

Original articles

Timing and evolution of periventricular haemorrhage in infants weighing 1250 g or less at birth

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SUMMARY The brains of 50 consecutively admitted infants who weighed 1250 g or less at birth were examined with real time ultrasound. Of 30 (60%) who had periventricular haemorrhage (PVH), 19 (63%) bled on the first day and 17 (57%) showed extension of the initial haemorrhage on serial scans. The median age was 16 hours when PVH was first detected and 48 hours when PVH reached its maximum extent. Ventricular size at birth correlated with gestation. Progressive ventricular growth was seen after birth in infants both with and without PVH. Charts of normal ranges of ventricular size and head circumference were drawn up from birth to 10 weeks of age. All infants with PVH showed a transient increase in ventricular size at 2 weeks of age but most returned to normal by 6 weeks of age. Ventricular dilatation after PVH that was greater than the 95th centile for this population developed in 5 (31%) of 16 survivors, four of whom subsequently developed hydrocephalus, although none required ventriculo peritoneal shunting. The optimal timing for diagnosis with ultrasound is at the end of the first week for PVH and the second to third week for ventricular dilatation.

Although extreme prematurity has been identified as one of the most important antecedents of periventricular haemorrhage (PVH),^{1 2} no infant below 26 weeks' gestation³⁻⁶ and very few infants weighing 1000 g or less at birth have been included in previously published studies.^{7 8} Recent ultrasound studies showed that 60-70% of infants weighing 1000 g or less at birth had PVH, an incidence that is almost twice that reported in larger preterm infants.^{1 9 10} If PVH is to be prevented in this extremely preterm group the timing of its onset must be defined before antecedent factors can be evaluated. The purpose of this report is to describe the timing of onset and extension of PVH in a group of infants who weighed 1250 g or less at birth. No reports on normal ventricular size or the natural history of ventricular dilatation have been published for this weight group as all previous studies were in populations that included predominantly larger preterm infants.^{6 10-13} Data on early postnatal head growth are only available from 28-32 weeks' gestation.¹⁴⁻¹⁶ We therefore investigated longitudinal ventricular and head growth in those with and without PVH as well as the incidence and outcome of ventricular dilatation after PVH in our study group.

Patients and methods

During the 8 month study period 59 infants with a birthweight of 1250 g or less were admitted to this medical centre. Of these, 9 were excluded from the cerebral ultrasound study. Three excluded infants had multiple congenital anomalies: one had Potter's syndrome and left diaphragmatic hernia, one had tracheoesophageal fistula and cleft lip and palate, and one had hypoplastic lungs and adrenal hypoplasia. The other 6 excluded infants died shortly after birth, before scanning, at a mean age of 90 (range 15-195) minutes. Eight of the 9 excluded infants underwent full necropsy examination, which showed that five infants had had no PVH and one infant each had had germinal layer haemorrhage, intraventricular haemorrhage, and intracerebral haemorrhage.

The remaining infants weighing 1250 g or less were scanned at least daily for the first four days after birth and weekly thereafter until discharge or death. The mean age at the time of the first scan was 10 hours. All the infants who had PVH were scanned before 12 hours of age except two not born in this hospital but transferred later. All those in the group showing haemorrhage were actually scanned

every 12 hours until 72 hours of age except two who were scanned every 12 hours only until 48 hours of age.

