases of suicide attempts with these drugs are relatively rare. With propranolol Drs W Wermut and M Wójcicki (15 September 1973,

p 591) reported that even a fairly high single dose, 2000 mg, in a suicide attempt had no effect on blood pressure or pulse rate. They concluded that "the effect of propranolol on the healthy heart needs to be reconsidered." It is also well known that propranolol may be given in very high doses in the treatment of hypertension. Prichard¹ has been using doses up to 4000 mg daily and Kincaid-Smith and her co-workers² up to 2000 mg daily, but with a gradual titration of the optimal dose. It is therefore of interest to note that even a relatively small "massive" dose of propranolol can give rise to severe cardiac disturbances.

A woman aged 24 was recently treated in our department after a suicide attempt with 25 40-mg tablets of propranolol taken as a single dose together with some beer and 100 ml of whisky. On admission to hospital about two hours later she was comatose, without measurable blood pressure, and had pronounced sinus bradycardia with a pulse rate of about 35-40/min. Over the lungs sibilant rhonchi were auscultated. Atropine was given intravenously, but soon after admission asystole developed. External cardiac compression was immediately started, endotracheal intubation was performed, assisted ventilation was started, and bicarbonate was given intravenously. This, however, did not have any effect on cardiac activity, but after adrenaline had been given intracardially spontaneous sinus rhythm was restored, with adequate peripheral circulation. The patient was observed for five days and discharged without any signs of cardiac or cerebral damage. The concentration of propranolol in the serum was not measured.

It was suggested by Drs A J Boakes and B H Boeree (15 December 1973, p 675) that since a healthy subject resting in the supine position maintains an adequate cardiac output and blood pressure in the absence of sympathetic drive, beta-blockers in massive doses are not likely to represent a hazard. This case, however, shows that such a hazard does exist, though it is possible that the effect was potentiated by the simultaneous consumption of alcohol. One can, however, expect that the potential risk of cardiac arrest should be lower with those beta-adrenergic blocking drugs which have an intrinsic sympathomimetic activity.

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¹ Prichard, B N C, *British Journal of Hospital Medicine*, 1973, 10, 45.

² Kincaid-Smith, P, Fang, P, and Laver, M C, *Clinical Science and Molecular Medicine*, 1973, 45, 758.

IUD and congenital malformation

SIR,—Attention is drawn by Dr H Barrie (28 February, p 488) to the possible teratogenic effect on the developing fetus of copper released from intrauterine devices (IUDs) for contraception.

It has previously been shown¹ that copper released from such devices results in a significant increase in the local copper concentration in the intrauterine fluid. However, this does not result in a significant rise in serum copper or caeruloplasmin concentrations.^{2 3} Even if a significant rise did occur it is to be expected that the placenta would form an effective barrier to the transfer of the large (molecular weight 151 000) caeruloplasmin molecule to the fetus. As about 93% of copper in the maternal blood exists in the form of this enzyme only a small amount of free copper is

available to diffuse across the placenta to the fetus. This relative isolation of the developing fetus from copper is supported by the apparent normality of the majority of animal and human infants^{4 5} delivered from mothers using copper IUDs. As Dr Barrie points out, however, it is likely that such pregnancies are seriously under-reported, in addition to which closer examination of those fetuses which do not go to term but abort at an earlier stage might well reveal a different pattern.

In a recent case (reported in full elsewhere⁶) the rare opportunity was taken to estimate the cord blood copper and caeruloplasmin concentrations from a neonate conceived in the presence of a Gravigard IUD. The serum copper concentration was 2.5-5 times higher than the normal range⁷ for neonates of equivalent gestational ages and the serum caeruloplasmin (measured as copper oxidase by the same technique as by Canzler *et al.*) was 3.5-8 times the normal range. The maternal serum copper and caeruloplasmin concentrations were within the normal range. In this instance the neonate was apparently normal, although he died shortly after delivery, probably from immaturity.

Presumably if significant quantities of copper do not cross the placenta they must diffuse across the embryonic membranes and liquor to reach the fetus. Whichever route is taken we must conclude on present evidence that a fetus conceived in the presence of a copper IUD is incompletely isolated from its copper-containing environment. Until more is known of the effect of copper on human organogenesis it would be prudent to exercise caution in the use of copper IUDs.

