Correspondence

Standardization of insulin preparations and syringes

Sir,

We wish to comment on the article by McKinlay and Farquhar (1976) and to give the opinion of the International Study Group of Diabetes in Children and Adolescents—the association of paediatric diabetologists. At the meeting of the study group held in Belgium 25–26 June 1976, one of the sessions was entitled 'Standardization of types of insulins and syringes' (moderator, Prof. Ø. Aagenaes, Oslo).

Of course, the dual U-40/U-80 syringe is a source of dosage errors and the type of syringe with 2 graduated scales has to be discarded (Ernould *et al.*, 1973; Rosenbloom, 1974; Shainfeld, 1975). The use of U-100 insulins is certainly of great interest for diabetic adolescents and adults who need a larger number of units each day. But in children receiving small doses of insulin, the study group preferred the U-40 insulins because of greater accuracy in measuring the dose in the syringe, since a smaller concentration of insulin per ml allows easier reading of graduations on the syringe.

So paediatric diabetologists of the study group would like to maintain, in Europe, the existence of U-40 insulins for diabetic children. The ideal syringe must be graduated at 1-U increments, with graduations not too close, for only a single strength of insulin, and with no dead space (Shainfeld, 1975).

H. DORCHY*, Ch. ERNOULD, and
H. LOEB

*International Study Group of Diabetes in Children
and Adolescents*

(*Service de Pédiatrie, Hôpital Universitaire St.
Pierre, Rue Haute, 320, B-1000, Brussels, Belgium.)

References

- Ernould, Ch., Dorchy, H., Francois, B., Geussens, H., Mozin, M. J., and Loeb, H. (1973). *Guide du Jeune Diabétique*. Revue Médicale de Liège, Liège.
- McKinlay, I., and Farquhar, J. W. (1976). Use of 100 units/ml insulin in treatment of diabetic children. *Archives of Disease in Childhood*, **51**, 796–798.
- Rosenbloom, A. L. (1974). Advances in commercial insulin preparations. *American Journal of Diseases of Children*, **128**, 631–633.
- Shainfeld, F. J. (1975). Errors in insulin doses due to the design of insulin syringes. *Pediatrics*, **56**, 302–303.

Dr. Farquhar comments:

Our Belgian colleagues differ only in that they, like other Europeans, wish to retain U-40 preparations. I understand that there may be good economic reasons for this as well as the practical one of measuring low doses.

Colleagues in adult medicine however may argue to retain U-80 or even U-20 so that no change occurs. The International Diabetes Federation compromised in 1976 by accepting both U-100 and U-40 which may mean that North Americans will polarize toward one, Europeans toward another, and the insulin manufacturers make for one or other market. The British Standard 1619 insulin syringes (20 graduations in 1 ml; 40 graduations in 2 ml) have existed for over 20 years so that British children and parents are more fortunate than many in Europe who must still contend with 2 or even 3 graduation scales at the whim of manufacturers and nonconformist physicians. The British Diabetic Association would like to see all disposable insulin syringes in Britain conform to 1619 type. U-100 insulin was measured accurately enough down to 4 units (as in our Table 1). The syringes were well marked and of such a diameter as to space out the graduations. Parents preferred exerting a little more manipulative skill to risking their arithmetic in the way made necessary with varying insulin concentrations.

The insulin market has become as complex as the baby food one and is a sight more dangerous. If all currently available insulins have to exist in 2–3 concentrations in packets gay as coloured bunting at a regatta, some children will suffer, sometimes permanently, and the very real anxieties of their parents will continue. The exact concentration may matter more to manufacturers than to physicians. For the sake of diabetic children, their parents, nurses, and doctors, let us agree with industry on one concentration (U-50?) for all diabetics and on standardized syringes for all. If we compromised on U-50 in Europe and U-100 in North America the same standardized syringe could be used for both (50 graduations in 1 ml) or at least life would be less confusing for those whose diabetic practice is North Atlantic in outlook.

J. W. FARQUHAR
*Department of Child Life and Health,
University of Edinburgh,
17 Hatton Place, Edinburgh EH9 1UW.*

Stool sugars and pH in breast-fed neonates

Sir,

We have read with interest the article by Drs. Counahan and Walker-Smith on stool and urinary sugars in normal neonates (*Archives*, 1976, **51**, 517). They suggest that the greater proportion of breast-fed babies observed to have reducing substances in their stools may be related to the higher concentration of lactose in breast milk. In fact, the formula (prepacked half-cream Cow and Gate) given to the bottle-fed babies did not contain less lactose than human milk (7.1 g/100 ml).