Every week all surviving infants had their head circumferences measured and underwent ultrasound scans. This was done to follow the evolution of PVH and to monitor ventricular size in those with and without PVH. A Toshiba SAL 120 real time linear array scanner was used with a 5 MHz transducer, and the images were recorded on Polaroid film. Each scan was done in coronal and saggital planes through the anterior fontanelle and in axial and coronal planes through the temporoparietal bone. Ventricular size was assessed according to previously published methods.^{7 11 17 18} Scanning was carried out in the axial plane through the skull and in a coronal plane through the fontanelle. Calipers were used to measure the distance between the echo from the falx to the wall of the lateral ventricle. As this is not a true measurement of the size of the ventricle this distance was referred to as the ventricular index.^{7 11} In addition, the maximum width of the lateral ventricle at the level of the foramen of Munro was also measured with calipers.^{17 18} PVH was diagnosed when increased echoes consistently appeared at the same location in all planes. A study of diagnostic correlation at necropsy previously reported by us showed 90% accuracy in the diagnosis of PVH,¹⁹ similar to the previous experience of one of us (WS).²⁰ The limit of resolution of ultrasound image of PVH was 3 mm.

Results

The birthweight of the 50 infants was mean (SD), 888 (204) g, (range 430–1250 g) and their gestational age was mean (SD), 27 (4) weeks, (range 24–32 weeks). Table 1 shows selected perinatal data. The

Table 1 *Selected perinatal data*

	No (%)
Antenatal haemorrhage	11 (22)
Membranes ruptured before 24 hours of age	16 (32)
Born at this hospital	46 (92)
Apgar score <6 at 5 minutes	13 (26)
Type of delivery:	
Caesarean section	18 (36)
Vaginal vertex	21 (42)
Vaginal breech	11 (22)
Assisted ventilation	38 (76)
Hyaline membrane disease	31 (62)
Recurrent apnoea	27 (54)
Pneumonia	19 (38)
Patent ductus arteriosus	19 (38)
Seizures	14 (28)
Pneumothorax	9 (18)
Pulmonary hypertension	10 (20)
Pulmonary haemorrhage	9 (18)

overall incidence of PVH was 60%: germinal layer haemorrhage alone developed in 6 (20%) of those with PVH, intraventricular haemorrhage with or without germinal layer haemorrhage in 16 (53%), and intracerebral haemorrhage with or without either germinal layer or intraventricular haemorrhage in 8 (27%). Fig. 1 shows the distribution of haemorrhage with respect to gestation. Seventeen (81%) of 21 infants of 26 weeks or less gestation had PVH compared with 13 (45%) of 29 infants of more than 26 weeks ($P<0.005$). Ten (77%) of 13 infants weighing 750 g or less at birth had PVH compared with 13 (62%) of 21 infants weighing 751–1000 g and 7 (44%) of 16 infants weighing 1001–1250 g at birth ($P<0.05$).

Eighteen (90%) of 20 infants without PVH survived compared with 16 (53%) of 30 infants with PVH ($P<0.02$). None of the infants with PVH had treatment withdrawn because of ultrasound findings. The nursery survival rate also decreased with increasing severity of haemorrhage: all 6 infants with germinal layer haemorrhage, 9 (56%) of 16 with intraventricular haemorrhage with or without germinal layer haemorrhage, and one (13%) of 8 with intracerebral haemorrhage with or without either germinal layer or intraventricular haemorrhage survived ($P<0.01$).

In 19 (63%) of the 30 infants with PVH, haemorrhage developed within 24 hours. Of the 28 infants with PVH who underwent scanning before 12 hours of age, 15 (57%) had already developed haemorrhage. The median age when PVH was first detected was 16 hours (range a half to 48 hours). The median age when the haemorrhage was at a maximum was 48 hours (range 7–288 hours). No germinal layer haemorrhage or intraventricular

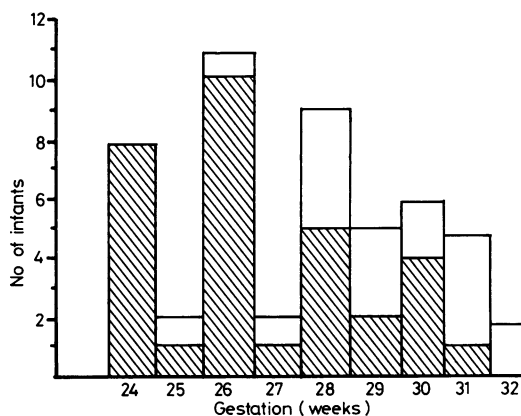


Fig. 1 *The distribution of PVH with respect to gestation. The shaded area indicates infants with PVH.*

