clude the possibility of a direct effect of metoclopramide and propantheline on absorption across the intestinal mucosa.

We have tested the effects of these compounds and of phenobarbitone on D-xylose absorption from rat small intestine in vitro. Everted sacs were used with Krebs phosphate buffer containing calcium and glucose.[4] Transport of 50 mM xylose was measured with a concentration gradient—that is, with buffer only and no xylose initially within the sac. The drugs were added to the mucosal and serosal solutions of alternative sacs at a concentration of 1 mmol/l. Phenobarbitone and metoclopramide significantly reduced xylose transport but propantheline had no such effect.

Our finding of inhibition by metoclopramide agrees with the clinical findings of Kendall[1] in individuals with normal gastrointestinal function. He also showed that propantheline increased urinary excretion, and presumably intestinal absorption, of xylose in one case of carcinoid syndrome. No such effect of propantheline was observed in our investigation in vitro.

The in-situ intestinal loop preparation with anaesthetized rats has been used to study antibiotic absorption. This showed good correlation when predicting antibiotic absorption in man. By contrast, results with the everted sac as a model for gastrointestinal absorption had to be interpreted with extreme caution.[5] Our results agree with this latter view. Thus phenobarbitone[6] and metoclopramide show similar effects on xylose absorption both in vivo and in vitro but there is no such correlation with propantheline.—We are, etc.,

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2 Nimmo, J., *et al.*, *British Medical Journal*, 1973, **1**, 587.
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Metaclopramide and Prolactin

SIR,—Dr. M. Shaklai and others (18 May, p. 385), reporting the occurrence of cardiac arrhythmia during the administration of metaclopramide, make reference to the fact that this drug is considered to be free of side effects in adults. In recent studies we have discovered that metaclopramide is a potent stimulator of prolactin release in both men and women when given intramuscularly, intravenously, or orally in a dose of 10 mg. Levels increased from 3- to 8-fold within five minutes of either an intramuscular or intravenous injection and within 60 minutes after oral administration; these levels remained elevated for at least eight hours. Long-term administration of metaclopramide has occasionally been associated with galactorrhoea.

Metaclopramide is a derivative of procainamide and we have previously reported[1] that a related compound, sulpuride, is also a very potent releaser of prolactin in man. In view of a recent report on the effects of prolactin on the rat heart in vitro, causing changes in both heart rate and amplitude of contraction and inducing dysrhythmia,[2] it would seem possible that the effects observed by Dr. Shaklai and his colleagues in their patient may be related to the elevation in the circulating prolactin. We are at present investigating the site of action of metaclopramide and the effects of other procainamide derivatives on prolactin secretion in man.—We are, etc.,

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1 Thorner, M. O., *et al.*, *Journal of Endocrinology*, 1974, **61**, 132.
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Isolation System for General Hospitals

SIR,—Professor N. R. Grist (8 June, p. 555) has overlooked the evidence[1] that spread of infection in infectious hepatitis derives from anicteric and preicteric cases. I suggest that it validates the statement in my letter (11 May, p. 331) and also that the modern attitude to the icteric form of infectious hepatitis is as misguided as was that of our ancestors to leprosy. But unlike us they had the excuse of not knowing that those whom they banished from their midst were the least infectious patients, if they were infectious at all.[2]—I am, etc.,

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Transplacental Passage of Chlordiazepoxide

SIR,—Benzodiapines are widely used in the management of eclampsia and fulminating pre-eclampsia. We were therefore interested to read the article by Dr. Jean E. Cree and her colleagues (3 November, p. 251) and the letter of Dr. J. Kanto and others (30 March, p. 641) on the use of diazepam in labour.

Over the past 18 months a regimen of chlordiazepoxide, hydrallazine, and frusemide has been used in St. Mary's Hospital to control severe pre-eclampsia and eclampsia. Chlordiazepoxide was chosen following the results reported by Lean and others.[1] One patient was given chlordiazepoxide 500 mg intravenously over a period of four hours before caesarean section. The baby had Apgar scores of 8 at 1 minute and 10 at 5 minutes but was unresponsive, hypotonic, hypothermic, and reluctant to feed for 48 hours. The atonicity persisted for a week but ultimately the baby did well. A full range of tests was normal but it was not possible to measure drug levels in mother or baby.

The similarity between this syndrome and that described by Dr. Cree and her colleague led us to do a pilot study of chloridiazepoxide levels in maternal and mixed cord blood at delivery in three patients with severe pre-eclampsia and in one with eclampsia who had been treated with the drug. The results (see table) showed that chlordiazepoxide crosses the placenta and may affect the neonate. None of the effects persisted but long-term minor sequelae cannot yet be ruled out. Bearing in mind the value of the drug in the treatment of a potentially dangerous condition, however, the therapeutic balance must be in favour of its judicious use. A fuller study is in progress.—We are, etc.,

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1 Lean, T. H., Ratnam, S. S., and Sivasamboo, R., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1968, **75**, 856.

Adjustment of Plasma Calcium Measurements

SIR,—We cannot agree with the statement of Dr. R. B. Payne and his colleagues (1 June, p. 504) that the clinical usefulness of their adjustment is enhanced by the inbuilt errors.

With a low ionized calcium level the adjustment applied is larger than it should be, whereas with a raised calcium level it is smaller. Thus only in cases where the adjustment is subtracted from the measured total will one observe the enhancement claimed by them. This, of course, requires that the albumin level be higher than normal. Where the albumin level is lower than normal the adjustment must be added, thus giving an adjusted total higher than it should be with low ionized calcium, and lower than it should be with high ionized calcium. It is well known that abnormalities of plasma albumin are generally towards low rather than high concentrations. In such circumstances the inbuilt error of the Payne adjustment, far from enhancing the usefulness of the correction tends to negate it.

Apart from recommending direct measurement of plasma ionized calcium, we agree with Dr. A. M. Parfitt (16 March, p. 520) that the McLean-Hastings nomogram is still the most appropriate way of allowing for variations in plasma protein because it is

Case No.	Chlordiazepoxide Dosage before Delivery		Last Dose and Time (hr) before Delivery	Birth Weight and Fetal Condition	Serum Chlordiazepoxide Levels (μg/ml)	
	7 days	24 hr			Mother	Cord
1	1,900 mg	100 mg	100 mg I.M. 15 hr	1,802 g. Apgar 7/1, 9/5. Listless, hypotonic, reluctant to feed, hypothermia 3 days	5·0	5·3
2	450 mg	400 mg	100 mg I.M. 6½ hr	900 g. No problems	3·2	3·4
3	300 mg	110 mg	100 mg I.M. 5 hr	2,602 g. Apgar 9/1, 10/5. Hypotonic, reluctant to feed	1·3	0·5
4	100 mg I.V. over last 8 hr			3,240 g. Apgar 9/1, 10/5. No problems	1·4	1·6