Original articles

Structure and evolution of echo dense lesions in the neonatal brain

A combined ultrasound and necropsy study

D I RUSHTON, P R PRESTON, AND G M DURBIN

Department of Pathology, University of Birmingham and Regional Neonatal Unit, Birmingham Maternity Hospital

SUMMARY Sixty seven of 216 infants weighing less than 2 kg at birth had cerebral lesions on ultrasonic scanning. Eight of 17 who had periventricular leukomalacia, with or without subependymal or intraventricular haemorrhage, or both, died. These and one larger baby were the subject of a combined ultrasound, and where appropriate, necropsy study. There was excellent correlation between the ultrasound and necropsy findings, only some of the earlier lesions of periventricular leukomalacia being missed by ultrasound. The data suggest it is now possible to distinguish periventricular leukomalacia and subependymal/intraventricular haemorrhage by ultrasound, that both lesions may be present in the same brain, that apparent parenchymal extension of an intraventricular haemorrhage is more probably the result of haemorrhage into ischaemic periventricular tissue, and that the term 'periventricular haemorrhage' should be abandoned since it confuses two lesions of differing aetiology and differing clinical importance. Future advances in neonatal brain ultrasound depend on accurate assessment of both the nature and site of lesions within the cerebral hemispheres and ventricular system since the interpretation of these parameters is of critical importance.

The periventricular regions of the brain of the preterm neonate are known to be particularly susceptible to circulatory disturbances. Two major groups of lesions are recognised, the subependymal haemorrhage (or germinal matrix haemorrhage) /intraventricular haemorrhage complex, simplistically related to hyperperfusion of the brain, and periventricular leukoencephalomalacia related to hypoperfusion.¹ There is growing evidence from follow up studies that the prognosis of the former disorder is good whereas it is frequently very poor with periventricular leukomalacia.²

The advent of techniques to show lesions of the neonatal brain during life has greatly extended knowledge about the genesis and natural history of these disorders but their exact inter-relation remains controversial.³ The relatively low resolution of early scanning instruments combined with ignorance of the natural history of the lesions prevented distinction between subependymal/intraventricular

haemorrhage and periventricular leukomalacia, the term periventricular haemorrhage being introduced to describe all echo dense lesions related to the walls of the lateral ventricles. Subsequent discussion of periventricular haemorrhage as a single entity has obscured the differences and associations between the lesions. In 1983 we described the ultrasound appearance of early periventricular leukomalacia before the cystic phase had developed.⁴ Other authors have confirmed our observations, though some stress the haemorrhagic nature of these lesions.^{5–7} Improved techniques now allow the distinction between these two groups of lesions, yet there are few combined ultrasonic and necropsy studies of either subependymal/intraventricular haemorrhage⁸ or periventricular leukomalacia.⁹

The present study endeavours to distinguish between these two major groups of lesions, particularly in the early phases of periventricular leukomalacia before cystic change has occurred, and to

correlate the ultrasonic findings with necropsy examinations of the brain. The results suggest that it is possible to divide the ultrasonic appearances into several categories, that is subependymal haemorrhage alone; subependymal haemorrhage and intraventricular haemorrhage; subependymal haemorrhage, intraventricular haemorrhage and periventricular leukomalacia; intraventricular haemorrhage and periventricular leukomalacia; and periventricular leukomalacia alone. In addition, it provides insight into the relation between the two groups of disorders and raises doubts about the concept of extension of subependymal/intraventricular haemorrhagic lesions into normal brain parenchyma.

Subjects and methods

A total of 216 infants—most babies weighing 2 kg or less and all weighing less than 1.5 kg—admitted to the regional neonatal unit at Birmingham Maternity Hospital were subject to ultrasound scanning as soon after birth as possible. In most this was undertaken on the first or second day of life, but in some outborn infants scanning was delayed till one or two days after admission to the neonatal unit. Thereafter, scans were performed three times a week for the first week and at least weekly until hospital discharge. A total of 67 heavier babies were scanned when clinically indicated, usually because of fits or abnormal movements.

