some burden and the site of recurrent infarctions. Apart from the few cases of myelosclerosis with splenic haemopoiesis most big spleens are associated with many harmful effects of the "big spleen" syndrome notwithstanding the basic disease state. Provided that splenectomy is not delayed until it becomes a last-ditch procedure it is likely to improve the quality if not the quantity of life in a chronically ill patient.

There is also a very real place for splenectomy in the management of the patient with undiagnosed splenomegaly. Most large series of splenectomies contain a group of patients in whom the cause for the splenic enlargement was uncertain before operation. Usually histological examination of the excised spleen will reveal the nature of the basic disease but in some patients meticulous histological examination will still fail to provide a diagnosis, and long-term follow-up over a period of years may be necessary to detect the frequent development of haematological disease, usually lymphoma. With gross splenomegaly and an uncertain diagnosis many advantages may accrue from splenectomy, even considering the appreciable risks of the operation itself.

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Suicide and attempted suicide

SIR,—The excellent article on "Suicide and attempted suicide" by Professor W H Trethowan (4 August, p 319) reminds us of the very great changes which have occurred not only in the law and the public's attitude to self-destruction but in the agents used in these forms of "communication between a person in distress and his environment," to use Professor Trethowan's own words. Few of these gestures, as he points out, prove fatal; but as the pharmaceutical scene has changed over the last 20 years so have the agents used in these gestures of despair.

We¹ reported in 1964 from St Stephen's Hospital, Fulham, on 126 patients (100 female, 26 male) admitted under our care into our general medical beds with suicidal gestures between 1955 and 1960. None died. One-third were considered straightforward and not suffering from psychiatric abnormalities; the other two-thirds were seen by the psychiatrist but only a small minority were transferred for psychiatric treatment and care. The agents most commonly used were barbiturates, as these were then the drugs most often present in the home drug cupboards; but now the more popular agents are the non-barbiturate sedatives and anxiolytics and the more popular analgesics. At the time of our study physical measures were very rarely used and gas fires in only 15%, mostly in the older age groups. Where such suicidal gestures were repeated the same agents, usually barbiturates, were often used again. M W Johns² has noted that hospital admissions due to acute barbiturate poisoning have decreased in England and Wales since 1965, roughly in parallel with barbiturate prescribing in the NHS, their place being taken by the less dangerous benzodiazepines and other agents.

It would seem that the most popular therapeutic agents of the day—that is, the ones in the family drug cupboard—will be the ones most likely to be used in these gestures

in the future as they have been in the past; but the fact that an agent, effective and non-toxic when used therapeutically in the correct dosage, can prove lethal when used for suicidal purposes in excessively high dosage, often with large amounts of alcohol, can hardly be set against it in terms of everyday therapeutics. What might be called pharmacological parasuicides, emotional gestures using whatever is in the home drug cupboard, occasionally prove fatal because of unanticipated side effects—for example, liver damage after ingestion of excessive amounts of paracetamol—but this risk will continue so long as drugs have side-effects and so long as the sad and distressed make these gestures of despair.

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¹ Taylor, D J E, *et al*, *Practitioner*, 1964, **192**, 251.

² Johns, M W, *British Medical Journal*, 1977, **1**, 1128.

Wernicke's encephalopathy

SIR,—Your leading article (4 August, p 291) suggests that Wernicke's encephalopathy should be both treated early and ideally prevented. It is a rare complication of chronic alcoholism, only occurring in those patients who have a genetic abnormality of transketolase, which binds thiamine pyrophosphate less avidly than normal.¹ If all alcoholics were recognised and tested for this abnormal enzyme the development of the condition could be prevented in those vulnerable to it by regular supplements of thiamine, if necessary by the parenteral route, in much the same way as many schizophrenics receive depot neuroleptics.

