possible whether or not: (a) the drug affects the production of milk; (b) the drug is excreted in the milk and, if so, whether the amount is of clinical significance; and (c) the amount excreted would adversely affect the neonate or infant. The information would then be readily at hand when the increasing number of lactating mothers consult their practitioners. I am trying to assemble such data to produce a useful reference to drugs which are safe rather than the negative lists which currently predominate.

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¹ Lewis, P, *Journal of Maternal and Child Health*, 1978, 3, 128.

² Harvey, D, *Modern Medicine (Great Britain)*, 1978, 23, 87.

Serum trypsin concentrations in diabetes mellitus

SIR,—The paper by Dr P Dandona and others on serum trypsin concentrations in diabetic subjects (21 October, p 1125) is an interesting contribution to the accumulating evidence of dysfunction of the exocrine pancreas in diabetes. Their observation that serum trypsin concentrations are low in insulin-dependent diabetic patients, with a lesser decrease in diabetic patients treated with oral hypoglycaemic agents, certainly corresponds to the pattern of reduced pancreatic trypsin output described in similar groups of diabetic subjects.¹ (Exocrine pancreatic function in these patients was in fact studied in response to an intravenous infusion of secretin and cholecystokinin-pancreozymin and not to a Lundh test meal as the authors state.) However, while serum trypsin concentrations vary in different clinical conditions,² the value of this measurement as an index of the secretory capacity of the exocrine pancreas can only be inferred. Their interpretation that low serum trypsin concentrations in diabetic subjects are indicative of exocrine pancreatic deficiency would be strengthened if a direct correlation could be demonstrated with stimulated outputs of pancreatic trypsin in the same patients. It would also be interesting to know if the authors found a relationship between the serum trypsin concentrations and the duration of diabetes in each group of patients.

The authors further refer to our study demonstrating a direct relationship between exocrine pancreatic function and endogenous insulin secretion³ (as measured by C-peptide concentrations) to support their premise that the abnormality of serum trypsin concentrations parallels the degree of beta-cell deficiency in their diabetic patients. We observed a significant correlation between endogenous insulin secretion and the outputs of pancreatic amylase and bicarbonate in a group of insulin-dependent diabetic patients but could not demonstrate a relationship with pancreatic trypsin output, although the latter was undoubtedly diminished in diabetes.³ Animal studies have also failed to show that insulin will enhance pancreatic protease enzyme secretion in alloxan diabetic rats.^{4,5}

The effect of endocrine factors on pancreatic trypsin production and secretion are not well established and dietary carbohydrate restriction in diabetes is another factor which may influence trypsin secretory capacity and serum trypsin levels. Therefore, while it is likely that low serum trypsin concentrations in diabetes are secondary to exocrine pan-

creatic dysfunction, the suggested relationship to the severity of beta-cell deficiency cannot be supported by present evidence.

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¹ Frier, B M, *et al*, *Gut*, 1976, 17, 685.

² Elias, E, Redshaw, M, and Wood, T, *Lancet*, 1977, 2, 66.

³ Frier, B M, *et al*, *Diabetologia*, 1978, 14, 301.

⁴ Ben Abdeljlil, A, Palla, T C, and Desnuelle, P, *Biochemical and Biophysical Research Communications*, 1965, 18, 71.

⁵ Adler, G, and Kern, H F, *Hormone and Metabolic Research*, 1975, 7, 290.

Repeatability and reliability

SIR,—Discussing observer variations in their useful series of articles about epidemiology Drs Geoffrey Rose and D J P Barker note (7 October, p 1006) that repeatability is less satisfactorily known as reliability.

If reliability is defined as the degree of agreement between different observations it is possible to distinguish test-retest reliability, or repeatability, when the observations are made on different occasions by the same or different observers, and single test inter-rater reliability, when the observations are made on the same occasion by different observers; these two measures have produced different results regarding the presence of a psychiatric symptom.¹

Reliability is thus a more generic concept than repeatability.

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¹ Wing, J K, *et al*, *British Journal of Psychiatry*, 1967, 113, 499.

Autoimmunity in juvenile diabetics and their families

SIR,—Dr Eva Kohner (19 August, p 568) has criticised our paper (15 July, p 165), in which we tentatively suggested that autoimmune diabetes has a stronger tendency to run in families and might be more liable to complications than in non-autoimmune families. She states that diabetic microangiopathy is a manifestation of the duration of the disease and also points out that the seven patients in our study developing proliferative retinopathy were all diabetics of long standing.

HLA typing of the patients with retinopathy has, however, provided a little further evidence that some diabetics may be more liable to complications than others. The 10 patients in our study with diabetic retinopathy (who were all members of autoimmune families) had a significantly higher frequency ($P < 0.05$) of HLA-B8 than diabetics without complications (see table). There is also a tendency, not

Distribution of HLA antigens in diabetics with and without retinopathy

Antigen	Retinopathy (n = 10)	No complications (n = 70)
A1	6 (60%)	26 (37%)
B7	2 (20%)	14 (20%)
B8	8 (80%)	29 (41%)
B15	2 (20%)	30 (43%)
BW35	1 (10%)	8 (11%)
A1 B8	5 (50%)	21 (30%)
B8	2 (20%)	8 (11%)
without A1		

statistically significant, towards a higher frequency of B15 among diabetics without complications. This is, of course, a very small series, but the frequency of B8 among our patients with retinopathy is virtually identical to that reported recently by Dr R G Larkins and his colleagues (29 April, p 1111) among 16 patients with proliferative retinopathy in Australia.

We agree entirely with Dr Kohner about the importance of both duration and degree of control in determining the development of complications but suggest that there is at least some evidence that a subgroup of diabetics (those with serological evidence of autoimmunity and HLA-B8) may be more liable. This suggestion certainly warrants further investigation, since if this is shown to be correct diabetologists might pay special attention to such patients.

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Tetracycline preparations for children

SIR,—It should by now be common knowledge among practitioners that tetracyclines stain and deform the developing teeth. The antibiotics section of the current edition of *MIMS* is headed by the statement, "Tetracyclines should not be used in the latter half of pregnancy or in children up to 12 years of age." However, the following tetracycline preparations are listed in the same publication with recommended dosages for children: Achromycin V syrup (Lederle); Deteclo syrup (Lederle); Ledermycin drops; Ledermycin syrup; Megaclor syrup (Pharmax); Mysteclin syrup (Squibb); Terramycin syrup (Pfizer); Vibramycin syrup (Pfizer). There are a number of other tetracycline preparations, manufactured by Berk, Glaxo, and ICI, in syrup form and therefore liable to be prescribed to children.

It is therefore small wonder that we continue to encounter cases of tetracyclines being prescribed to pregnant mothers or children.

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Paget's disease of bone among British migrants to Australia

SIR,—Earlier this year (24 June, p 1655) we reported on the radiological prevalence of Paget's disease in British migrants to Australia, showing it to be higher than in a comparable Australian resident population and lower than in a British resident population. We have since completed a case-control study on age at migration and place of origin in Britain among the British migrants, exploring further the possible reasons for these differences in prevalence rates. The particular aims were to ascertain whether migrants with Paget's disease had emigrated at a later age and came more often from areas of higher prevalence within Britain in comparison with migrants without Paget's disease.

Forty-eight cases of Paget's disease were identified among the British migrants in the