The apparatus used was an ATL Mark III small wheel sector scanner with a 5 MHz transducer using the anterior fontanelle as an acoustic window. The babies were scanned in their incubators without disturbance, and a set of standard views was recorded at each examination, including anterior, middle, and posterior coronal sections and right and left parasagittal sections.

Eight infants with abnormal scans indicative of periventricular leukomalacia died. In these cases a necropsy was performed by DIR, who was unaware of the scan data when the brains were examined. Necropsies were performed in all babies dying with other abnormalities or with normal scans, the vast majority by DIR and the remainder by an experienced consultant perinatal pathologist. In all cases where periventricular leukomalacia, subependymal, or intraventricular haemorrhages had been identified on scan, lesions were subsequently confirmed at necropsy.

Results

Sixty seven of the 216 infants who weighed 2 kg or less at birth had abnormal scans (Table 1). Seventeen were found to have an ultrasound appearance

of periventricular leukomalacia with or without subependymal or intraventricular haemorrhages, or both. One further heavier baby was found to have periventricular leukomalacia on ultrasound. These 18 infants are the subject of this study. Ten are still alive (Table 2), most with major neurological defects.

Clinical data. Fifteen of the 18 babies had a birthweight of between 0.96 and 1.75 kg (mean 1.2 kg), and gestational age was 26 to 33 weeks (mean 29 weeks). Ten had birth asphyxia as evidenced by low Apgar scores or a low cord blood pH <7.25 with a base excess of -10, or both. Nine infants required mechanical ventilation. Three of these infants were ventilated from birth, two of whom had a clinical diagnosis of hyaline membrane disease; five required later ventilation for hyaline membrane disease; and one infant was ventilated for excessive lung fluid and hypercarbia.

Five infants were not asphyxiated at birth. Four subsequently required ventilation—two for hyaline membrane disease, one for lung fluid, and one outborn baby during transfer from an outlying unit.

Six of the nine infants who required ventilation for hyaline membrane disease developed air leaks—five had pneumothorax (56%), and one developed interstitial emphysema. The current incidence of pneumothorax associated with hyaline membrane disease in this hospital is 28%. Serious hypotension was observed in three infants. Convulsions occurred in seven of the 15 infants.

The three remaining infants had very different clinical histories. Case 9, a first twin weighing 0.77 kg, had normal ultrasound scans until age 61 days, two days after a profound hypotensive episode associated with fulminating necrotising enterocolitis

Table 1 *Classification of cerebral lesions in relation to birthweight in 67 low birthweight infants with abnormal ultrasound findings and one larger infant*

Classification	Birthweight <2 kg (range 560–1980 g, mean 1404 g) (n=216)	Birthweight >2 kg (range 2140–4250 g, mean 3045 g) (n=67)
SEH	34 (3)	
SEH PVL	2 (1)	
SEH IVH	16 (15)	
SEH IVH PVL	6 (4)	
IVH PVL	1	
IVH PVL	8 (3)	1 (case 8)
Total of abnormal ultrasound appearances excluding malformations	67 (26)	1

SEH=subependymal haemorrhage; IVH=intraventricular haemorrhage; PVL=periventricular leukomalacia.

Figures in brackets represent numbers that did not survive.

Table 2 Clinical details, ultrasound findings, and outcome in 18 infants with periventricular leukomalacia (PVL)

