Discussion

Although several predisposing factors have been identified[1-3] the trigger for febrile convulsion remains elusive. Previous studies have shown slowing of background rhythms during and after pyrexial illnesses[3] and during artificially induced fever.[4] The background rhythms in the present study were generally slower than expected for the children's ages but no fluctuation with temperature was detected, suggesting the slowing is caused by an effect of the infection other than fever.

It has been suggested that fever precipitates reflex anoxic seizures that progress to typical febrile convulsions.[6] None of the present children had asystole, and seizure activity occurred independently of cardiac rhythm. We are unable to exclude asystole as the final precipitating event for clinically observable seizures, but seizure activity in this study could not be attributed to anoxia. Our findings did not help to predict early recurrences of febrile convulsion.

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Weight as the best standard for glomerular filtration in the newborn

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SUMMARY The relation between surface area and body weight changes dramatically in infancy. In 31 healthy infants of 27 to 40 weeks' gestation, variations in glomerular filtration rate were reduced more than twofold by choosing glomerular filtration rate/kg body weight rather than glomerular filtration rate/m^2. The former provides the most useful and practical index of renal function in the neonate.

Although the use of surface area for standardising glomerular filtration rate minimises age and weight dependent variations in children and adults, this has never been tested in infancy, when surface area:weight changes most dramatically. We have, therefore, tested glomerular filtration rate data from preterm and term babies to find which standard reduces the variation most effectively.

Patients and methods

Thirty one well babies of 27 to 40 weeks' gestation weighing 0·68 to 3·7 kg were studied between 2 and 7 days of age. Twenty five (81%) of the infants were below the 50th centile for weight and 11 (35%) were below the 10th. Glomerular filtration rate was measured by the 24 hour constant inulin infusion method[1] on average three times for each baby, and the mean value taken. Surface area was estimated by Boyd's formula[2] and a weight index was calculated as weight:50th centile weight. The study had the approval of the local ethical committee, and informed parental consent was obtained.

Results

Glomerular filtration rate values varied more than 10 fold between babies (0·50 to 5·71 ml/min), but only fivefold when expressed per unit surface area (4·5 to 22·6 ml/min/m^2) and less than threefold when expressed per unit body weight (0·59 to 1·56 ml/min/kg). Glomerular filtration rate/m^2 and glomerular filtration rate/kg were each positively correlated with weight ($P<0·001$), gestational age ($P<0·001$), and weight index ($P<0·05$). Multiple

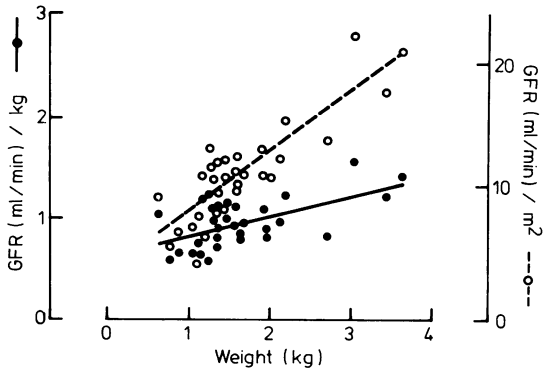

Fig. 1 *Regression of glomerular filtration rate (GFR)/m² and glomerular filtration rate (GFR)/kg on weight in 31 babies in the first week of life. Each point is the mean value for one baby.*

For glomerular filtration rate/m²; y = 3·67 + 4·55x, r = 0·82, P<0·001.
For glomerular filtration rate/kg; y = 0·623 + 0·196x, r = 0·60, P<0·001.

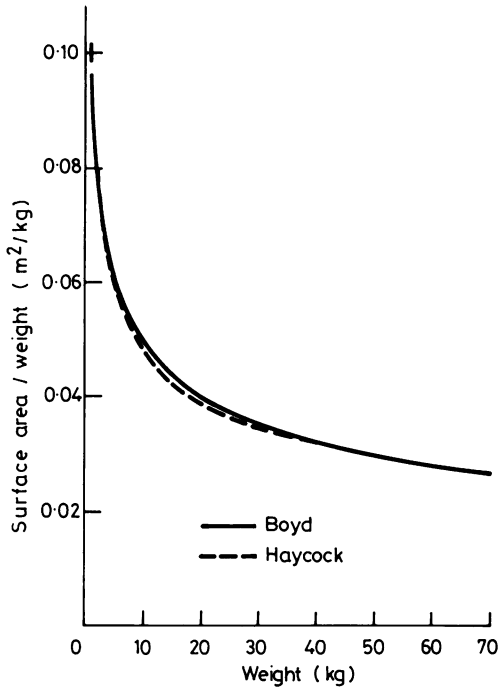

Fig. 2 *Relation between surface area to weight ratio (SA/W) and body weight, calculated (a) from Boyd[2] and (b) from Haycock et al[7] using the 50th centile values from national height and weight standards.*

regression analysis, however, showed that when weight was accounted for there was no longer any association with either gestation or weight index (P> 0·25 in each case). The slope of the regression line relating glomerular filtration rate/m² to body weight is two and a half times steeper than that for glomerular filtration rate/kg (P<0·05) (Fig. 1). Glomerular filtration rate/m² therefore shows wider variations between infants of different sizes than glomerular filtration rate/kg.

