regarded as incompatible with clinical medicine.

The construction of questionnaires remains a ticklish problem. I have recently attempted to simplify my own questionnaire¹ by identifying and rejecting redundant questions. A correlation matrix was drawn up from 100 consecutive completed forms. The matrix showed which pairs of questions were or were not obtaining substantially the same information from the patient. If they were, then one of the pair could be left out. Furthermore, even elementary cluster analysis of the matrix revealed significant grouping of symptoms. "Neurotic" and "senile" groups were easily definable, and a more detailed factorial analysis is at present being undertaken. The emergence of factors—that is, symptom patterns—raises interesting questions as these do not always seem to correspond to our preconceived notions of so-called objective diagnoses.

Anyone who uses questionnaires will soon find himself fascinated and stimulated by the light they throw on the theory and practice of the medical interview.—I am, etc.,

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¹ Hall, G. H., *British Medical Journal*, 1972, 1, 42.

Radiographic Location of the Dalkon Shield

SIR,—The use of radiographic methods to establish the possible expulsion or translocation of a Dalkon Shield entails considerable irradiation of the patient, especially if one of the "soft tissue" techniques suggested by Dr. Ursula E. Mountrose and Mr. L. Whitehouse (1 June, p. 503) is used and both anteroposterior and lateral films are taken.

In the majority of cases an ultrasonic scan of the uterus through a full bladder is all that is required.^{1,2} The procedure is quick, simple, and free from harmful irradiation.

The Dalkon Shield in the uterus is arrowed. The vagina (V) and bladder (B) are clearly seen.

All types of intrauterine devices can be readily shown (see fig.). If the uterus is empty, then x-rays will of course be necessary to exclude translocation.—I am, etc.,

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¹ Cochrane, W. H., and Thomas, M. A., *Radiology*, 1972, 104, 623.

² MacKay, D., and Mowat, J., *Lancet*, 1974, 1, 652.

Lactose Intolerance in San Populations

SIR,—In a recent paper (6 April, p. 23) we described the investigation of a San ("Bushman") population for lactose tolerance and animadverted on the possibility (to which others^{1,2} have drawn attention) that the supplementation with dried milk of the diet of peoples in which adult tolerance of lactose is very unusual might be inadvisable. We have recently investigated two further Khoisan peoples by the same methods and present a brief summary of our findings.

The populations investigated were:

(1) the ǀhūa:, a small San group found scattered in southern Botswana, the subject of some speculation regarding the affiliations of their language, which appears not to fall into any of the hitherto reorganized Bush groups;³ and (2) the Nama of Keetmanshoop, representatives of the largest extant group of Khoi ("Hottentots"), resident in the semi-desert south of South-west Africa. The ǀhūa:, like the !Kung, are not known ever to have been cattle-keepers or milk-drinkers; some of them do, however, live in a client/patron relationship with cattle-keeping Kgalagadi, and the latter, in common with the other Tswana, use both fresh and sour milk.⁴ The Khoi peoples first enter recorded history⁵ as cattle-keepers, and though the Nama of Keetmanshoop today possess few bovine cattle they do have an abundance of goats, whose milk they drink both fresh and sour.

Lactose tolerance tests were performed on 34 ǀhūa:, but nine were excluded from the final calculations because of close family relationship or technical faults. Of the remaining 25, two proved to be tolerant, giving a phenotypic frequency for lactose tolerance of 8%. With the exception of three children about 10 years old, all of them intolerant, all persons in the ǀhūa: series were adult. Among the Keetmanshoop Nama the results, after the exclusion of closely related individuals, showed a 50% frequency among children (4 out of 21); the difference was significant at the 5% level ($\chi^2=4.18$ for 1 D.F.).

The frequency of lactose-tolerant individuals in San populations seems to be turning out to be rather higher than the hypothesis put forward by Simoons,⁶ that lactose tolerance represents an advantageous adaptation consequent on the development of dairying, would lead one to expect. Moreover, the significant difference between adults and children among the Nama would appear to favour the possibility that induction of lactase in response to milk-drinking plays a larger part in the production of adult tolerance than has previously been supposed, were it not that the youngest member of our series, a 7-year-old, was lactose tolerant. It seems to us that our latest findings may be of some interest in the study of human evolution.