Case no (Figures)	Birth- weight (kg)	Echo dense phase of PVL			Cystic PVL Age at appearance (days)	Ventricular enlargement	Echo densities consistent with haemorrhage	Age at death (days)	Necropsy findings/neurological status
		Age at appearance (days)	Location/ adjacent to	Side					
1	0.90	4-7	Anterior horn Body of ventricle	Bilateral	11-14	Present	Bilateral SEH	26	Old R subependymal haemorrhage. Bilateral periventricular cysts R>L. Ischaemic neuronal change.
2 (1)	0.96	1-3	Anterior horn Body of ventricle	Bilateral	—	—	Bilateral SEH IVH	6	Oedematous friable brain. Bilateral IVH and PVL. Cerebellar softening R>L. Ischaemic neuronal change.
3 (6 a, b)	1.00	0-3	Anterior horn Body of ventricle	Bilateral	—	—	L SEH	5	L subependymal haemorrhage. R IVH. Disruptive haemorrhage. Bilateral haemorrhagic PVL.
4 (4 a, b)	1.04	—			0-14 Bilateral lesions	Present	Nil	42	Cerebral cortical softening R occipito-parietal and L motor regions. Bilateral cystic PVL. Basal ganglia gliosis
5 (5 a, b)	1.07	—			0-14 Bilateral lesions	Present	Nil	23	Bilateral PVL R>L. Cerebral oedema. Minor subarachnoid haemorrhage
6 (7 a, b, c)	1.34	0-2	Anterior horn Body of ventricle	Bilateral	—	—	R SEH bilateral IVH	4	Massive L PVL. Micro R PVL. Bilateral IVH. Post fossa haemorrhage. Pontine neuronal necrosis
7 (2, 3a, 3b)	1.45	1-4	Body of ventricle	R	—	—	Bilateral SEH IVH	3	Cerebral oedema. Massive R IVH with surrounding PVL. Sloughing of ventricular wall. L subependymal haemorrhage. Necrosis and feruginisation of neurones of basal ganglia. Microscopic PVL on L.
8	1.75	0-1	Anterior horn Body of ventricle	Bilateral	—	—	—	4	Gross cerebral oedema. Bilateral PVL. L IVH. Diffuse iron staining of leptomeninges.
9	0.77	61-63	Anterior horn Body of ventricle	Bilateral	67-74	Present	—	Alive	Global retardation. Spastic quadriplegia.
10	0.98	0-2	Posterior horn Body of ventricle	R	9-12	Present	R SEH IVH	Alive	Good at 2 years.
11	1.12	0-1	Anterior horn	R	9-13	Present	L Choroid plexus	Alive	Hydrocephalic with shunt. Mild spastic quadriplegia. R arm better than L. Developmental delay.
12	1.18	3-5	Anterior horn	R	10-20	—	R SEH	Alive	Normal at 18 months.
13	1.27	0-1	Anterior horn Body of ventricle	L	7-40	Present	—	Alive	R hemiplegia, possibly asymmetrical tetraplegia
14	1.34	0-2	Anterior horn Body of ventricle	Bilateral	8-10	Present	—	Alive	Spastic quadriplegia. Global retardation
15	1.52	0-3	Posterior horn Anterior horn Body of ventricle	L	6-9	Present	L SEH IVH	Alive	Right hemiplegia.
16	1.57	0-8	Temporal horn Anterior horn Body of ventricle	R	13-34	Present	—	Alive	Severe retardation and spasticity. Spastic quadriplegia.
17	1.85	61-67	Posterior horn Anterior horn Body of ventricle	Bilateral	67-80	Present	—	Alive	Spastic quadriplegia.
18	2.76	1-7	Anterior horn Body of ventricle	Bilateral	8-17	Present	—	Alive	Severe retardation and spasticity

R=right; L=left; SEH=subependymal haemorrhage; IVH=intraventricular haemorrhage.

which required jejunostomy and resection of gangrenous bowel. Case 17, also of low birthweight, had been discharged home from another hospital only to be readmitted because of convulsions. Several hours of hypoxia ensued. The baby was transferred to this neonatal intensive care unit and required ventilation before the convulsions were controlled with large doses of anticonvulsants. Case

18 was delivered by forceps after a prolonged period of fetal distress. He had multiple fits in the neonatal period.

Ultrasound findings. Sixteen of the 18 babies developed abnormal echo dense lesions in the periventricular white matter of the cerebral hemispheres. In 14 the lesions were discovered within 8

Fig. 1 Mid coronal section of the brain in case 2 showing large bilateral subependymal haemorrhages. Confluent with these are triangular dense lesions typical of periventricular leukomalacia.

