Table Proportion of infants abnormal at follow up

Degree of periventricular haemorrhage	Subependymal haemorrhage	Intraventricular haemorrhage (No VPS)	Parenchymal extension (No VPS)	All	Subependymal/intraventricular haemorrhage only
Ventricular enlargement	1/3	4/9 (1)	14/16 (7)	19/28*	5/12†
No ventricular enlargement	3/28	3/10	1/1	7/39*	6/38†

* $\chi^2 = 15$, $P < 0.001$; † $\chi^2 = 2.2$, $P > 0.1$. VPS = ventriculo-peritoneal shunt.

Abnormal outcome is strongly associated with ventricular enlargement ($P < 0.001$). However, ventricular enlargement is also strongly associated with the degree of haemorrhage, in particular the presence of parenchymal extension of a bleed. Twelve of 50 babies with subependymal haemorrhage or simple intraventricular haemorrhage, and 16 of 17 with parenchymal extension of intraventricular haemorrhage (PAR H) had ventricular enlargement. Only 2 babies with PAR H appeared normal at follow up. It seems that the association of ventricular enlargement with poor outcome in this study is largely due to the bias introduced by the poor outcome of babies with large haemorrhages. If infants with subependymal or intraventricular haemorrhage alone are considered the relation between ventricular enlargement and outcome is no longer statistically significant. A similar bias is likely to have occurred in the study of Palmer *et al.* in that 12 of 14 babies without ventricular enlargement had small bleeds, while only 1 of 10 babies in the ventricular enlargement group had small bleeds ($P < 0.005$). Until larger numbers are available it will not be possible to allow for the effect of bleed size in analysis of the effect of ventricular enlargement on subsequent outcome. It is also not possible to conclude that ventricular enlargement has a greater effect than bleed size on subsequent development. This has implications for the rationale of conducting a trial of early intervention by cerebrospinal fluid drainage in posthaemorrhagic ventricular enlargement.

Reference

- Palmer P, Dubowitz LMS, Levene MI, Dubowitz V. Development and neurological progress of preterm infants with intraventricular haemorrhage and ventricular dilation. *Arch Dis Child* 1982; **57**: 748–53.

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Plasma terbutaline levels in asthma

Sir,

The reported safety of oral terbutaline in a dose of 250 $\mu\text{g/kg}$ in children prompts me to comment.¹ As a regular prescriber of this drug I have found a marked individual variation in response. Doses as high as 140 $\mu\text{g/kg}$ have caused tremor severe enough to render writing impossible and recently a dose of 330 $\mu\text{g/kg}$ (7.5 mg) has been reported to cause seizures.^{2 3}

It should be noted by your readers that Dinwiddie *et al.*

studied only 5 patients.¹ In a larger and more comprehensive study it has been shown that doses in excess of 100 $\mu\text{g/kg}$ produce side effects with no improvement in pulmonary function.²

References

- Dinwiddie R, Gewitz M, Van Der Laag H, Frame MH. Plasma terbutaline levels in asthma. *Arch Dis Child* 1983; **58**: 223–4.
- Ardal B, Beaudry P, Eisen AH. Terbutaline in asthmatic children: a dose-response study. *J Pediatr* 1978; **93**: 305–7.
- Friedman R, Zitelli B, Jardine D, Fireman P. Seizures in a patient receiving terbutaline (letter). *Am J Dis Child* 1982; **136**: 1091–2.

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Dr Dinwiddie comments:

Our clinical experience of oral terbutaline, often given in the higher dose in children, is at variance with Dr Blumenthal's. We have found that children are generally more tolerant of this drug and that higher proportionate doses are often required to produce a therapeutic effect. It was this experience that prompted us to undertake the present study.

We agree that there is individual variation with this as with any drug and the dose must always be tailored to the patient and his response to treatment. Our small study does, however, show that children may be given doses of up to 250 $\mu\text{g/kg}$ with good response and usually no untoward side effects. We should point out, however, that the maximum dose of 5 mg as stated in our paper should not be exceeded.

