demonstrated a most simple outpatient technique of excising the sinus and cleaning out any tracts under local anaesthesia. Over the last six years I have used this method for almost a hundred patients and the rate of recurrence has been negligible. The procedure takes less than 10 minutes, only a dry dressing is required, and many patients return to work the following day. Most patients can then attend to their own dressings, and one or two follow-up visits to the clinic are all that is required before discharge. Instead of six inpatient days with the foam elastomer sponge those treated by the "Lord" technique spend more like six minutes in the hospital.

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Early thymectomy for myasthenia gravis

SIR,—I have long accepted the value of early thymectomy in myasthenia gravis¹ and I therefore read with interest Mr A E Kark's (6 September, p 593) and Mr C Grimshaw's (4 October, p 40) comments.

No one would deny that a less mutilating surgical procedure must benefit the patient (and also the surgeon), but what worries me is the likelihood that anything less than a full exposure of the anterior mediastinum may result in a procedure which is less than a total thymectomy. The following case illustrates this.

A woman aged 41 underwent trans-sternal thymectomy for generalised myasthenia. A typical fleshy thymus gland weighing 10 g was removed. It must be stressed that the gland was clearly delineated and easily dissected in its entirety, and one would have been justified in assuming that the whole thymus had been removed. However, a final look round before closure revealed fatty masses on either side and extending into the lung hila. These were then dissected and also examined histologically. Section of the thymus revealed thymic tissue with areas of adipose tissue between lymphoid aggregates, germinal centers being very prominent. Section of both lateral fatty masses revealed adipose tissue with fragments of thymic tissue similar to the histological features noted in the main thymus gland.

While it is known that ectopic thymic tissue is not uncommon, the above findings have been noted and proved histologically on numerous occasions, and this is the main reason for my continuing to use the trans-sternal approach.

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¹ Lange, M J, *British Journal of Surgery*, 1960, 48, 285.

Diagnosis of gastric cancer

SIR,—The article by Dr A W Segal and others (21 June, p 669) emphasises the poor diagnostic yield of direct vision gastric biopsy in relation to gastric carcinoma. Their result of only 70% biopsy confirmation of carcinoma is by no means in keeping with experience in other centres. Kasugai reports a 92.8% positive biopsy correlation in 751 proved gastric carcinomas.¹

In all but four of 130 gastric carcinomas examined by endoscopy at this hospital in just over four years the diagnosis was confirmed by biopsy evidence. Two of the patients with the false-negative biopsy results

were recognised by the endoscopist to have advanced carcinoma. There were no false-positive biopsies. We take 8-12 bites routinely of all doubtful or suspicious ulcers, using the Olympus GFB or JFB instruments. Our current policy is that surgery for cancer is not performed unless a positive biopsy report is obtained. However, if a lesion is suspected of being malignant endoscopy and biopsy are repeated until x-ray, endoscopy, and biopsy findings correlate.

Dr Segal and his colleagues do not refer to the problem of the diagnosis of early gastric cancer, which is so well recognised by Japanese workers.²

Despite the falling standardised mortality rate in Australia for gastric cancer³ the recognition of these early lesions does much to increase survival figures. In our experience with early gastric cancer⁴ the reliance on biopsy and its interpretation is paramount and the overall value of direct-vision gastric biopsy cannot be over-emphasised.

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¹ Kasugai, T, and Kobayashi, S, *American Journal of Gastroenterology*, 1974, 66, 199.

² Murakami, T, *Pathomorphological Diagnosis*, Gann Monograph II, p 53. Tokyo, University of Tokyo Press, 1974.

³ Scott, G, *Cancer Forum No 5*, Australian Cancer Council, August 1975, p 250.

⁴ Barrett, P J, *et al*, *Gut*. In press.

Paradoxical effect of pindolol

SIR,—Drs Hendrika J Waal-Manning and F O Simpson (19 July, p 155) report on nine cases among 260 hypertensive patients whose blood pressure (BP) fell when the dose of pindolol was reduced. From our experience with pindolol in hypertension the incidence of this so-called "paradoxical" effect may be more general than is suggested.

We have recently carried out a controlled study,¹ in which a reduction of the pindolol dosage from about 30 mg daily to about 20 mg daily consistently gave a further reduction in blood pressure.

Of 38 patients with essential hypertension (WHO grade 1) with a diastolic BP of 100-129 mm Hg, 20 were treated with pindolol and 18 with propranolol for 14 weeks after an initial placebo period of four weeks. The patients were examined six times—initially, after the placebo period (visit 2), after a pretreatment period, after four weeks' treatment with the full dosage of pindolol (29 mg daily) or propranolol (232 mg daily), after four weeks' further treatment with an individually adjusted dose of pindolol (average 29 mg daily) or propranolol (average 241 mg daily) (visit 5), and finally after a

further four weeks' treatment during which the individual doses were reduced by one-third by the elimination of the midday dose so that patients received medication in the morning and evening only (visit 6).