On the right the dense area extends throughout the hemisphere sparing only the cortex and basal nuclei.

Fig. 2 Parasagittal slice of left cerebral hemisphere in case 7.

The ventricle contains a small quantity of free blood clot (in continuity with a massive intraventricular haemorrhage (R)). There is a subependymal haemorrhage and there are multiple early lesions of periventricular leukomalacia in the roof of the ventricle (arrowed).

Fig. 3 (a) Parasagittal section of the right cerebral hemisphere in case 7.

There is a very large subependymal haemorrhage in the floor of the ventricle, a mass of more diffuse echoes representing intraventricular blood clot and a dense mass (arrowed) extending from the ventricle upwards towards the cortex which represents periventricular leukomalacia.

(b) Parasagittal slice of right cerebral hemisphere of case 7.

The intraventricular haemorrhage has been removed to show sloughing of the lateral wall of the ventricle and massive haemorrhagic periventricular leukomalacia extending to immediately beneath the cerebral cortex.

days of birth (range 0 to 8 days, mean 2.1 days). The mean birthweight was 1.37 kg (range 0.9 kg to 2.76 kg). Two further infants (cases 9 and 17) developed echo dense lesions in the periventricular white matter between the 61st and 67th day of life. The lesions were bilateral in nine infants and unilateral in seven. Five of the unilateral lesions were right sided. The lesions were situated in the white matter adjacent to the anterior horns and bodies of the lateral ventricles. In two, the lesions were more extensive affecting the posterior and temporal horn regions (Fig. 1). The shape of the lesions was similar tending to be triangular on coronal section with the base to the cortex and the apex to the ventricle. The margin stops short of the cortex including the lateral sulcus and insula and varies in appearance ranging from a clear demarcation (Fig. 1) to a more diffuse pattern (Fig. 7a(L) below). These lesions occur at the site of the boundary zone between cortical and central blood supplies, that is the watershed zones in the periventricular white matter.

Nine infants had additional echo densities consistent with haemorrhage in the following sites: germinal matrix with no evidence of intraventricular haemorrhage in two, (Fig. 2), germinal matrix with intraventricular haemorrhage in six (Figs. 3(a) and 3b), and choroid plexus alone in one.

Eleven of the 16 infants who had the characteristic

echo dense lesions in the periventricular white matter went on to develop echo free areas (periventricular cysts) in sites corresponding to the original echo dense lesions (Figs. 4(a) and 4(b)). The mean time interval was 14 days from birth (range 6 to 40 days) in nine babies, within 20 days of the convulsions in one (case 17) and after 11 days of severe necrotising enterocolitis in one (case 9). One baby (case 1) died on day 26.

The remaining two infants in this series who had infrequent scans were found to have echo free areas in the periventricular region on the 14th day of life (Figs. 5(a) and 5(b)). These babies died at 42 and 43 days respectively. Five of the 16 infants who had characteristic echo dense lesions died aged 6 days or less while in the echo dense phase. Ten further babies with echo dense or cystic lesions are alive (Table 2).

Pathology. The pertinent pathological features of the eight deaths are detailed in Table 2. In all cases there was either complete or partial correlation between the findings on ultrasonic scanning and at necropsy. Where only partial agreement was shown there were explanations for the discrepancy as follows:

(a) Some lesions were in a very early stage of their

Fig. 4(a) Right periventricular cyst in case 4 seen in anterior coronal section.

(b) Coronal section case 4.

A well formed cyst with a smooth lining lying immediately above the roof of the dilated lateral ventricle on the right side.

Fig. 5(a) Posterior coronal section in case 5 showing extensive bilateral periventricular cysts with linear echoes which correspond to the septae seen in Fig. 5(b).

(b) Coronal section case 5 showing bilateral cystic periventricular leukomalacia (PVL).

The cysts are traversed by septae (visible on the scan). There is no evidence of haemorrhage on the left but there are focal bleeds into the PVL on the right. The space arrowed is artefact. The lateral ventricles are dilated.