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¹ Oster, G K, *Fertility and Sterility*, 1972, 23, 18.

² Hagenfeldt, K, *Contraception*, 1972, 6, 119.

³ Daunter, B, and Elstein, M, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, 80, 644.

⁴ Chang, C C, and Tatum, H J, *Contraception*, 1973, 7, 413.

⁵ Tatum, H J, *American Journal of Obstetrics and Gynecology*, 1973, 117, 602.

⁶ Alderman, B, *Proceedings of the Royal Society of Medicine*. In press.

⁷ Canzler, E, Brosch, G, and Schlegel, C, *Zentralblatt für Gynäkologie*, 1972, 94, 646.

SIR,—In recent weeks the intrauterine device (IUD) as a method of fertility regulation has been receiving something of a bad press in daily and weekly newspapers. Some of this can be attributed to misreporting or to sensationalism for its own sake, but the article by Dr H Barrie (28 February, p 488), relating to fetal abnormality associated with IUD use is, I believe, even more damaging.

I found Dr Barrie's article difficult to understand as I could find no evidence in it to support the conclusions he draws. The claim that "the possibility of a causal association [between IUD use and congenital abnormality] is consistent with the known hazards of intrauterine devices" is puzzling. What evidence is there for this claim? No published study that has assessed the outcome of pregnancy among IUD users has revealed evidence of a causal link between IUD use and congenital malformations.

A further puzzling aspect of the article is the suggestion that it was the copper content of the IUDs that was to blame. The two devices described were the Gräfenberg ring and the Dalkon Shield, both of which carry

only trace copper. In the United Kingdom at the present time approximately one-third of all IUDs fitted are devices which carry very large amounts of surface copper. For example, the Gravigard (Copper-7), the Gyne-T (Copper-T), and the Copper Omega. These devices carry 200 mm² or more of surface copper yet no reports of congenital abnormalities associated with the use of these devices have been received.

The second case cited by Dr Barrie is based almost entirely on conjecture and certainly does not fit with his belief that this is "experimental evidence." There are uncertainties relating to the device model—the Dalkon Shield was named by the mother after being shown illustrations and samples three months after the delivery. The device was not found at delivery and it would be equally reasonable to assume that the device had been expelled before conception occurred.

The family planning research unit in the University of Exeter has been collecting data on IUDs fitted in 20 centres situated in various parts of the United Kingdom for a number of years. At present over 100 000 medical records relating to 25 000 IUD fittings are held in Exeter. All pregnancies reported are followed up to assess the outcome of that pregnancy. Since April 1972 317 completed pregnancies have been recorded and details of the pregnancy outcome published.¹ In summary, 33% of these pregnancies ended in spontaneous abortion, 35% were terminated, 3% were ectopic pregnancies, and 21% proceeded to full term (the outcome of the remaining 8% is not known). No congenital abnormalities were reported among these full-term births.

At the present time it is estimated that about 400 000 women in the United Kingdom are using IUDs. For almost all IUD models the pregnancy rate during the first year of use lies between 2.0 and 4.0 per 100 users.² Taking the lower figure, this yields approximately 8000 pregnancies among women wearing IUDs. According to evidence collected in this unit and summarised above approximately 1 in 5 of these pregnancies will go to term. If 5% of all babies are born with congenital abnormalities, as Dr Barrie states, one would expect approximately 80 malformed infants to be born to mothers wearing IUDs in the United Kingdom as a whole. It would be double this figure if the higher pregnancy rate (4.0%) was taken. From the above evidence it is possible to argue that the incidence of congenital abnormality is reduced in infants born to mothers wearing an IUD. This is clearly a dubious hypothesis, but at the present time there is more evidence to support it than there is to support the contrary hypothesis put forward by Dr Barrie.

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¹ Snowden, R, *FPA Medical Newsletter*, No 59, 1976.

² Snowden, R, *Journal of Biosocial Science*, 1975, 7, 367.

Immunisation against whooping cough

SIR,—I wonder if Professor G T Stewart's evidence has all been published or whether I shall upset him again by writing too soon—his published article¹ has little in common with the "raw data" he sent me. He asks (6 March, p 583) why I associate the new vaccine with the recent decline in whooping cough, whereas a "greater decline . . . occurred before it began to