You also suggest fortifying foodstuffs with thiamine. Vitamin depletion in alcoholics has been studied by Thomson,² who found many contributory mechanisms, including malnutrition, malabsorption, increased metabolic demands, and impaired utilisation. The only logical way round this would be to incorporate high doses of thiamine in alcoholic beverages before consumption, say 5 mg in a pint of beer, and 50 mg in a bottle of spirits. This could be done during manufacture or during inspection for duty purposes. After all, we have long accepted vitamin fortification of our breakfast cereal and margarine.

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¹ Blass, J P, and Gibson, G E, *New England Journal of Medicine*, 1977, **297**, 1367.

² Thomson, A D, *Clinics in Endocrinology and Metabolism*, 1978, **7**, 405.

SIR,—Your leading article (4 August, p 291) rightly draws attention to the frequency with which this eminently treatable but potentially fatal condition is missed. We are preparing a report of the results of a recent 24-month study of all patients referred to a single medical service screened for the presence of an "alcohol problem." In this period 73 such patients were identified, an incidence of 3%. Of these no fewer than nine had the Wernicke-Korsakoff syndrome, and none had been diagnosed before admission. Polyneuropathy was present in 10, tremor in 14, and cerebellar degeneration in three, with response to vitamin B complex in many instances.

A full clinical nutritional examination revealed virtually no other evidence of

deficiency. Liver involvement was frequent. A seven-day dietary recall showed a deficient thiamine intake in about 90% of these patients, a higher incidence of deficiency than for any other nutrient.

The close association with alcoholism, with its rising rate and especially high incidence in Scotland, gives cause for concern. Recognition by general practitioners of early thiamine deficiency in alcoholics might be life saving. You call for preventive measures—control of alcoholism and fortification of foodstuffs. The former is difficult to achieve but the latter in the form of increased fortification of bread, from which nearly one-third of our thiamine comes, would be simple, cheap, and safe.

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Herpetic proctitis and sacral radiculomyelopathy in homosexual men

SIR,—Mr P L Samarasinghe and others (11 August, p 365) have drawn attention to the importance of herpetic proctitis in homosexual men. Severe anorectal herpes infections may be the commonest cause of acute urinary retention in young men. We in fact described two such cases in 1975.¹

The appearance of the rectal mucosa in the cases described by Mr Samarasinghe ranged from "hyperaemia and oedema to frank ulceration." *Chlamydia trachomatis* can cause exactly this picture of inflammatory rectal change² but, of course, not (to my knowledge) the associated neurological syndrome. In my series of homosexual men with herpetic proctitis, of which I hope to publish fuller details soon, ulceration was present on the anal mucosa up to the anorectal junction. Above this point—that is, on the rectal mucosa itself—no ulceration was present, but rather a hyperaemia that ranged from mild to severe, with areas of haemorrhage. Two asymptomatic excretors of virus (Mr Samarasinghe's "silent shedders") both had a normal anorectal mucosa as seen by the naked eye, but showed obvious hyperaemic change when the rectum was viewed and magnified through an operating microscope. The absence of ulceration on non-squamous-celled epithelium, however, is not a new observation: Coutts³ observed hyperaemia and haemorrhage only on the urethral mucosa in patients with herpetic urethritis as long ago as 1948.

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¹ Goldmeier, D, Bateman, J R M, and Rodin, P, *British Medical Journal*, 1975, **1**, 425.

² Goldmeier, D, *A Study of Non-specific Proctitis in Homosexual Men*. MD thesis, University of London.

³ Coutts, W E, *British Journal of Venereal Diseases*, 1948, **28**, 205.

Relation between herpes simplex virus and carcinoma

SIR,—The paper on herpetic proctitis by Mr P L Samarasinghe and others (11 August, p 365), reporting urinary dysfunction as a complication, was of considerable interest and served also as a reminder of interrelation

between the herpes simplex virus and its human host. In view of the hardening evidence implicating the herpes simplex virus type 2 (HSV 2) as an important aetiological factor in cervical carcinoma, one cannot escape wondering whether this agent has a similar role in some types of rectal and perianal carcinoma (particularly in the increasing male homosexual population).