Fig. 6(a) Mid coronal section of the brain in case 3 showing a left subependymal haemorrhage (SEH) and bilateral periventricular leukomalacia (PVL) lesions.

(b) Coronal section of left hemisphere case 3.

Haemorrhagic PVL (arrowed) is sited in the typical area of 'parenchymal extension' of an intraventricular haemorrhage. There is a small SEH. The ventricular wall is intact.

Fig. 7(a) Anterior coronal section in case 9 showing large bilateral subependymal haemorrhages (SEH).

The ventricle is completely obscured on the left but can be seen displaced upwards on the right. Bilateral periventricular leukomalacia (PVL) lesions are seen, typically triangular on the right whilst the lesion on the left is more extensive.

(b) Sagittal section of the left hemisphere in case 6 showing the large SEH, intraventricular haemorrhage (IVH), and PVL lesions forming an extensive composite and confluent echo dense area.

(c) Left cerebral hemisphere case 6.

There is the remnant of a large IVH visible in the midline. The hemisphere has ruptured on removal of the brain from the skull to show the lateral wall of the ventricle has sloughed to reveal underlying haemorrhagic PVL.

evolution. Thus early periventricular leukomalacia was not always detected (Fig. 2);

(b) Some lesions evolved or extended between the last scan and death (Figs. 2, 3(b));

(c) New lesions occurred between the last scan and death.

Haemorrhagic periventricular leukomalacia occurred either as a distinct lesion which was not in continuity with subependymal haemorrhage (Figs. 6(a) and 6(b)), or more typically as a combined lesion in association with massive intraventricular haemorrhage (Figs. 7(a), (b), and (c)). In the latter example the dual nature of the lesions of intraventricular haemorrhage and periventricular leukomalacia is clearly evident on the right side, and their separate nature was readily seen at necropsy (Fig. 7(c)). On the left side (Figs. 7(a) and (b)) the echo is less well defined due to the larger intraventricular haemorrhage which has filled the ventricle distorting the basal ganglia and displacing the original subependymal haemorrhage downwards. The lateral margin of the haemorrhage merges with the surrounding periventricular leukomalacia, which is identified by its site. The lateral border between the echo density and the cortex is ill defined.

Discussion

The advent of ultrasonic scanning has greatly increased our understanding of the nature and evolution of lesions of the neonatal brain, not least in emphasising the very high incidence of pathology in babies weighing less than 1.5 kg at birth.³ The recognition of this abundance of pathology has led to a need for the identification of early lesions for both therapeutic and prognostic reasons. The limits, however, of ultrasonic resolution are uncertain, though it is known that some areas of the brain are beyond the reach of the scanner and lesions of less than 3 mm diameter are unlikely to be recognised.⁸ It is therefore essential for comparative studies to be made whenever both ultrasonic and necropsy data are available.

The pathological distinction between uncomplicated subependymal/intraventricular haemorrhage^{9 10} and periventricular leukomalacia¹¹ is usually clear, though the latter may also be haemorrhagic. Periventricular leukomalacia is generally considered to be a form of hypoxic-ischaemic encephalopathy peculiar to the neonate, the anatomical distribution of the lesions coinciding with the junctional zone between the ventriculopetal and ventriculofugal components of the arterial circulation within the cerebral hemispheres.¹ The end stage of periventricular leukomalacia is either focal gliosis with or

without calcification, when the initial lesions are small, or periventricular cysts when they are more extensive.

Subependymal/intraventricular haemorrhage is attributable to the vulnerability of the germinal matrix to haemorrhage, consisting as it does of masses of neuroblasts traversed by poorly supported very thin walled vascular channels which, if engorged, are particularly likely to rupture leading initially to local and then to intraventricular haemorrhage. It may be assumed that this pattern of evolution is determined, at least in part, by the relative resistance of the surrounding structures to extension of the haemorrhage, a factor of considerable importance when the origin of the so called disruptive parenchymal extensions of intraventricular haemorrhage is examined.

