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Peri/intraventricular haemorrhage: a cranial ultrasound study on 5286 neonates

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Abstract

Objective: We launched a prospective cranial ultrasound study at the Department of Obstetrics and Gynaecology of the University of Giessen. In this study we examined the incidence and severity of brain damage in neonates and related them to various obstetrical risk factors. *Study design:* More than 90% of all neonates born between 1984 and 1988 were included in the study (n=5286) and were screened by ultrasound for cerebral abnormalities on 5–8 days post-partum. The relation between the incidence of peri/intraventricular haemorrhages (PIVH) and obstetrical risk factors were analyzed by contingency tables. *Results:* The most frequent abnormality was PIVH (3.6%) of various degrees (grade I–III). Periventricular leucomalacia, porencephalia, subarachnoidal haemorrhages, and hydrocephali were rare (≤0.2%). The incidence of PIVH increased progressively with decreasing gestational age, e.g. from 1.6% at 38–43 weeks up to 50.0% at 24–30 weeks of gestation. A large percentage of babies with PIVH were clinically normal. In immature neonates there was a close inverse relationship between Apgar score at 1, 5 and 10 min and both incidence and severity of PIVH. This was in contrast to findings in mature neonates where a marked increase in the incidence of PIVH was found only with Apgar scores as low as 0–4 points. The relation between the incidence of PIVH and both cardiotocography and arterial cord blood pH was poor, independent of the gestational age. The incidence of PIVH was increased in growth retarded fetuses (pH≤7.29), premature rupture of membranes, fever sub partu and gestosis. It is interesting to note that in mature fetuses there was no difference in the incidence of PIVH between vaginally delivered (0.8%) and sectioned breech presentations (2.1%). In preterms at 35–37 weeks with prolonged labour and secondary cesarean section, the incidence of PIVH was very high (11.2%). *Conclusion:* From the present study we conclude that the incidence of PIVH especially in immature neonates is highly associated with low Apgar scores at birth. Since the Apgar score reflects the clinical condition and the degree of circulatory centralisation of neonates that is influenced by various ante- and intranatal risk factors, a protective obstetrical management is necessary to reduce the incidence of PIVH in neonates.

Keywords: Cranial ultrasound; Peri/intraventricular haemorrhage; Preterm neonates; Term neonates; Apgar score; Umbilical blood pH; Cardiotocogram

1. Introduction

The successful reduction of perinatal mortality almost to the optimal attainable level has meant that mortality has become less significant as a measure of the quality of obstetric care (Perinatal Statistics-Hessen, 1989). Instead infant morbidity, i.e. degree of asphyxia during birth, clinical condition post-partum, brain damage as well as neurological and mental development throughout childhood and adolescence must be taken into closer consideration when assessing standards of perinatal management.

Even with expert analysis of the cardiotocogram, acid-base status and clinical condition of the infant post-partum, the probability of cerebral damage is still very difficult to estimate [1–5]. This problem, which often becomes the focus of lawsuits and conflicting opinions, essentially arises from a lack of concrete data. For instance, prospective studies with large patient populations are needed to investigate the relation between risk factors arising during

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pregnancy, birth and post-partum and the occurrence of brain damage, such as peri- or intraventricular haemorrhage in newborns [3–6].

To examine the incidence and severity of cerebral morbidity in neonates systematically, the Departments of Paediatrics as well as of Obstetrics and Gynaecology at the Justus-Liebig University in Giessen collaborated in launching a prospective cranial ultrasound study of all infants born there between 1984 and 1988. The results of these examinations were related to obstetric data and procedures. Attention was focused on the correlation of these factors to the incidence of peri- and intraventricular haemorrhages (PIVH), since these are by far the most common forms of brain damage.

The present study was limited to neonates born in the Department of Obstetrics and Gynaecology of the University of Giessen so that it can be assumed that the obstetric and paediatric care of the infants was constant over the period mentioned. Some preliminary results have already been published elsewhere [7].

2. Materials and methods

From 1984 to 1988, a cranial ultrasound study was carried out on all live-born infants on the day of discharge of the mother (5–8 days post-partum) from the Department of Obstetrics and Gynaecology at the University of Giessen. Infants who had to be transferred to the Children's Hospital directly post-partum were screened in the neonate ward there. Some of the infants with abnormal findings were then monitored daily.