We should like to thank the Director, Professor J. F. Murray, and the Deputy Director, Professor J. Metz, of The South African Institute for Medical Research, as well as the Directors of Medical Services of Botswana and South West Africa, the medical superintendent and staff of Keetmanshoop Hospital and the District Surgeon, Keetmanshoop, the Rev. Fr. Jansen, the Sister Superior and staff of the Don Bosco Nama Laerskool, Keetmanshoop, Mr. Thompson of the S.A.I.M.R. Laboratories in Keetmanshoop, Mr. Tony Traill, the Ministry of Commerce and Industry, Gaborone, Botswana, and, of course, the 77 volunteers who made the whole project possible. The work of the unit is

supported in part by the Medical Research Council of South Africa.

—We are, etc.,

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¹ Cook, G. C., and Kajubi, S. K., *Lancet*, 1966, 1, 725.

² Jersky, J., and Kinsley, R. H., *South African Medical Journal*, 1967, 41, 1194.

³ Traill, A., *African Studies*, 1973, 32, 25.

⁴ Schapera, I., *The Tswana*. London, International African Institute, 1953.

⁵ Nienaber, G. S., *Hottentots*. Pretoria, Van Schaik, 1963.

⁶ Simoons, F. J., *American Journal of Digestive Diseases*, 1970, 15, 695.

B.M.A. and B.M.S.A.

SIR,—On behalf of past members of the British Medical Students Association, we would like to express our sincere gratitude to the B.M.A. for all the help that they gave the association over the years. We would also like to thank Mr. A. E. Vince for his hard work and forbearance in dealing with our many problems.—We are, etc.,

H. G. STURZAKER
J. E. P. SIMPSON
ALAN BAILEY
MICHAEL GARRAWAY

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Temporarily Dependent Patients in General Practice

SIR,—I would like to reply to the letters of Drs. Joyce E. Leeson and R. J. Robertson (18 May, p. 385). It is impossible to say whether the patients described in my article (30 March, p. 625) are ill or not ill in the absence of a universally accepted definition of illness; hence my use of such terms as "undiagnosed," "successfully untreated," and "ill in the accepted sense of the word."

These patients were called "temporarily dependent" because, having come to their doctor with no objective evidence of disease and having been given no pharmacologically effective treatment, they made no further effort to seek help either by returning to me, as they were invited to do, or to any of my three partners, as they could easily have done. The implication is that in that particular situation at that particular time they were in a state which was altered and improved by reassurance from their doctor. Dr. Robinson's point is well taken. It would have been more accurate to say "patients who received no pharmacologically effective treatment."—I am, etc.,

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Drugs and Xylose Absorption from Intestine

SIR,—Absorption of xylose from the human intestine has been reported¹ to be decreased by metoclopramide and increased by propantheline. These drugs also alter the absorption of paracetamol² and digoxin.³ These effects were thought to be due to delayed gastric emptying³ or to altered gastrointestinal motility.³ The indirect evidence quoted in support of this view does not ex-

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.¹ 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 Kendall² 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 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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1 Kendall, M. J., *British Medical Journal*, 1973, 2, 179.

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

3 Manninen, V., *et al.*, *Lancet*, 1973, 1, 398.

4 Wass, M., and Evered, D. F., *Biochemical Pharmacology*, 1970, 19, 1287.

5 Perrier, D., and Gibaldi, M., *Journal of Pharmaceutical Sciences*, 1973, 62, 1486.

6 Matthews, D. M., *Journal of Physiology*, 1966, 182, 468.

Metoclopramide and Prolactin

SIR,—Dr. M. Shakkai and others (18 May, p. 385), reporting the occurrence of cardiac arrhythmia during the administration of metoclopramide, 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 metoclopramide 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 metoclopramide has occasionally been associated with galactorrhoea.

Metoclopramide is a derivative of procainamide and we have previously reported¹ that a related compound, sulphuride, 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. Shakkai 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 metoclopramide 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.

2 Nassar, B. A., *et al.*, *British Medical Journal*, 1974, 2, 27.

Isolation System for General Hospitals

SIR,—Professor N. R. Grist (8 June, p. 555) has overlooked the evidence¹ 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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1 Gowen, G. H., *Lancet*, 1964, 2, 478.

2 Easton, H. G., *World Medicine*. In press.

Transplacental Passage of Chlordiazepoxide

SIR,—Benzodiazepines 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 chlordiazepoxide 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 900 g. No problems	5.0	5.3
2	450 mg	400 mg	100 mg I.M. 6½ hr		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