The table shows how the BP changed between visits. At visit 5 the BP reductions on pindolol and propranolol were similar; further reductions followed on pindolol treatment when the dose was lowered and given only twice daily during the last four-week period. The results with propranolol were somewhat different: the systolic, diastolic, and mean pressure decreased up to visit 5 but increased again after dosage reduction and the change to twice-daily administration.

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¹ Bjerle, P, *et al*, *Current Therapeutic Research*. In press.

Serum cholesterol and enzyme-inducing agents

SIR,—We read with interest the report by Dr Risto Pelkonen and others (11 October, p 85) of increased serum cholesterol levels in patients receiving phenytoin. We have recently completed an investigation of the effects of phenobarbitone on serum lipids in healthy young volunteers (the results of which have been submitted for publication elsewhere). We similarly found a significant increase in the level of total serum cholesterol occurring within three weeks, which was entirely accounted for by a rise in low density lipoprotein cholesterol. Total serum triglycerides and very low density lipoprotein triglycerides were not altered, although a significant rise in low density lipoprotein triglycerides did occur. Evidence that drug-metabolising enzymes were induced was provided by a considerable increase in antipyrine clearance.

Microsomal enzyme induction, an effect of both phenobarbitone and phenytoin, would be a possible mechanism for the rise of serum cholesterol, since the rate-limiting enzyme for cholesterol biosynthesis, β -hydroxy- β -methylglutaryl-CoA reductase, is microsomally located.¹ Increased hepatic and intestinal cholesterol synthesis has been produced experimentally in phenobarbitone-treated animals.^{2,4}

Raised levels of serum cholesterol have previously been shown in persons receiving phenobarbitone,⁵ in children on anti-convulsant therapy,⁶ and in a patient undergoing medical treatment with phenobarbitone for gallstones.⁷ Therefore we would agree that a rise in serum cholesterol is a

	High dose visit 2→5		Reduced dose visit 5→6	
	Pindolol	Propranolol	Pindolol	Propranolol
No of patients	20	18	20	16*
Mean dosage change (mg)	0→29	0→241	29→176	241→176
Resting BP changes:				
systolic (mm Hg)	-17.0	-14.4	-3.1	+3.6
diastolic (mm Hg)	-10.7	-8.6	-1.1	+4.1
mean (mm Hg)	-12.9	-10.5	-1.7	+4.0

*Two patients were excluded since they did not follow the dosage instructions.

risk in patients receiving long-term phenobarbitone or phenytoin therapy.

Exposure to enzyme-inducing agents such as drugs, industrial and agricultural chemicals, pesticides, food additives, etc, is a hazard of living in the more highly developed countries. It is tempting to speculate that the differences in serum cholesterol between such populations and those of less affluent countries, which have never been fully explained by differences in dietary intakes of animal fat,^{8,9} may in part be due to differences in their degree of enzyme induction.

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- 1 Siperstein, M D, *Current Topics in Cellular Regulation*, ed B Horecker and E Stadtman, vol 2, p 65. New York, Academic Press, 1970.
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- 7 Coyne, M J, et al, *New England Journal of Medicine*, 1975, **292**, 604.
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Use and effectiveness of IUDs

SIR,—The Family Planning Research Unit in the University of Exeter has for some years been collecting data on the use and effectiveness of IUDs. Data from 25 000 fittings, with 8000 additional fittings each year, are processed and evaluated to give detailed information on a number of IUD models. Part of our work is the follow-up of women who have become pregnant when wearing an IUD.

The table¹ shows that the incidence of ectopic pregnancy is far lower than was suggested in your leading article (31 May, p 458). Your rate of one ectopic pregnancy in every five pregnancies is clearly an error, for the studies you cite in evidence give a crude rate of 1 in 25 pregnancies. Our data give a comparable ectopic pregnancy rate of 1 in 29 IUD pregnancies. The paper by Mr A K Thomas (27 September, p 747) rightly draws attention to the need to study all IUDs in relation to septic abortion. Our experience suggests that the incidence of spontaneous abortion is high among pregnant women wearing IUDs irrespective of the IUD model worn (see table). I am unaware of any deaths

in Britain attributable to the wearing of an IUD. However, two among the 317 pregnancies reported to our unit ended in septic spontaneous abortion during the mid trimester.

I agree with Mr Thomas that pregnancy associated with an IUD is a potentially serious condition, but I believe that a registry system for all IUD fittings would be a cumbersome, complicated, and probably unworkable system for identifying low-incidence medical complications such as he describes. More useful, perhaps, is a system which can quickly adapt to selected problems as they arise. Such a system requires a careful follow-up of a large number of IUD fittings in various parts of the country. It is this follow-up system that differentiates a prospective, flexible approach to problems as they arise from the retrospective, more rigid approach of a registry system on all IUD fittings.