While haemorrhage and cysts are readily visualised by ultrasound, it is as yet uncertain at which stage in the evolution of periventricular leukomalacia echo densities are first seen. Pathologically hypoxia-ischaemia of the periventricular white matter leads to cellular swelling, oedema, necrosis, and liquefaction.¹² Secondary haemorrhage may occur into necrotic tissue,¹³ probably as a reflow phenomenon. Ultrasonically, the periventricular leukomalacia lesion in the early phase has a characteristic triangular shape in coronal section and is situated lateral and superior to the ventricle. More extensive lesions may affect the whole hemisphere, sparing only the cortex and thalamic nuclei. The echo density of the lesions may gradually decrease on the lateral margins as the cortex is approached, producing a blurred edge. This reflects both the irregularity of the extent of the infarction, which is clearly seen at necropsy (Figs. 1 and 3(b)), as well as the variability in the evolution of the lesion, the most advanced pathology being nearer the midline. In sagittal sections the lesions lie lateral and superior to the ventricle, and though irregular, follow the outline of the ventricle.

It is likely that liquefaction and haemorrhage will produce similar appearances on scan and that not all periventricular leukomalacia identified in the precystic stage by ultrasound is necessarily haemorrhagic.^{5 6 9} In 1983 we described the ultrasound appearance of periventricular leukomalacia.⁴ Our observations have been confirmed by the combined ultrasound and necropsy study of Nwaesei *et al.*,⁹ these authors reporting examples of non-haemorrhagic infarction detected by ultrasound. They emphasise that haemorrhage is not a prerequisite for the detection of infarction by ultrasound, a finding supported by the present study (Fig. 5(b)). When considered in the knowledge of the different anatomical distribution of subependymal/intra-

ventricular haemorrhage and periventricular leukomalacia,⁶ the clinical value of periventricular haemorrhage as a descriptive term must be questioned since both liquefactive and haemorrhagic lesions will be included in the spectrum. Indeed, we would suggest that periventricular haemorrhage has outlived its usefulness in that it confuses not only aetiological discussion but also the categorisation of patients included in trials of various therapeutic regimens.

The present study confirms the high incidence of brain lesions in small babies (31% in those with a birthweight under 2 kg). Periventricular leukomalacia was detected in a quarter of the abnormal scans and confirmed at necropsy in all deaths. In half of these cases both periventricular leukomalacia and subependymal/intraventricular haemorrhagic lesions occurred in the same brain. Furthermore, while the most extensive acute or early periventricular leukomalacia was found in association with intraventricular haemorrhage it did occur with subependymal haemorrhage and in isolation, suggesting that concurrence of the lesions is not necessarily an indication of a direct relation between them. A major sequelae, however, of a large intraventricular haemorrhage must be hypotension, and therefore hypoperfusion and ischaemia of the periventricular white matter. The substantial loss of blood may also result in disturbance of the coagulation status of the neonate. On correction of the hypotension, haemorrhagic periventricular leukomalacia and necrosis of the ventricular wall may ensue. This may then be interpreted erroneously as an extension of the intraventricular haemorrhage from the ventricular lumen rather than sloughing of the ventricular wall secondary to ischaemia.

It has been suggested^{14, 15} that direct parenchymal extension of intraventricular haemorrhage may not occur, and that destruction of the cerebral substance may be the result of bleeding into a primary ischaemic lesion. Our own data and those of Nwaesei *et al*⁹ support this opinion in showing that non-haemorrhagic and haemorrhagic periventricular leukomalacia occur at the characteristic site of apparent parenchymal extension of intraventricular haemorrhage (above and lateral to the roof of the lateral ventricles) in some infants who do not have intraventricular haemorrhage (Fig. 6(b)). We would further suggest that the physical structure of the brain, the differing but consistent anatomical sites of the two major forms of pathology, and the ultrasonic evolution and echo dense characteristics of the two lesions are inconsistent with either direct extension of subependymal haemorrhage or disruption of the ventricular wall by an intraventricular haemorrhage in the presence of an otherwise normal