2.1. Cranial sonography

Sonographic examination of the neonate brain was performed through the anterior fontanelle in coronal and sagittal section using high resolution sector transducers (Siemens Sonoline SL (1984), 5 MHz, Siemens Model RA1 (1980), 7.5 MHz). The coronal section ran along the level of the foramina interventricularia through the lateral ventricle and the third ventricle so that asymmetrical findings such as one-sided lateral ventricle enlargement with or without displacement of the interhemispheric fissure, could be diagnosed easily. Sonographically, brain haemorrhages appear as unusual localized areas of high echo-density.

PIVH was by far the most common form of brain damage diagnosed by ultrasound (Table 4). PIVHs were recorded photographically by the sonographer who had observed them and categorized in one of three grades of severity [8]. To exclude variance in these judgements, all findings were checked by another experienced examiner (V.K.). Ambiguous findings were excluded from the study.

The categorization into grades of severity I–III was used in preference to the four grade division proposed by Papile et al. [9] for computer-tomographical examinations. Grade I in the present study corresponds to Papile's grades I and II combined together. The reasonings behind this are first that possible slight ventricular haemorrhages cannot be excluded sonographically in overt cases of subependymal haemorrhage, and second that current knowledge suggests that there is little difference between the effects of grade I and grade II cerebral haemorrhages on the psychomotor development of the child.

In order to relate the cranial ultrasound findings to the obstetric data, the entire information contained in the birth records was encoded and fed into a data-bank (Institute of Medical Statistics, University of Giessen).

2.2. Statistics

The results are presented as means±standard deviation (S.D.). The quantitative and qualitative variables were compared using the chi-square test for contingency tables (statistical program: SPSS). Gestational age was identified to be the most important confounding factor affecting the incidence of PIVH. This was taken into account in statistical analyses. Although PIVH in term fetuses was a rare event in this study, we thought it worthwhile to present these data, since PIVH in term neonates may be nonetheless a sign of non-optimality in obstetrical management. Particularly, because we were able to demonstrate in a preliminary evaluation of a controlled follow-up examination of the studied children that cerebral haemorrhage in term neonates is associated with signs of minimal brain dysfunction (labyrinth test). Neonatal risk factors such as resuscitation, sepsis, pneumothorax and others were observed only in a small number of babies. This number was much too low to perform a statistical analysis. For the sake of brevity, only those obstetrical risk factors were presented that correlated to the incidence of PIVH. The occasional discrepancies between the total number of measurements and the size of the patient population (n= 5286), arose from missing data.

3. Results

Of the 5799 live-born babies delivered between 1984 and 1988, 5286 (91.1%) neonates (51.1% male, 48.9% female) underwent cranial ultrasound screening. In 38 babies gestational age could not be assessed. The basic obstetric data for the neonates and the distribution of the various modes of delivery and of the obstetric risk factors are given in Tables 1–3.

Pathological findings revealed by cerebral ultrasound screening are shown in Table 4. The most common abnormalities (3.6%) were slight (grade I), moderate (grade II) and severe PIVH (grade III) (n=191), usually accompanied by ventricular asymmetries. Periventricular

Table 1
Neonates

	24–43 weeks	24–30 weeks	31–34 weeks	35–37 weeks	38–43 weeks
Age of gestation (weeks)	39.2±2.5	28.3±1.5	32.7±1.1	36.4±0.8	40.0±1.0
Weight (g)	3220±686	1087±317	1794±448	2614±504	3424±481
Length (cm)	51.0±3.5	37.0±3.8	43.1±3.4	47.8±2.9	51.6±2.4
pH[a]	7.28±0.07	7.28±0.09	7.28±0.10	7.28±0.08	7.28±0.07

Data are given as means±S.D.
[a]Umbilical artery.

Table 2
Mode of delivery/presentation of fetuses

Mode of delivery	24–43 weeks (n=5286)		24–30 weeks (n=102)		31–34 weeks (n=212)		35–37 weeks (n=531)		38–43 weeks (n=4403)	
	%	N	%	N	%	N	%	N	%	N
Spontaneous delivery	72.2	3817	12.7	13	23.1	49	58.8	312	77.5	3413
Cesarean section	14.8	783	61.8	63	62.7	133	28.6	152	9.7	429
Vacuum	9.1	479	0	0	2.4	5	7.9	42	9.8	430
Vag. breech delivery	3.0	156	5.9	6	1.4	3	3.6	19	3.0	130
Assisted vag. delivery	0.9	49	19.6	20	10.4	22	1.1	6	0.02	1
Presentation of fetuses	(n=5281)		(n=102)		(n=212)		(n=531)		(n=4399)	
Vertex	92.2	4873	60.8	62	67.5	143	87.6	465	94.7	4166
Breech	7.2	380	37.3	38	26.4	56	12.2	65	5.1	225
Transverse	0.5	28	2.0	2	6.1	13	0.9	5	0.2	8

leucomalacia, porencephalia, subarachnoidal haemorrhages and post-haemorrhagic hydrocephali were rare (≤0.2%).