Our unit systematically collects data from 20 IUD fitting centres situated in England, Scotland, and Wales and, in collaboration with these centres, has developed procedures for the follow-up of IUD fittings. As a result we can respond to requests for information at relatively short notice. This was the case when the FDA requested information during their hearings on the Dalkon shield last year. Low-incidence complications will continue to arise, especially as the number of IUD fittings is increasing. What we need is a large scale but flexible follow-up system in selected fitting centres which will assist in identifying such complications as soon as possible after they appear.

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- 1 Family Planning Research Unit, University of Exeter, *Report 15*. Exeter, University of Exeter, 1974.

Stereotaxic neurosurgery for cerebral palsy

SIR,—I was interested to read your recent leading article on this subject (20 September, p 665) especially as it mentions the experience in my own group. I would contest, however, the last paragraph, in which you suggest that stereotaxic surgery is unlikely to be widely undertaken on children with cerebral palsy because of the need to perform the operation under general anaesthesia, making accurate localisation impossible. The cases reported,¹ however, had the passage of the probe and its final placement monitored using electro-physiological recording from cerebellar cortex, white matter, and deep nuclei, an essential aid in placing accurate lesions. The use of depth recording and

stimulation in increasing stereotaxic accuracy has been known for many years and has been reported extensively.²⁻⁴ For this reason I think it is likely that stereotaxic procedures will be increasingly performed on children with cerebral palsy as the results of such treatment become increasingly successful.

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- 1 Gornall, P, Hitchcock, E, and Kirkland, I S, *Developmental Medicine and Child Neurology*, 1975, **17**, 279.
- 2 Albe-Fessard, D, et al, *Journal of Neurosurgery*, 1968, **29**, 173.
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- 4 Gillingham, F J, *Journal of Neurosurgery*, 1966, **24**, Suppl, p 382.

Diazepam withdrawal symptoms

SIR,—I was interested in Drs Indira Vyas and M W P Carney's letter (4 October, p 44) describing a case of withdrawal fits following prolonged medication with diazepam. I recently had two patients who developed withdrawal phenomena on stopping taking diazepam despite the fact that they had been immediately changed to another benzodiazepine tranquilliser, oxazepam.

A young woman had a severe long-standing anxiety neurosis partially controlled on diazepam 10 mg three times a day, which she had been receiving for about a year. She felt that the drug had lost its efficacy and requested a change. She was started on oxazepam 30 mg three times a day but within 48 hours of the changeover she developed marked shaking. She put herself back on to the former dose of diazepam and over the next few days the shaking subsided.

A middle-aged woman with an obsessive compulsive neurosis had been receiving diazepam 10 mg three times a day for two years. She was changed to oxazepam 30 mg three times a day at her request and within 48 hours of the changeover developed severe limb shaking and became unable to stand. Intravenous diazepam dramatically alleviated the symptoms, but over the next few hours they gradually returned. She was restarted on oral diazepam 10 mg three times a day and the shaking subsided within a few days.

These two patients were unknown to each other and had no psychological dependence on diazepam as it was changed at their request. It is most likely, therefore, that they had both developed a physical dependence on diazepam, which is more markedly sedative and muscle-relaxant than the oxazepam to which they were changed. It is suggested that some degree of physical dependence occurs on diazepam when given in large doses for long periods of time.

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Outcome of pregnancy in 317 women who completed a pregnancy when wearing an IUD

"Completed" pregnancies	All IUDs		Dalkon shield		Gravigard		Lippes loop		"M" Device		Antigon		Other IUDs	
	No 317	Rate	No 149	Rate	No 64	Rate	No 43	Rate	No 24	Rate	No 23	Rate	No 14	Rate
Full-term births	66	(1:5)	31	(1:5)	14	(1:5)	12	(1:4)	2	(1:12)	4	(1:6)	2	(1:7)
Spontaneous abortion*	104	(1:3)	50	(1:3)	11	(1:6)	18	(1:3)	15	(1:2)	9	(1:3)	1	(1:14)
Induced abortion*	109	(1:3)	49	(1:3)	32	(1:2)	8	(1:5)	5	(1:5)	8	(1:3)	7	(1:2)
Uterine perforation followed by pregnancy	2	(1:159)	0	(—)	0	(—)	2	(1:27)	0	(—)	0	(—)	0	(—)
Ectopic pregnancy	11	(1:29)	5	(1:30)	0	(—)	3	(1:14)	0	(—)	2	(1:12)	1	(1:14)
Pregnancy outcome not known (but not now pregnant)	25	(1:13)	14	(1:11)	7	(1:9)	0	(—)	2	(1:12)	0	(—)	2	(1:7)

*As stated by doctor reporting on the pregnancy.