cerebral hemisphere. Equally in the more mature infant, in whom the germinal matrix has involuted,^{6, 8} it is possible that parenchymal haemorrhages in areas of periventricular leukomalacia may rupture into the ventricles providing an explanation for intraventricular haemorrhage in these babies. The basic pathology underlying the seeming rather than real extension of intraventricular haemorrhage into the cerebral hemispheres is, in our opinion, ischaemic necrosis of the underlying cerebrum, be it haemorrhagic or non-haemorrhagic. Furthermore, echo dense lesions in the anatomical watershed zones of the periventricular white matter, notably on the superolateral aspects of the lateral ventricles, are, in our opinion, indicative of periventricular leukomalacia whether they occur in isolation or in the presence of subependymal/intraventricular haemorrhage.

Perusal of published ultrasonic scans would suggest that periventricular leukomalacia has gone unrecognised in the past, particularly where it has occurred concurrently with intraventricular haemorrhage. This has almost certainly been compounded by the failure of pathologists to recognise periventricular leukomalacia at necropsy. This is particularly likely to occur if the unfixed neonatal brain is sliced immediately on removal from the skull. The finding of an intraventricular haemorrhage is often considered to be the end point of the morphological investigation and any disruption or softening of the adjacent brain is taken to be an integral part of the subependymal/intraventricular haemorrhage complex.

In conclusion, we suggest that the well established pathological distinction between subependymal/intraventricular haemorrhage and periventricular leukomalacia has been blurred by the introduction of the term periventricular haemorrhage and that the latter should now be dropped. Ultrasonic techniques allow the distinction between these lesions, and since their prognosis differs considerably every attempt should be made to separate them during life. We therefore advocate that the ultrasonic classification of these lesions should follow the scheme used in Table 1. Such an approach is not only of critical importance in the counselling of parents but is also of crucial importance in the assessment of any treatment introduced to improve the outcome in either category.

We thank the medical and nursing staff of the Regional Neonatal Unit for their care and cooperation in managing these small infants, Mr T Stevens for photographic assistance, and Miss G Hayes for secretarial help.

References

- ¹ Pape KE, Wigglesworth JS. *Haemorrhage, ischaemia and the perinatal brain*. (Clinics in Developmental Medicine Nos 69/70.) London: Heinemann and Spastics International Medical Publications, 1979.
- ² Levene MI, Dubowitz LMS, de Gispigny, LCh. Classifying intraventricular haemorrhage. *Lancet* 1983;ii:49.
- ³ Anonymous. Ischaemia and haemorrhage in the premature brain. [Editorial]. *Lancet* 1984;ii:847-8.
- ⁴ Preston PR, Rushton DI, Durbin GM. Ultrasound periventricular echo densities in neonatal brains. *Lancet* 1983;ii:459.
- ⁵ Hill A, Nelson GL, Clark HB, Volpe JJ. Haemorrhagic periventricular leukomalacia. Diagnosis by real-time ultrasound and correlation with autopsy findings. *Pediatrics* 1982;69:282-4.
- ⁶ Levene MI, Wigglesworth JS, Dubowitz V. Haemorrhagic periventricular leukomalacia in the neonate. A real time ultrasound study. *Pediatrics* 1983;71:794-7.
- ⁷ Dolfin T, Skidmore MB, Fong KW, Hoskins EH, Shannan AT, Hill A. Diagnosis and evolution of periventricular leukomalacia. A study with real time ultrasound. *Early Hum Dev* 1984;9: 105-9.
- ⁸ Szymonowicz, W, Schaffler K, Cussen LJ, Yu VYH. Ultrasound and necropsy study of periventricular haemorrhage in preterm infants. *Arch Dis Child* 1984;59:637-42.
- ⁹ Nwaesei CG, Pape KE, Martin DI, Becker LE, Fitz CR. Periventricular infarction diagnosed by ultrasound. A post mortem correlation. *J Pediatr* 1984;105:106-10.
- ¹⁰ Hambleton G, Wigglesworth JS. Origin of intraventricular haemorrhage in the preterm infant. *Arch Dis Child* 1976;51:651-9.
- ¹¹ Banker BQ, Larroche J-L. Periventricular leukomalacia of infancy. A form of neonatal anoxic encephalopathy. *Arch Neurol* 1962;7:386-410.
- ¹² Dereuck J, Chattha AS, Richardson EP. Pathogenesis and evolution of periventricular leukomalacia in infancy. *Arch Neurol* 1972;27:229-36.
- ¹³ Armstrong D, Norman MG. Periventricular leukomalacia in neonates. *Arch Dis Child* 1974;49:367-75.
- ¹⁴ Flodmark O, Becker LE, Harwood-Nash DC, Fitzhardinge PM, Fitz CR, Chuang SH. Correlation between computed tomography and autopsy in premature and full-term neonates that have suffered perinatal asphyxia. *Radiology* 1980;137:93-103.
- ¹⁵ Volpe JJ, Herscovitch P, Perlman JM, Raichle ME. Positron emission tomography in the newborn. Extensive impairment of regional cerebral blood flow with intraventricular haemorrhage and haemorrhagic intracerebral involvement. *Pediatrics* 1983; 72:589-601.