3.1. Gestational age

The relation between gestational age and the incidence of PIVH in neonates is shown in Table 5. The frequency of all three grades of haemorrhage increases with decreasing duration of pregnancy. Preterms born before the end of the 30th week of pregnancy had grade I–III brain haemorrhages in 50% of cases, 43% of which were moderate to severe (grade II–III). The lowest incidence of PIVH was noted for births between 38 and 43 weeks.

3.2. Birth weight

Body-weight at birth also correlated closely with the incidence of PIVH (Table 5). This relation can be seen

Table 3
Risk factors

	24–43 weeks (n=5286)		24–30 weeks (n=102)		31–34 weeks (n=212)		35–37 weeks (n=531)		38–43 weeks (n=4403)		P
	%	N	%	N	%	N	%	N	%	N	
Preterm membrane rupture	15.9	843	45.1	46	39.2	83	29.6	157	12.8	557	***
Pathologic heart rate pattern	12.5	663	41.1	42	36.8	78	17.5	93	10.1	450	***
Prolonged labor	11.5	606	0.0	0	3.3	7	8.7	46	12.5	553	***
Gestosis	7.3	386	13.7	14	15.1	32	10.9	58	6.3	282	***
Meconium stained amniotic fluid	4.7	248	1.0	1	0.9	2	2.4	13	5.2	232	***
Hypertension	3.0	158	6.9	7	6.6	14	3.6	19	2.7	118	***
Hypotension	0.3	15	0.0	0	0.5	1	0.2	1	0.3	13	
Growth retardation	3.6	189	8.8	9	6.1	13	9.8	52	2.6	115	***
Vaginal bleeding before 28 weeks of gestation	2.3	123	8.3	8	3.5	7	3.2	17	2.0	91	***
Vaginal bleeding after 28 weeks of gestation	1.9	102	6.3	6	15.1	14	6.6	35	1.1	47	***
Maternal diabetes mellitus	1.2	64	0.9	1	4.2	9	1.9	10	1.0	44	***
Fever sub partu	0.8	44	6.0	6	1.4	3	0.4	2	0.7	33	***
Rh-Incompatibility	0.5	26	1.1	1	1.9	4	0.9	5	0.4	16	**
Fetal malformation	0.6	29	1.1	1	2.8	6	0.6	3	0.4	19	***
Amnionitis	0.1	6	4.9	5	0.5	1	0.0	0	0.0	0	***

Significant differences between gestational groups are indicated by *P<0.05; **P<0.01; ***P<0.001.

Table 4 -
Sonography of neonatal brains

	24–43 weeks (n=5286)		24–30 weeks (n=102)		31–34 weeks (n=212)		35–37 weeks (n=531)		38–43 weeks (n=4403)		P
	%	N	%	N	%	N	%	N	%	N	
Total number of PIVH	3.6	191	54.9	56	17.0	36	5.6	30	1.6	69	***
degree 1	1.8	92	11.8	12	9.0	19	3.4	18	1.0	43	***
degree 2	1.0	55	14.7	15	4.2	9	1.5	8	0.5	23	***
degree 3	0.8	43	28.4	29	3.8	8	0.6	3	0.06	3	***
Asymmetry of lateral ventricles	3.8	200	49.0	50	18.4	39	4.1	22	2.0	89	***
Enlarged lateral ventricles	2.6	137	42.2	43	11.8	25	4.0	21	1.1	48	***
Periventricular leucomalacia	0.2	9	2.0	2	0.9	5	0.0	0	0.04	2	***
Displacement of interhemispherical fissure	0.2	11	5.9	6	1.9	4	0.2	1	0.0	0	***
Porencephalia	0.2	9	2.9	3	2.4	5	0.2	1	0.07	3	***
Subarachnoidal haemorrhage	0.02	1	0.0	0	0.0	0	0.0	0	0.02	1	

Significant differences between gestational groups are indicated by *P<0.05; **P<0.01; ***P<0.001.

most clearly in the case of severe haemorrhages (grade III), the incidence of which was found to rise almost exponentially (0.0%, 0.1%, 2.0%, 10.3% and 31.0%) with decreasing birth weight (Table 5).