Intracranial calcification and childhood medulloblastoma

Sir,

We read with interest the paper by Pearson *et al.*¹ on intracranial calcification in survivors of childhood medulloblastoma. They observed intracranial calcification in 3 of 5 survivors of medulloblastoma who had undergone surgery and radiotherapy but had not had chemotherapy.

We would like to report a boy, now aged 16 years, who developed intracranial calcification following cranial irradiation and partial surgical removal of a cerebellar

astrocytoma. He presented at the age of 11 years with a 2 month history of ataxia and evidence of raised intracranial pressure. A posterior fossa tumour was partially removed and a ventriculo-atrial shunt inserted. Histology showed this to be an astrocytoma. His initial CAT scan showed no calcification. He received a 3 week course of irradiation as follows:

Dose(Gy)	Fractions	Duration(days)	Fields	Source
45	15	21	^R Lateral 6 MeV	

Five years later computerised axial tomography showed right occipital lobe calcification (Figure). Since operation and radiotherapy there has been a gradual deterioration in mental function and he is now at a school for the educationally subnormal.

This shows that intracranial calcification may occur in children who receive intracranial irradiation at a later age than those described by Pearson¹ and that it is not confined to children who are treated for medulloblastoma. Our patient and the 3 patients of Pearson¹ who developed intracranial calcification have educational problems. It seems more likely that calcification reflects the extent of the radiation damage than that calcification per se is harmful. The practical point is that children who have cranial irradiation need their educational progress monitored in view of the progressive intellectual deterioration that may occur.

Figure Computed tomography scan showing calcification in right occipital lobe.

Reference

- ¹ Pearson ADJ, Campbell AN, McAllister VL, Pearson GL. Intracranial calcification in survivors of childhood medulloblastoma. *Arch Dis Child* 1983; **58**: 133-6.

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Reference ranges for plasma creatinine

Sir,

In presenting the reference ranges for plasma creatinine in the newborn, Dr Rudd and his colleagues have made certain assumptions that could be misleading in interpreting the data presented.¹ They have excluded from their study infants who were oliguric, and were therefore considered to be in acute renal failure as a consequence of birth asphyxia. If this was the sole criterion for the diagnosis of acute renal failure they may well have included in their analysis infants with degrees of renal insufficiency who had never become oliguric, and excluded oliguric infants who were not in acute renal failure.²

The authors state that there was an appreciable increase in plasma creatinine values in babies who had required mechanical ventilation for respiratory distress syndrome. This finding agrees with the clearance studies of Guignard *et al.*, who showed a reduced glomerular filtration rate in infants with respiratory distress syndrome.³ Having made this assumption the authors then offer a reference range for plasma creatinine in which they have combined mean values for babies breathing spontaneously and babies requiring mechanical ventilation for respiratory distress syndrome from 7 days of postnatal age without having shown that infants previously ventilated subsequently achieve a normal glomerular filtration rate.

In normal term infants plasma creatinine is known to reach stable values within the first week of life and those for preterm infants towards the end of the first month.^{4,5} From the present study the findings would suggest that stable values for plasma creatinine in term infants are not reached until at least 14 days of age and that values obtained before this are not a reliable index of renal function.

The authors have produced a complicated formula from which a value for plasma creatinine may be calculated given the gestational and postnatal age. The value of the formula is questionable as the authors themselves clearly state that the range of calculated 'normal' values based upon it is wider than that derived from their empirical data.

References

- ¹ Rudd PT, Hughes EA, Placzek MM, Hodes DT. Reference ranges for plasma creatinine during the first month of life. *Arch Dis Child* 1983; **58**: 212-5.
- ² Mathew OP, Jones AS, James E, Bland H, Groshong T. Neonatal renal failure: usefulness of diagnostic indices. *Pediatrics* 1980; **65**: 57-60.