Similarities between the mucosa of the cervix and the rectum certainly exist—for example, they both have glandular columnar epithelia and a squamocolumnar junction. Investigations similar to those which have established a close relationship between HSV 2 infection and carcinoma of the cervix would be of interest in rectal and perianal cancer.

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Blindness after treatment for malignant hypertension

SIR,—It was with great interest that I read the account by Dr D H Cove and others (28 July, p 245) of two young women who became blind following treatment for malignant hypertension. In December 1976 I had a similar, but not identical, experience with an 18-year-old girl who presented with malignant hypertension. Her blood pressure fell quite gently over a five-day period, during which time her initial blurring of vision became worse. After her papilloedema had resolved she developed bilateral optic atrophy. This patient, fortunately, still has some useful vision, although she has been registered as partially sighted.

In this patient there was no precipitous drop in blood pressure to explain the optic nerve damage, and I wonder whether the optic atrophy in these three young females might be a direct result of severe papilloedema rather than the fall in blood pressure. The fact that this tragic complication has now been described in three young women raises the possibility that there are hormonal factors involved, for otherwise one might have assumed it more likely in older patients with pre-existing vascular degeneration.

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Maturity-onset diabetes

SIR,—In their article on maturity-onset diabetes (7 April, p 938) Drs V Anne Ropner and J Anderson state that there is no reason to discontinue propranolol in diabetic patients receiving oral hypoglycaemic drugs. At the same time they point out that beta-blockers may potentiate hypoglycaemia and mask the warning symptoms and signs. In fact beta-blockers cause little or no potentiation of the actual fall in blood sugar after the administration of insulin,¹⁻⁴ and rarely seem to mask the warning symptoms.

Propranolol has been shown experimentally to delay recovery from hypoglycaemia induced by insulin,¹⁻⁴ and even to cause a temporary secondary fall in blood sugar during the recovery period³; while other beta-blocking drugs have little, if any, effect on the recovery from insulin reactions. The following case shows that this effect of propranolol is not

just of theoretical interest, but also of practical importance in the management of diabetics.

A 26-year-old hypertensive insulin-dependent diabetic recently became pregnant. Her hypertension had been treated with propranolol in a dose of 80 mg twice daily for the past two years. She volunteered that she had been taking considerably longer to recover from insulin reactions since taking the drug, and that hypoglycaemic symptoms sometimes recurred before she had fully recovered. Insulin reactions would still tend to occur during the pregnancy, when good diabetic control is so important; and as propranolol leads to a marked rise in blood pressure and bradycardia in addition to the adverse metabolic effects during insulin reactions⁵ the drug was stopped. Metoprolol was considered to be a safe alternative and was given in a dose of 100 mg twice daily. Insulin reactions still occurred, but the patient now found that she recovered from them normally.

Hypoglycaemia usually occurs in diabetics receiving insulin, but it may also occur when oral hypoglycaemic drugs are used, especially the longer-acting agents, and in the elderly. Whereas insulin reactions are usually recognised and rectified by the patient, hypoglycaemic symptoms due to oral drugs, particularly confusion, may be insidious and protracted and they could be seriously accentuated by propranolol.

Drs Ropner and Anderson rightly advise careful monitoring when combining therapy with oral hypoglycaemic drugs and propranolol, but we feel it would be wiser to choose a cardioselective beta-blocker such as metoprolol.

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¹ Deacon, S P, and Barnett, D, *British Medical Journal*, 1976, **2**, 272.

² Newman, R J, *British Medical Journal*, 1976, **2**, 447.

³ Davidson, N McD, *Scottish Medical Journal*, 1977, **22**, 69.

⁴ Deacon, S P, et al, *British Medical Journal*, 1977, **2**, 1255.

⁵ Lloyd-Mostyn, R H, and Oram, S, *Lancet*, 1975, **1**, 1213.

⁶ Sandström, B, *British Journal of Obstetrics and Gynaecology*, in press.