3.3. Apgar score

Of all variables reflecting the clinical condition of the child during delivery and thereafter, the Apgar score at 1, 5 and 10 min after birth correlated best with the incidence of PIVH (Table 6). There were, however, marked differences between preterm and mature neonates (Table 6; Fig. 1). While the incidence of PIVH in premature neonates rose dramatically with decreasing 1-min Apgar scores, in mature neonates the overall incidence of haemorrhage was no higher for those with lower 1-min Apgar scores (5–7 points) than in infants with scores of 8–10 points. A marked increase in the incidence of PIVH (9.1%) was found only with Apgar scores as low as 0–4 points and was still moderate compared to the corresponding value for preterm neonates with these scores (Fig. 1). These findings, together with the fact that no severe PIVH occurred either in mature infants with Apgar scores of between 5–7 or in severely asphyxiated mature neonates (0–4 Apgar points), show that babies born at full-term unlike the preterms can tolerate asphyxia to a certain amount.

An equally important finding was that, in preterms (≤37 weeks) born in optimal physical condition (1-min Apgar scores: 8–10), there was a low overall incidence of PIVH (5.8%) and a very low incidence of severe haemorrhages (0.4%) contrasting to the corresponding value (15.4%) for preterm neonates with only 0–4 Apgar points. These results show that the combination of premature birth and asphyxia is associated with a particularly high risk of PIVH in newborns. Conversely, PIVH in preterms can be largely avoided if the fetuses are born in good clinical conditions.

3.4. Acid-base status

In 98.3% of all infants subjected to cerebral cranial ultrasound screening (n=5194), the arterial cord blood-pH was also analyzed. The correlation between acid-base status of the arterial cord blood and the incidence of PIVH

Table 5
Peri/intraventricular haemorrhage — gestational age and birth weight

Risk factor	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
Gestational age (weeks)	24–30	102	11.7	12		14.7	15		28.4	29		50.0	56	
	31–34	212	11.2	19		4.2	9		3.8	8		17.0	36	
	35–37	531	3.4	18		1.5	8		0.6	3		5.6	30	
	38–43	4403	1.0	43	***	0.5	23	***	0.07	3	***	1.6	69	***
Birth weight (g)	24–43	5279												
	0–1000	58	8.6	5		15.5	9		31.0	18		55.2	32	
	1001–1500	97	11.3	11		11.3	11		10.3	10		33.0	32	
	1501–2500	488	5.5	27		1.8	9		2.0	10		9.4	46	
	2501–4000	4161	1.1	46		0.6	23		0.1	4		1.8	73	
	4001–6000	475	0.6	3	***	0.6	3	***	0.0	0	***	1.2	6	***

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on gestational age and birth weight was established for each grade of PIVH as well as for the total group of PIVH. Significant differences are indicated by ***P<0.001.