haemorrhage developed after 96 hours of age and all but one intracerebral haemorrhage had developed by this age (Table 2). Extension of haemorrhage was noted in 17 (57%) infants with PVH (Table 3). Gestation was mean (SD), 25.7 (1.5) weeks in the 17 infants with progression of PVH compared with 28.0 (2.1) weeks in the 13 infants who did not show progression of PVH ($P < 0.05$). When germinal layer haemorrhage developed early (median 12 hours) progression of haemorrhage was likely but when it developed late (median 42 hours) this was unlikely. Intracerebral haemorrhage was always diagnosed after an intraventricular haemorrhage had developed and itself developed at a median age of 40 hours (range 8–288 hours).

Longitudinal data for head circumference and ventricular measurements for the first 10 weeks of life were derived from 30 nursery survivors who were of appropriate weight for gestational age (AGA). Data from the four small for gestational age (SGA) survivors were excluded from the analysis. All infants both with and without PVH were included in the data for head circumference growth as the differences in the two groups were not significant. After an initial shrinkage of head size during the first week, the mean growth rate of head circumference was 0.75 cm/week once birthweight was regained (Fig. 2).

The ventricular index at birth correlated linearly

Table 2 Age at development of germinal layer haemorrhage (GLH), intraventricular haemorrhage (IVH), and intracerebral haemorrhage (ICH)

Postnatal age (hours)	No (%) infants		
	GLH (n=27)	IVH (n=24)	ICH (n=8)
	No (%)	No (%)	No (%)
By 24	15 (56)	10 (42)	2 (25)
By 48	26 (96)	19 (79)	5 (63)
By 72	26 (96)	20 (83)	6 (75)
By 96	27 (100)	24 (100)	7 (88)

Table 3 Progression of PVH

Type of haemorrhage	% of infants (n=30)	Median age at diagnosis (hours)	
		Initial haemorrhage	Extension of haemorrhage
Progression of PVH			
GLH to IVH	9 (30)	16	55
IVH±GLH to ICH	6 (20)	19	58
GLH to IVH to ICH	2 (7)	6	62, 162*
No progress of PVH			
GLH	6 (20)	31	
IVH±GLH	7 (23)	16	

*GLH → IVH, median 62 hours; IVH → ICH, median 162 hours.

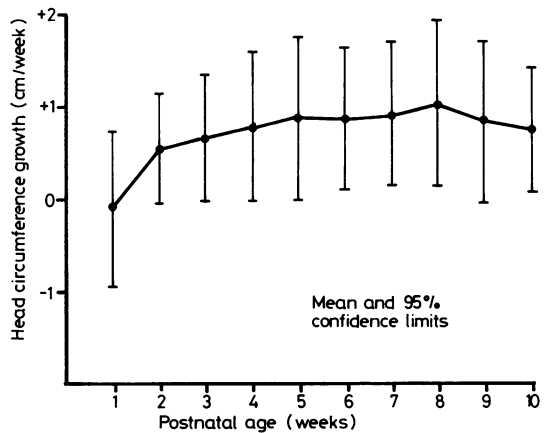


Fig. 2 Growth rate of head circumference.

with gestation from 24–31 weeks (Fig. 3). The 14 AGA survivors with PVH and the 16 AGA survivors without PVH all showed progressive growth of ventricles after birth (Fig. 4). In the group with PVH there was a transient increase in ventricular index at 2–3 weeks of age. The increase was seen as early as 6 days and as late as 22 days after haemorrhage. The mean ventricular index for the group with PVH returned to normal by 6 weeks of age. Although all