Discussion

The ratio of glomerular filtration rate to surface area hardly changes between age 2 years and adulthood, while surface area:weight falls by about 40%. Surface area:weight ratio alters much more dramatically, however, during infancy (it is about four times higher for a baby of 27 weeks' gestation than for an adult) and falls by one third between 27 weeks' and term (Fig. 2). For a physiological function to vary with surface area, its value per kilogram in early life would have to be large and change very rapidly. To maintain a glomerular filtration rate of 80 ml/min/m², a baby of 27 weeks' gestation would need to filter 8 ml/min/kg, whereas the figure for an adult would be 2 ml/min/kg.

The metabolic rate determines the need for the excretion of waste products. Basal metabolic rate and glomerular filtration rate correlate in older children and adults in that they each vary closely with surface area. Metabolic rate has been expressed both as metabolic rate/m² and metabolic rate/kg in newborn infants; the advantage of using metabolic rate/kg is shown by data previously presented by one of us.[3] The effects of environmental temperature and postnatal age on metabolic rate were easily recognised because size related variations were eliminated. If the same data are expressed per surface area, the regression of metabolic rate/m² on both weight and gestation (P<0·01) almost masks the effects of the other factors. Our finding that glomerular filtration rate is more closely related to weight than surface area in newborns, therefore, fits well with the data on metabolic rate.

The use of surface area to 'correct' neonatal glomerular filtration rate may be more than a mere extrapolation of convention; it may relate to the unifying 'law of surface area'. This century old law has, however, been shown to be invalid, and its use has led to many false conclusions.[4] Over 30 years ago, McCance and Widdowson[5] argued that the incorrect selection of surface area as a basis for comparison had delayed the understanding of juvenile renal function, but predicted pessimisti-

cally that changes in established practice would be opposed.

A major disadvantage of standardising glomerular filtration rate to surface area is that formulas for estimating surface area from weight or weight and length are based on relatively few actual measurements in the smallest weight range and have never been systematically tested in babies of varying body proportions. Practical neonatal management decisions, including those regarding calorie intake, temperature control, and fluid, electrolyte, and drug administration are almost universally made on the basis of body weight, which can be measured directly. Even workers who standardise their glomerular filtration rate results/m^2 generally calculate the doses of their test substances per kg body weight. For research findings to be usefully assimilated and applied clinically, they should be expressed in the same way as other parameters.

It has been argued that it would be logical to relate glomerular filtration rate to the size of the fluid pool affected by the kidney[5 6] but this has three disadvantages. Firstly, like surface area, fluid volumes would be estimated rather than measured. Secondly, no single fluid space would be appropriate to all aspects of renal function; total body water would be best for urea and water handling,[5] and extracellular fluid volume for inulin or mannitol clearances.[6] Thirdly, like surface area:weight, the total body water:weight and extracellular fluid volume:weight ratios fall with increasing postconceptual age, exaggerating the rises in glomerular filtration rate with increasing body size.

We have shown that weight, the only reference standard that can be actually measured and is clinically useful, is the best index for neonatal glomerular filtration rate measurement. To expect a single standard to apply to all patients weighing from 1 to 70 kg is simplistic, however, and could be misleading. It is better to consider glomerular filtration rate/kg as useful in the newborn period and glomerular filtration rate/m^2 as convenient in older children, and not to place physiological importance on either approach.

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Cushing's syndrome and bronchial carcinoid tumour

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SUMMARY Adrenal function test results in a girl with Cushing's syndrome and a bronchial carcinoid tumour suggested pituitary dependent hypercortisolism. Resolution after excision of the tumour indicated that her condition had been caused by ectopic adrenocorticotrophic hormone secretion. Conventional tests of adrenal function may be misleading in cases of adrenocorticotrophic hormone secreting bronchial carcinoid tumours.

The aetiology of Cushing's syndrome can usually be determined from the serum adrenocorticotrophic hormone concentration and the response of urinary corticosteroids to high dose dexamethasone and metyrapone.[1] In some circumstances, however, these investigations may be misleading.[2] We report a patient who seemed to have pituitary dependent hypercortisolism but was subsequently shown to have an adrenocorticotrophic hormone secreting bronchial carcinoid tumour.