Table 6
Peri/intraventricular haemorrhage — Apgar score

Risk factor	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
Apgar 1 min	24–43	5280												
0–4		148	10.8	16		7.4	11		10.8	16		29.1	43	
5–7		422	3.8	16		4.0	17		5.2	22		13.3	56	
8–10		4710	1.3	59	***	0.6	27	***	0.1	5	***	1.9	91	***
	24–30	101												
0–4		48	14.6	7		12.5	6		29.2	14		56.3	27	
5–7		41	7.3	3		17.1	7		36.6	15		61.0	25	
8–10		12	8.3	1		16.7	2		0.0	0	*	25.0	3	(*)
	31–34	211												
0–4		34	17.7	6		5.9	2		2.9	1		26.5	9	
5–7		98	8.2	8		6.1	6		6.1	6		20.4	20	
8–10		79	6.3	5		1.3	1		1.3	1		8.9	7	*
	35–37	530												
0–4		22	4.6	1		4.6	1		4.6	1		13.6	3	
5–7		101	4.0	4		2.0	2		1.0	1		7.9	8	
8–10		407	3.2	13		1.2	5		0.3	1	*	4.7	19	(*)
	38–43	4438												
0–4		44	4.6	2		4.6	2		0.0	0		9.1	4	
5–7		182	0.6	1		1.1	2		0.0	0		1.7	3	
8–10		4212	1.0	40	*	0.5	19	***	0.1	3		1.5	62	***
Apgar 5 min	24–43	5279												
0–4		19	21.0	4		21.0	4		5.3	1		47.4	9	
5–7		152	6.6	10		4.6	7		9.2	14		20.4	31	
8–10		5108	1.5	77	***	0.9	44	***	0.5	28	***	2.9	150	***
	24–30	101												
0–4		5	20.0	1		40.0	2		20.0	1		80.0	4	
5–7		35	11.4	4		14.3	5		34.3	12		60.0	21	
8–10		61	9.8	6		13.1	8		26.2	16		49.2	30	
	31–34	212												
0–4		3	33.3	1		33.3	1		0.0	0		66.7	2	
5–7		42	11.6	10		0.0	0		2.3	1		13.9	6	
8–10		166	7.8	13		4.8	8	*	4.2	7		16.9	28	(*)
	35–37	529												
0–4		6	16.7	1		16.7	1		0.0	0		33.3	2	
5–7		31	3.2	1		0.0	0		3.2	1		6.5	2	
8–10		492	3.3	16		1.4	7	**	0.4	2		5.3	26	*
	38–43	4437												
0–4		5	20.0	1		0.0	0		0.0	0		20.0	1	
5–7		43	0.0	0		4.7	2		0.0	0		4.7	2	
8–10		4389	1.0	42	***	0.5	21	***	0.07	3		1.5	66	**
Apgar 10 min	24–43	5274												
0–4		4	50.0	2		0.0	0		0.0	0		50.0	2	
5–7		33	12.1	4		12.1	4		15.2	5		39.4	13	
8–10		5237	1.6	85	***	1.0	51	***	0.7	37	***	3.3	174	***
	24–30	100												
0–4		1	0.0	0		100.0	1		0.0	0		100.0	1	
5–7		12	16.7	2		16.7	2		41.7	5		75.0	9	
8–10		87	10.3	9		13.8	12		26.4	23		50.6	44	
	31–34	209												
0–4		9	0.0	0		0.0	0		0.0	0		0.0	0	
5–7		7	28.6	2		0.0	0		0.0	0		28.6	2	
8–10		202	8.4	17		4.5	9		4.0	8		16.8	34	
	35–37	528												
0–4		0	0.0	0		0.0	0		0.0	0		0.0	0	
5–7		9	11.1	1		11.1	1		0.0	0		22.2	2	
8–10		518	3.3	17		1.4	7	(*)	0.6	3		5.4	28	(*)
	38–43	4437												
0–4		2	50.0	1		0.0	0		0.0	0		50.0	1	
5–7		5	0.0	0		0.0	0		0.0	0		0.0	0	
8–10		4430	1.0	42	***	0.5	23		0.07	3		1.5	68	***

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on Apgar score was established for each grade of PIVH as well as for the total group of PIVH. Significant differences are indicated by (*)$P<0.10$; *$P<0.05$; **$P<0.01$; ***$P<0.001$.

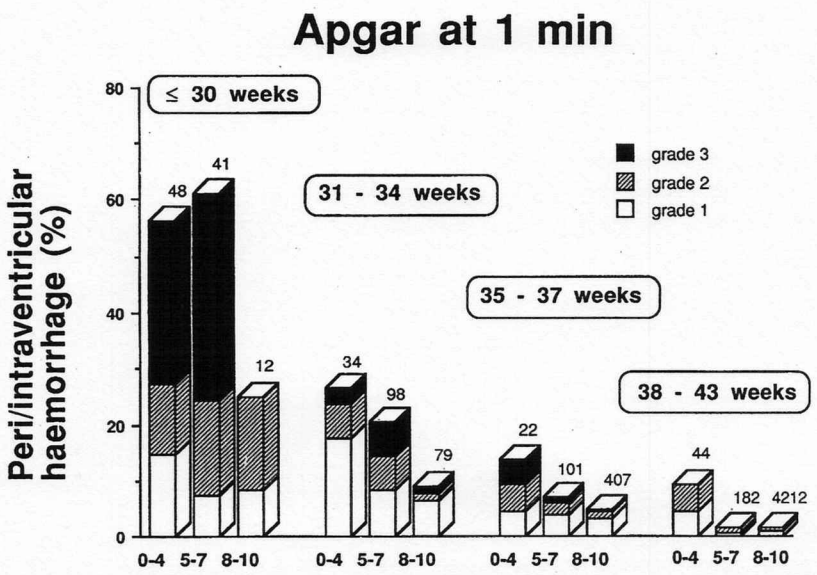

Fig. 1. Incidence of peri/intraventricular haemorrhage in neonates depending on the 1-min Apgar score.

was poor (Table 7). No correlation at all was found between base deficit (BE) and PIVH (data not shown).