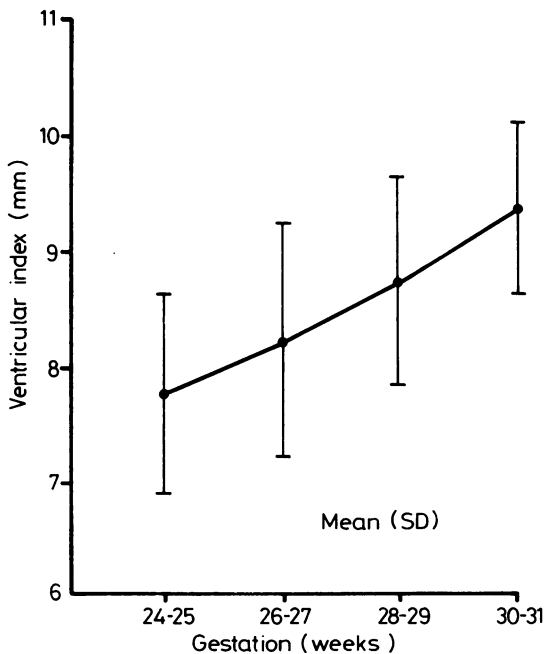


Fig. 3 Mean (SD) ventricular index on day of birth.

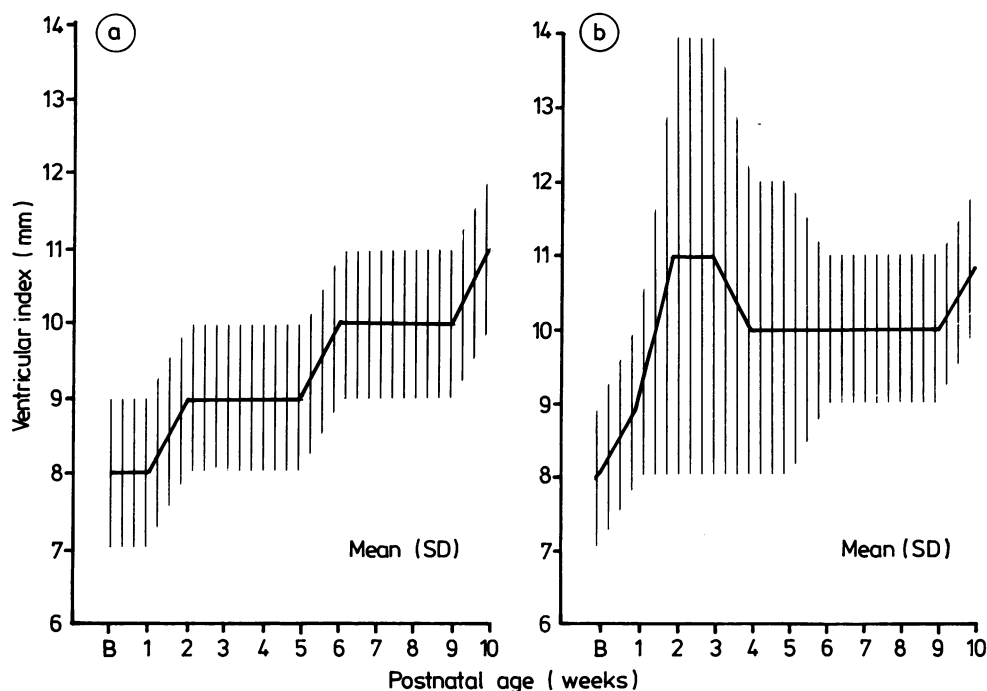


Fig. 4 Postnatal ventricular growth in infants with no PVH (a) and those with PVH (b). The single line represents the mean and the shaded area the standard deviation.

infants showed a progressive increase in ventricular index postnatally, especially during the first three weeks, for those in the group with PVH, ventricular dilatation, defined as a ventricular index greater than the 95th centile for the group without PVH, developed in only 5 (31%) of 16 survivors with PVH.