Serum free thyroxine in pregnancy

SIR,—In a previous communication¹ we presented serum free thyroxine (FT4) values during each trimester of pregnancy as measured by the Corning Immophase kit.² Over 30% of our values were in the hypothyroid range, so we were forced to question the methodology of the kit. Subsequent discussions and correspondence³ cast doubt on the derivation of the FT4 result from the measured kit parameters and offered alternative methods of manipulating the raw data. We would like to point out that Corning Medical have now modified the instructions which accompany the kit concerning the calculation of the results.

We have recalculated our FT4 results and the revised means are shown in the accompanying table together with similar means for total T4 and thyroxine-binding globulin (TBG). The latter values were also measured by Corning kits. The trend we originally reported, that FT4 falls significantly during the trimesters of pregnancy, is still apparent but now 90% of the FT4 values are within the range of the non-pregnant controls.

We now believe that the Corning FT4 kit in its original form was subject to at least two different errors which acted in opposition. One, an error in the method of manipulating the data, tended to decrease FT4 values and this has now been corrected. The other, a non-specific binding effect, which is operator dependent, would tend to increase the FT4 values with increasing TBG concentrations. Since we did not measure the non-specific binding we are unable to correct for this effect, but this might be the explanation of the significant rise in the FT4 mean in the first trimester over the mean of the control group. We suggest that TBG rises significantly during this period before any change in FT4 which may occur.

As the Corning kit gives an indirect method of measuring FT4 we have compared our FT4 values with the total T4/TBG ratio, which is recommended as an indicator of thyroid state by several workers (for example, Burr, *et al*),⁴ especially in abnormal TBG states. The significant downward trend is even more marked using this ratio, and in the third trimester 11 out of 19 values (58%) are below the lowest control value and are at risk of giving rise to misdiagnosis. Moreover, from theoretical considerations this ratio might be expected to fall during pregnancy without an associated fall in FT4.

Clearly, a precise, reliable, and cheap method of determining FT4 in abnormal states, such as pregnancy, is still awaited. The Corning kit will give euthyroid values for about 90% of pregnant patients, but direct FT4 values are needed before we can confidently state that FT4 values fall during pregnancy and remain low until term.

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¹ Boss, M, Djahanbakhch, O, and Kingstone, D, *British Medical Journal*, 1978, **3**, 1496.

² Free T4 ¹²⁵I Radioimmunoassay Test System. Corning Medical, Halstead, Essex.

³ Ekins, R, *Lancet*, 1979, **1**, 1190.

⁴ Burr, W A, et al, *British Medical Journal*, 1977, **1**, 485.

SIR,—Low serum free thyroxine (T4) concentrations during pregnancy have been reported in your columns by Boss *et al*.¹ However, the commercial radioimmunoassay kit used by these workers (FT4 Immophase, Corning Medical) has recently been criticised^{2,3} on the grounds that the presence in serum of raised serum thyroxine-binding globulin (TBG) concentrations leads to anomalous results using the method as originally described.

It is clearly important that changes in binding protein concentration should not artefactually influence free T4 measurements since these are primarily undertaken when a suspected variation in serum T4 binding undermines the diagnostic usefulness of total serum thyroxine determination. Modification of the method of calculation of assay

Corrected FT4, T4, and TBG concentrations and T4:TBG ratios (means and standard deviations)

	No of subjects	FT4 (pmol/l)	T4 (nmol/l)	TBG mg/l	T4:TBG
Controls	22	17.6 ± 2.19	101 ± 16.6	21.8 ± 12.9	3.69 ± 0.61
First trimester	22	20.2 ± 2.70	138.5 ± 19.0	32.2 ± 7.4	3.46 ± 0.66
Second trimester	28	18.4 ± 3.3	162.5 ± 22.5	45.2 ± 7.3	2.86 ± 0.64
Third trimester	19	15.6 ± 2.7	152.3 ± 25.2	50.1 ± 9.6	2.41 ± 0.52

Conversion: SI to traditional units—FT4: 1 pmol/l ≈ 0.078 ng/100 ml. T4 1 nmol/l ≈ 0.78 ng/ml.