In mature newborns, unlike PIVH grade I (15.4%), PIVH grade II and grade III did not increase during severe acidemia (pH<7.00). Within the preterm groups, two infants with an umbilical blood pH below 7.00 had a slight to moderate haemorrhage. Furthermore, PIVH was observed in 27.3% of neonates with pH-values of 7.09 and 7.00 after premature delivery but in no infants with this acid-base status at full-term (Table 7).

3.5. Heart rate pattern

Pathological heart rate pattern as assessed by cardiotocography was noted in 12.5% of cases and was closely related to gestational age ($P<0.001$; Table 3). Thus the cardiotocogram was pathological in 41.1% of preterms born before the end of the 30th week of pregnancy, while in mature neonates born between the 38th and 43rd weeks of pregnancy all except 10.1% were normal.

The relation between pathological cardiotocograms and PIVH is given in Table 8. The incidence of PIVH in the total group of preterms (≤37 weeks) with pathologic heart rate pattern was significantly higher than in that without pathologic heart rate pattern (18.8% vs. 13.0%; $P<0.05$). We were not able to confirm this observation when the preterm group was further subdivided (Table 8). After the 37th week of pregnancy, no further correlation could be found between cardiotocogram findings and PIVH.

3.6. Premature rupture of membranes

The most common complication occurring during delivery was premature rupture of the membranes (15.9%; Table 3). There was a significant correlation between each grade of PIVH and premature rupture of membranes in the total group of patients, but not in the various subgroups (Table 9).

3.7. Prolonged labour

Prolonged labour occurred in 11.5% of births (Table 3), but was not associated with a higher risk of PIVH either in term neonates or those born before the 35th gestational week. Preterm babies born between the 35th and 37th weeks did, however, have a significantly higher incidence of grade 2 and 3 PIVH ($P<0.01$) (Table 9). A case study analysis of the seven newborns in question revealed that all of them had been delivered by cesarean section after prolonged labour, suggesting that in at least some of these cases haemorrhaging might have been avoided by earlier operative intervention.

3.8. Gestosis

Gestosis, which is very often concomitant with premature birth, was diagnosed in 7.3% of pregnancies (Table 3). However, a correlation between gestosis and the PIVH was found only for the total group of patients, but not for each grade of PIVH or for the various subgroups of babies (Table 9).

3.9. Fetal growth retardation

An intrauterine growth retardation (<10th weight percentile) was observed in 3.6% of cases, with a higher incidence in preterms (8.7%) than in infants born at full-term (2.6%) ($P<0.001$) (Table 3). Independent of the duration of pregnancy, the arterial cord blood pH corre-

Table 7
Peri/intraventricular haemorrhage — umbilical blood pH

Risk factor	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
pH	24–43	5194												
0–6.99		18	16.7	3		5.6	1		0.0	0		22.2	4	
–7.09		64	4.7	3		3.1	2		1.6	1		9.4	6	
–7.19		361	2.8	10		0.8	3		0.8	3		4.4	16	
–7.29		2436	1.8	44		1.1	26		0.5	13		3.4	83	
–7.50		2315	1.3	31	***	0.9	21		1.0	24		3.3	77	***
	24–30	98												
0–6.99		0	0.0	0		0.0	0		0.0	0		0.0	0	
–7.09		7	28.7	2		28.6	2		14.3	1		71.4	5	
–7.19		11	9.1	1		0.0	0		18.2	2		27.3	3	
–7.29		34	14.7	5		23.5	8		23.5	8		61.8	21	
–7.50		46	8.7	4		6.5	3		34.8	16		50.0	23	
	31–34	210												
0–6.99		4	25.0	1		25.0	1		0.0	0		50.0	2	
–7.09		5	0.0	0		0.0	0		0.0	0		0.0	0	
–7.19		19	10.5	2		0.8	0		0.0	0		10.5	2	
–7.29		70	7.1	5		4.3	3		4.3	3		15.7	11	
–7.50		112	8.9	10		4.5	5		4.5	5		17.8	20	
	35–37	523												
0–6.99		1	0.0	0		0.0	0		0.0	0		0.0	0	
–7.09		10	10.0	1		0.0	0		0.0	0		10.0	1	
–7.19		53	7.6	4		5.7	3		1.9	1		15.1	8	
–7.29		205	4.9	10		1.0	2		0.5	1		6.3	13	
–7.50		254	1.2	3	(*)	1.2	3		0.4	1		3.2	8	*
	38-43	4363												
0–6.99		13	15.4	2		0.0	0		0.0	0		15.4	2	
–7.09		42	0.0	0		0.0	0		0.0	0		0.0	0	
–7.19		278	1.1	3		0.0	0		0.0	0		1.1	3	
–7.29		2127	1.1	24		0.6	13		0.5	1		1.8	38	
–7.50		1903	0.7	14	***	0.5	10		1.0	2		1.4	26	***