Measurement of the width of the lateral ventricle as an alternative method of assessing ventricular size also gave similar results.^{17,18} The normal range was 1–4 mm during the first four weeks of life and 1–5 mm during the next 6 weeks. In the group with PVH there was a maximal increase at 2–3 weeks of age with a gradual return to the normal range at 7 weeks of age. Ventricular dilatation, again defined as ventricular size greater than the 95th centile for the group without PVH, developed in five (31%) of 16 survivors with PVH based on this method.

Hydrocephalus was defined as when both ventricular index and head circumference growth were greater than the 95th centile. Four of the five survivors of PVH with ventricular dilatation developed hydrocephalus, which arrested spontaneously in one infant and after treatment with serial cerebrospinal taps in three infants. Hyd-

rocephalus was also noted in one of the nursery deaths. Two (11%) of the 18 survivors without PVH had ventricular dilatation. Both were small for their gestational age. They were considered to have cerebral atrophy as their head growth continued at the lower limit of normal. Neither infant showed evidence of PVH at any time and one had a porencephalic cyst.

Discussion

Two previous studies using real time ultrasound scanning reported a similar incidence of PVH in infants weighing 1250 g or less and in the 250 g subgroups.^{1,10} These reports differ in that there were fewer infants weighing 1250 g or less and 58% and 100% respectively of their study populations were born elsewhere compared with only 8% in this series. One other study used computed tomography to scan brains of infants weighing 1250 g or less, 45% of whom were born elsewhere, and reported a low incidence of 32%.²¹ Seventeen (81%) of 21 infants of 26 weeks or less gestation had PVH in the present series. The incidence of PVH in infants with this very short gestation has not been reported

except in one study, which described a 93% incidence of PVH in 15 infants of 26 weeks or less gestation.¹

The different grades of PVH in the present series were compared with those previously reported in study populations that included larger preterm infants (Table 4). The higher overall incidence in the present study group seemed to be accounted for by a higher percentage of infants with intracerebral haemorrhage. The populations of previous studies differed considerably in that two did not include infants below 26 weeks' gestation,^{3 5} one included very few infants weighing 1000 g or less,⁸ and two included infants weighing up to 2500 g.^{1 13} All infants in this series with germinal layer haemorrhage only survived; this type of haemorrhage is associated with a good long term prognosis.²² Seven, however, of the 8 infants with intracerebral haemorrhage died, contributing appreciably to the high mortality of infants weighing 1250 g or less with PVH.

Haemorrhage developed within 24 hours in 63% of infants with PVH in this study compared with 40–74% previously reported in larger infants.^{1 8 10} The median age at which PVH was first detected was 16 hours compared with the second day as described in one study.¹ It was reported that the haemorrhage usually progressed.^{1 23} Extension of the initial haemorrhage developed in 43% of infants in one study compared with 57% in the present series.¹⁰ The results from these three studies contrast with one that found only 6% of haemorrhages progressed.⁸ The fact that 30% of the study population were over 1500 g in that study may account for the difference in their findings. The rate of progression was comparatively more rapid in the present series as the median age when the haemorrhage reached its maximum extent was 48 hours compared with the fourth day in a previous study.¹ All but one of the 17 haemorrhages that extended had de-

veloped by 96 hours of age compared to 6 of 16 reported in another study.¹⁰

Previous studies have shown that the incidence of ventricular dilatation after PVH in survivors ranged from 30–100%.^{2 5 9 10 12 13} The reason for these observed differences is that the diagnosis of ventricular dilatation in all these studies was qualitative and subjective. To assess the true incidence of ventricular dilatation, enlargement beyond a normal range must be known. Based on a cross sectional centile chart of ventricular size in infants without PVH over the gestational age of 26–42 weeks,¹¹ 39% of survivors of PVH were found to have ventricular dilatation that exceeded two SD.⁶ Their study population included all neonatal admissions irrespective of birthweight or gestation. None was below 26 weeks' gestation. All their 6 infants between 26 and 28 weeks' gestation when scanned serially showed ventricular dilatation. In the present study we measured postnatal ventricular growth using the ventricular index similar to the above study. The merits of this method compared with others have previously been reviewed.¹¹ We determined the range of ventricular index and ventricular width in infants weighing 1250 g or less without PVH for the first 10 weeks of life, thus allowing those infants with a ventricular size greater than the 95th centile to be identified. On this basis 31% of surviving infants with PVH and in the same weight group were recognised to have excessive ventricular dilatation even if head growth was initially not abnormal.