Correspondence to Dr D I Rushton, Birmingham Maternity Hospital, Queen Elizabeth Medical Centre, Birmingham B15 2TG.

Received 24 April 1985

Commentary

MALCOLM LEVENE

Leicester University Medical School

In the past two or three years a profound change has occurred in the understanding of intraventricular haemor-

rhage. It is now generally accepted that ischaemic periventricular lesions can be recognised in life and distinguished as separate from intraventricular haemorrhage, although they both may occur in the same brain. Rushton *et al* have provided further evidence for this and also stress that ischaemic lesions may occur well beyond the neonatal period in infants who develop surgical complications or severe seizures. They also confirm the poor prognosis as only two of their 10 infants surviving periventricular leucomalacia were normal at follow up.

The fundamental differences in aetiology between the popular notion of hyperperfusion leading to intraventricular haemorrhage and hypoperfusion causing periventricular leukomalacia makes it necessary to rethink our attitudes towards the prevention of the former. Uncomplicated subependymal haemorrhage may indeed prove to be a useful marker for those brains that have been well perfused and are at lower risk of subsequent neurodevelopmental handicap. Rushton and his colleagues have, however, extended their speculation well beyond accepted facts when they suggest that all parenchymal 'haemorrhage' in the preterm (and perhaps mature) brain is ischaemic in origin. The evidence for this is lacking but it is also true that evidence for direct parenchymal extension after intraventricular haemorrhage is equally poor. A mass of blood clot found at necropsy in the soft brain of a long dying infant makes elucidation of the precise pathophysiological process almost impossible. An ischaemic rim to the haemorrhagic lesion may be either primary or secondary. An *in vivo* study using positron emission tomography¹ showed extensive ischaemia in the hemisphere in which parenchymal haemorrhage had occurred but was not done early enough to determine the primary event.

How then can this fundamental question of ischaemia versus haemorrhage be answered? It is unlikely that either position emission tomography or nuclear magnetic resonance spectroscopy² can be used early or frequently enough to recognise the primary process. A portable and non-invasive technique is required to investigate cerebral haemodynamics prospectively from birth. At present Doppler ultrasound is the most promising tool. Modern combined real time and pulsed Doppler machines offer both safety and convenience. Further advances in our understanding of this important question may come from this direction.

References

- ¹ Volpe JJ, Herscovitch P, Perlman JM, Raichle ME. Positron emission tomography in the newborn. Extensive impairment of regional cerebral blood flow with intraventricular hemorrhage and hemorrhagic intracerebral involvement. *Pediatrics* 1983; 72:589-601.
- ² Hope PL, Costello AM, Cady EB, *et al*. Cerebral energy metabolism studied with phosphorous NMR spectroscopy in normal and birth asphyxiated infants. *Lancet* 1984;ii:366-9.