We have recently analysed specimens of stools from 78 normal term neonates ranging in age from 2 to 15

days. There were 58 breast-fed and 20 bottle-fed infants. The latter were fed a formula of humanized cows' milk (Similac-20). Though the lactose content of this formula is almost identical to that of human milk (7.2 vs. 7.0 g/100 ml, respectively), as is shown in Tables 1 and 2,

Table 1 Reducing substances in stool (Clinitest)

Reducing substances (%)	<0.5	0.5-2.0	Total
Breast-fed	8	50	58
Similac-20	16	4	20
Total	24	54	78

$\chi^2 = 31.02$, $P < 0.001$.

Table 2 Stool pH

Stool pH	4.4-6.0	6.1-7.2	Total
Breast-fed	52	6	58
Similac-20	7	13	20
Total	59	19	78

$\chi^2 = 23.89$, $P < 0.001$.

significantly more breast-fed neonates had 0.5% or more reducing substances in their stool as well as acid stool (pH between 4.4 and 6.0). As was observed by Counahan and Walker-Smith, in our series also estimation of stool pH was an unreliable index for lactose absorption. The caloric content of human milk is identical to that of Similac-20 (67 cal/100 ml). Since the average weight gain during the first 2 weeks of life of the formula-fed infants exceeded that of the breast-fed infants, food consumption, and therefore lactose intake of the former might have been even greater. Thus, in our study lactose intake was not a determinant in the trend for higher levels of reducing substances and lower pH in the stools of breast-fed neonates. Further investigations will be required in order to determine the exact contribution of the different gut flora in breast-fed infants to the observed differences in stool sugar content and pH.

M. NITZAN* and Z. ROSENFELD
Division of Paediatrics, Beilinson Medical Center,
Tel Aviv University Medical School, Petah Tikva,
Israel.

(*Section of Developmental Biochemistry,
National Institute of Child Health and Human
Development, Bldg 10, Rm. 13N260,
NIH, Bethesda 20014, USA.)

Dr. Walker-Smith comments:

I was pleased to see the letter of Drs. Nitzan and Rosenfeld confirming our finding that breast-fed infants have increased stool reducing substances. This observation supports the view that breast-fed babies have a temporary 'physiological malabsorption' of lactose. I agree that there is not a higher concentration of lactose in breast milk as compared to the artificial feeding formula used,

and so this cannot account for the greater proportion of breast-fed infants who have increased levels of stool reducing substances. Some other explanation must be sought, including the contribution of gut flora, but the inter-relationships between faecal sugar, pH, and flora is likely to be very complex. Whether the primary event in this inter-relationship is unabsorbed lactose entering the colon of breast-fed infants, influencing their colonic pH and flora, or whether small intestinal flora in such infants modifies the absorption of lactose is unknown and warrants investigation.

J. A. WALKER-SMITH
Department of Child Health,
Queen Elizabeth Hospital for Children,
Hackney Road, London E2 8PS.

Haemolytic uraemic syndrome in sibs

Sir,

The occurrence of multiple cases of a disease in some families does not by itself provide irrefutable evidence for genetic predisposition for that disease. This appears to be the case in the haemolytic-uraemic syndrome (HUS), which has been reported to affect multiple sibs in some families (Kaplan *et al.*, 1975). The reports of simultaneous occurrence of the disease in unrelated adopted sibs (Chan *et al.*, 1969) and the presence of asymptomatic mild cases in family contacts (Tune *et al.*, 1974), along with a well-recognized predilection of the disease to appear in endemic (Gianantonio *et al.*, 1964) and epidemic (McLean *et al.*, 1966) forms in various parts of the world, however, appear to implicate environmental agents, namely infections, as causative factors.

In a review of 41 sibships with multiple cases of HUS, Kaplan and associates (1975) could distinguish two groups of families on the basis of (1) the interval between onset of disease in affected sibs, (2) geographical location (endemic versus nonendemic) of the families and, (3) severity of the syndrome as indicated by mortality. The authors speculated that the milder disease occurring simultaneously in sibs in families living in endemic areas could be attributed to environmental agents, while genetic factors may have played an important role in severe form of the disease occurring in sibs after longer intervals in families living in nonendemic areas.

We have seen a New York City family in which 2 male infants were affected with HUS with an interval of 2 years between the cases. The parents were healthy non-consanguineous black Americans. Both parents and 2 sisters (7- and 1-year-old, respectively) were in good health. The first infant was born in December 1970 and died in May 1971, the second was born in February 1973 and died in August 1973. The clinical picture included gastroenteritis, haemolytic anaemia, disseminated intravascular coagulopathy, hypertension, and renal failure. Necropsy was performed on the second infant only, and showed widespread fibrin thrombi in arterioles and capillaries throughout both kidneys.