It is traditionally taught that hydrocephalus should be suspected when serial head circumference measurements show a rate of head growth that deviates from the normal intrauterine growth curves in association with bulging fontanelle and widened sutures. Growth data, however, available for seriously ill infants from 28–32 weeks' gestation showed that there is considerable growth retardation in the first weeks after birth, even with satisfactory nutrition.^{14–16} Infants who later developed hydrocephalus were found to follow the fetal growth curve.¹⁶ Data on rate of growth of head circumference in our series of infants weighing 1250 g or less are therefore essential to identify those who had excessive head growth. Fig. 2 shows that this roughly corresponded to an increase in head circumference of more than 2 cm/week in the first 10 weeks after birth, which is the risk period for the development of hydrocephalus.²⁴ We also found a shrinkage of head size during the first week similar to that reported in infants weighing 2000 g or less,²⁵ but no reduction in ventricular size was apparent, though this has been reported.¹¹

The incidence of hydrocephalus in studies that

Table 4 Incidence of PVH in previous series of infants. Individual study populations used as denominators for percentages

Study population	PVH No (%)	GLH No (%)	IVH ±GLH No (%)	ICH ±IVH/GLH No (%)
≤1250 g	30 (60)	7 (14)	15 (30)	8 (16)
<1500 g ³	20 (43)	3 (7)	14 (30)	3 (7)
<1500 g ⁵	20 (51)	5 (13)	12 (31)	3 (8)
<1500 g ¹⁰	35 (55)	14 (22)	6 (9)	15 (23)
≤1500 g ²	35 (55)	6 (9)	19 (30)	10 (16)
≤1500 g ⁹	46 (46)	20 (20)	24 (24)	2 (2)
<33 weeks ¹	36 (38)	11 (12)	21 (22)	4 (4)
<33 weeks ¹³	94 (35)	21 (8)	61 (23)	12 (4)
'High risk' ⁸	47 (27)	15 (10)	25 (17)	7 (5)

included larger preterm or term infants varied from 8–30% of survivors with PVH.^{2 5 9–13} The diagnosis of hydrocephalus was based on qualitative assessment of 'progressive' ventricular dilatation in most of these reports. Ventricular dilatation may progress in the absence of symptoms,²⁴ but it has been shown that intracranial pressure is normal in ventricular dilatation and does not begin to rise until one or two days before a rapid increase in head circumference.¹² It is unknown at present whether the ventricular dilatation itself is harmful. Three of the four infants with excessive ventricular dilatation and excessive head growth as defined above showed symptoms of increased intracranial pressure and required serial cerebrospinal taps. Although this procedure, instituted prophylactically from the onset of PVH, has been shown in a controlled trial not to be effective in preventing the development of hydrocephalus,²⁶ it is useful as a treatment for hydrocephalus.²⁷ It allows time for arrest of ventricular dilatation, which often develops naturally,²⁴ and avoids the need for ventriculoperitoneal shunting while extremely preterm infants are still sick.

Based on the data from this study, an ultrasound scan performed at the end of the first week will diagnose the presence and maximum extent of PVH, and a repeat scan at 2–3 weeks of age will show maximal ventricular dilatation. Serial scans if necessary will monitor the infants with dilated ventricles until the condition resolves or is stabilised. In addition, cerebral ultrasound scanning provides a way of assessing the effectiveness of medical and surgical treatments.

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