LETTERS TO THE EDITOR

Early complications of diabetes mellitus

Sr. — Dr Gibb and her colleagues have described in detail their findings of early physiological changes of renal function in children with type 1 insulin-dependent diabetes mellitus (IDDM). They conclude that an abnormally raised urine albumin excretion is associated with a high glomerular filtration rate and that serial follow up of these early markers is required to study their predictive roles in the development of nephropathy in IDDM. My concern regarding this statement is the suggestion that the measurement of glomerular filtration rate should be routine in children with diabetes.

Both glomerular filtration rate and renal plasma flow increase significantly with a variety of hormonal and metabolic disturbances. These include hyperinsulinaemia, hyperglycaemia, increased concentrations of circulating growth hormone, hyperketonaemia and hyperglycaemia. The effect of glycaemia on the glomerular filtration rate measurement is erratic and influences the analysis of renal plasma flow when estimated by para-aminohippurate (RN Dalton, C Turner, SA Greene, et al. Abstract presented at meeting of the Renal Association, 1987).

The subjects in the study of Gibb et al had diabetes of several years' duration and all had poor diabetic control with glycated haemoglobin (HbA1c) 11.2 to 13.4% compared with a normal range of 5.0 to 8.0%. The measurements of the glomerular filtration rate were undertaken after breakfast, which, from their description, almost certainly contained a considerable amount of carbohydrate. It is therefore likely that the blood glucose concentration during the glomerular filtration rate measurement period was abnormally raised resulting in glycosuria. Therefore, the design of their study may account for the abnormally raised glomerular filtration rate and the observation of a normal size kidney assessed by ultrasonography. I would contest that if glomerular filtration rate is to be measured in diabetic children, an attempt to standardise the metabolic milieu is necessary. Such manoeuvring would make routine measurement of glomerular filtration rate a difficult procedure for most paediatricians.

S A GREENE
Department of Child Health, Ninetinells Hospital and Medical School, Dundee DD1 9SY

Sr. — We would like to add our comments to the recent report of Gibb et al on early markers of renal dysfunction in diabetic children. Using two consecutive overnight urine collections we measured urinary albumin excretion in 64 type 1 diabetics, expressing the results as the geometric mean of the urine albumin concentration ratio (UA/UC). The diabetic children (boys and girls) ranged in age between 4 and 18 years, with duration of disease from 6 months to 14 years and did not show any evidence of clinical diabetic nephropathy. Fourteen out of these patients (22%) showed UA/UC values above the normal range (obtained in 57 matched healthy controls): this prevalence is similar to that found by Dr Gibb et al and by other authors, but greater than in other recent reports. At variance with the results of Dr Gibb et al, all the prepubertal diabetics showed normal UA/UC, while all the children with increased UA/UC were older than 13 years; four out of these 14 subjects were at Tanner stage 2 and 3, while 10 were at stages 4 and 5. The patients with increased UA/UC had significantly higher mean four year values for glycated haemoglobin (HbA1c) than matched subjects with normal UA/UC (mean (SD) 11.2+2.5) compared with 8.1 (2.3) (p<0.001), confirming a strong association between long term glycaemic control and microalbuminuria. Moreover, we have measured glomerular filtration rate in 38 children with diabetes duration greater than five years, using 67Tc-dipyridamole percutaneous renal clearance as the safe and convenient method of assessing renal function in children: in contrast to the findings of Dr Gibb et al we were not able to demonstrate any significant difference in glomerular filtration rate between the diabetics with normal and those with increased urinary albumin excretion (130-6 (4.31) compared with 133-2 (5.99) mg/min/1.73 m²).

Nevertheless, in agreement with the data of Dr Gibb et al, no significant linear correlation was observed between glomerular filtration rate and either UA/UC (r=0.14, p>0.05) or albuminuria (r=0.11, p>0.05). Furthermore, in our children, glomerular filtration rate measurement when repeated a year later was remarkably consistent and the association with urine albumin excretion and renal size remained. The predictive value of hyperfiltration in IDDM cannot be determined from cross sectional studies and our one year follow up results merely confirm associations noted at baseline. We therefore suggested that much longer follow up is required to determine the predictive value of hyperfiltration in diabetes.

The observation of Dr Gibb et al, that at each stage we state or suggest that glomerular filtration rate should routinely be performed on all children with IDDM. At the present stage of knowledge, this would be quite wrong outside the research situation.


Dr Gibb comments:
Dr Greene suggests that complicated and invasive clamping techniques be used to standardise the metabolic milieu of children with IDDM before the measurement of glomerular filtration rate. He suggests that glycosuria may cause underestimation of these children. We measured glycosuria throughout the glomerular filtration rate procedure in these children, and in accordance with his statement that the association with glomerular filtration rate was 'erratic', we observed no correlation at all between the two variables.

Furthermore, in our children, glomerular filtration rate measurement when repeated a year later was remarkably consistent and the association with urine albumin excretion and renal size remained. The predictive value of hyperfiltration in IDDM cannot be determined from cross sectional studies and our one year follow up results merely confirm associations noted at baseline. We therefore suggested that much longer follow up is required to determine the predictive value of hyperfiltration in diabetes.

At no stage did we state or suggest that glomerular filtration rate should routinely be performed on all children with IDDM. At the present stage of knowledge, this would be quite wrong outside the research situation.


Sr. — In response to the recent comments of Dr Gibb et al, we should like to emphasise the lack of correlation between the two variables. We determined renal plasma flow using arterial and venous blood samples and the dipyridamole clearance technique. The flow was calculated assuming a mean hematocrit of 45% and a mean red cell volume of 71 fL. The results were expressed as g/min/1.73 m². The subjects were 28 children between the ages of 8 and 16 years with duration of diabetes mellitus ranging from 6 months to 10 years. The mean (SD) albumin excretion was 3.7 (2.4) mg/min/1.73 m². In none of the children was a significant correlation found between renal plasma flow and albumin excretion.

Intravenous immunoglobulin in HIV infection

Sr. — Hague and colleagues have reported the use of intravenous immunoglobulin in eight children infected with human immunodeficiency virus (HIV). They have been enthusiastic about its beneficial effects on both weight gain and frequency of infectious episodes. Furthermore they suggest that the intravenous immunoglobulin treatment resulted in significant saving of costs, despite the expense of the treatment, as a result of a decrease in the number of days the children spent in hospital.

We do not use routine intravenous immunoglobulin in children with symptomatic HIV infection and do not consider that their clinical course has been any worse than the children described by Hague et al. Five symptomatic children aged 22 months to 10 years infected vertically with HIV are attend- ing the Hospital for Sick Children, Great Ormond Street, London. Failure to thrive in the first 18 months of life was prominent in the two children documented since birth, but resolved spontaneously with no specific treat- ment. In addition, numbers of infectious episodes and admissions to hospital were more frequent in the early months of life in all children. If we had begun intravenous immunoglobulin treatment at the onset of symptoms we might be claiming the apparent success of this treatment. Furthermore, based on the cost estimates of Hague et al we would have cost the National Health Service over £50 000.

There are major difficulties in the interpre- tation of uncontrolled studies of treatment efficacy, especially in a disease which is vari- able, and where the outcome measures may be related to age. HIV infection in children has