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on umbilical pH was established for each grade of PIVH as well as for the total group of PIVH. Significant differences are indicated by (*)$P<0.10$; *$P<0.05$; **$P<0.01$; ***$P<0.001$.

lated closely with the incidence of PIVH in growth retarded fetuses (Table 9).

3.10. Maternal fever during birth

Fever (>38.0°C) was measured in 0.8% of mothers ($n=44$) during birth. Eleven of these gave birth before the 37th week of pregnancy and 33 after (Table 3). An increased maternal body temperature during birth at full-term was not accompanied by PIVH, whereas in six of the 11 preterm neonates (<37 weeks) it was (Table 9). In preterms this corresponds to a 54.4% risk in comparison with a 13.9% risk for the control group ($P<0.01$).

3.11. History of abortion

There was only a low correlation between incidence of PIVH and previous abortions (Table 9).

Table 8
Peri/intraventricular haemorrhage — pathologic heart rate pattern

Risk factor	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
Pathologic	24–43	663	3.5	23	***	2.4	16	***	1.8	12	**	7.6	51	***
Heart rate pattern	24–30	42	9.5	4		19.1	8		23.8	10		52.4	22	
	31–34	78	7.7	6		5.1	4		2.6	2		15.4	12	
	35–37	93	5.4	5		1.1	1		0.0	0		6.5	6	
	38–43	450	1.8	8		0.7	3		0.0	0		2.4	11	

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on pathologic heart rate pattern was established for each grade of PIVH, for the total group of PIVH, and for each category of gestational age. Significant differences are indicated by (*)$P<0.10$; *$P<0.05$; **$P<0.01$; ***$P<0.001$.

Table 9
Peri/intraventricular haemorrhage — other risk factors

Risk factor	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
Preterm rupture of membranes	24–43	843	2.8	24	*	1.9	16	*	1.9	16	***	6.6	56	***
	24–30	46	6.5	3		13.4	6		30.4	14		50.0	23	
	31–34	83	9.6	8		3.6	3		1.2	1		14.5	12	
	35–37	152	0.0	0	*	2.6	4		0.7	1		3.3	5	
	38–43	557	1.4	8		0.5	3		0.0	0		2.0	11	
Prolonged labor	24–43	606	1.2	7		1.8	11	(*)	0.3	2		3.3	20	
	24–30	0	0.0	0		0.0	0		0.0	0		0.0	0	
	31–34	7	14.3	1		0.0	0		0.0	0		14.3	1	
	35–37	46	2.2	1		8.7	4	***	4.4	2	*	15.2	7	**
	38–43	553	0.9	5		1.3	7	*	0.0	0		2.2	12	
Growth retardation	24–43	189	3.2	6		4.2	8	***	2.1	4		9.5	18	***
	24–30	9	11.1	1		22.2	2		22.2	2		55.6	5	
	31–34	13	15.4	2		15.4	2		7.7	1		38.5	5	(*)
	35–37	52	5.8	3		3.9	2		1.9	1		11.5	6	
	38–43	115	0.0	0		1.7	2		0.0	0		1.7	2	
Growth retardation	24–43	62	1.6	1		3.2	2		1.6	1		6.5	4	
pH≥7.30	24–30	0	0.0	0		0.0	0		0.0	0		0.0	0	
	31–34	3	0.0	0		0.0	0		33.3	1		33.3	1	
	35–37	21	4.7	1		4.7	1		0.0	0		9.5	2	
	38–43	38	0.0	0		2.6	1		0.0	0		2.6	1	
Growth retardation	24–43	125	4.0	5		4.8	6	***	2.4	3		11.2	14	***
pH<7.30	24–30	9	11.1	1		22.2	2		22.2	2		55.6	5	
	31–34	10	20.0	2		20.0	2	(*)	0.0	0		40.0	4	
	35–37	31	6.5	2		3.3	1		3.3	1		12.9	4	
	38–43	75	0.0	0		1.3	1		0.0	0		1.3	1	
Fever sub partu	24–43	44	6.8	3	*	2.3	1		4.5	2	(*)	13.6	6	**
	24–30	6	16.7	1		16.7	1		33.3	2		66.7	4	
	31–34	3	66.7	2		0.0	0		0.0	0		66.7	2	
	35–37	2	0.0	0		0.0	0		0.0	0		0.0	0	
	38–43	33	0.0	0		0.0	0		0.0	0		0.0	0	
History of abortion	24–43	962	2.3	22		1.4	13		1.0	10		4.7	45	*
(n=1–2)	24–30	28	10.7	3		14.3	4		28.6	8		53.6	15	
	31–34	56	12.5	7		3.6	2		0.0	0		16.1	9	
	35–37	116	3.5	4		3.5	4		1.7	2		8.6	10	(*)
	38–43	762	1.1	8		0.4	3		0.0	0		1.4	11	
History of abortion	24–43	87	1.1	1		5.7	5	***	2.3	2		9.2	8	*
(n>2)	24–30	10	0.0	0		30.0	3		10.0	1		40.0	4	
	31–34	11	0.0	0		0.0	0		9.1	1		9.1	1	
	35–37	10	10.0	1		10.0	1		0.0	0		20.0	2	
	38–43	56	0.0	0		1.8	1		0.0	0		1.8	1	
Gestosis	24–43	386	3.1	12	(*)	2.1	8	(*)	1.0	4		6.2	24	**
	24–30	14	14.3	2		21.4	3		7.1	1		42.9	6	
	31–34	32	6.3	2		9.4	3		3.1	1		18.8	6	
	35–37	58	5.2	3		1.7	1		1.7	1		8.6	5	
	38–43	282	1.8	5		0.4	1		0.4	1		2.5	7	

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on risk factors was established for each grade of PIVH, for the total group of PIVH, and for each category of gestational age. Significant differences are indicated by (*)$P<0.10$; *$P<0.05$; **$P<0.01$; ***$P<0.001$.

3.12. Mode of delivery/vertex presentation

About 92.2% of infants were born from a vertex presentation (Table 2). Among the newborns delivered at full-term and presenting cranially the incidences of PIVH in those born spontaneously was slightly lower (1.4%) than in those delivered by vacuum extraction (2.8%) or cesarean section (2.1%) (Table 10).

For preterm infants born between the 35th and 37th weeks of pregnancy the situation was different. At 11.2%, the incidence of PIVH after a cesarean section was much higher than for spontaneous births (4.4%) or after vacuum extraction (2.5%) ($P<0.05$). It should however be noted that in seven out of 11 cases secondary cesarean sectioning was undertaken to curtail prolonged labour.

3.13. Mode of delivery/breech presentation

Of all the children included in the study, 380 (7.2%)

Table 10
Peri/intraventricular haemorrhage — fetal presentation and mode of delivery

Mode of delivery	Gestational age (weeks)	N	Grade 1			Grade 2			Grade 3			Total		
			%	N	P	%	N	P	%	N	P	%	N	P
Vertex presentation	24–43	4873												
Spontaneous delivery		3863	1.4	53		0.5	21		0.4	15		2.3	89	
Vacuum extraction		469	1.7	8		1.1	5		0.0	0		2.8	13	
Cesarean section	541	541	3.3	18	**	12.4	13	***	1.6	9	***	7.4	40	***
Vertex presentation	24–30	62												
Spontaneous delivery		32	15.6	5		9.4	3		31.3	10		56.3	18	
Vacuum extraction		0	0.0	0		0.0	0		0.0	0		0.0	0	
Cesareansection		30	10.0	3		16.7	5		13.3	4		40.0	12	
Vertex presentation	31–34	143												
Spontaneous delivery		69	10.1	7		2.9	2		1.4	1		14.5	10	
Vacuum extraction		4	0.0	0		0.0	0		0.0	0		0.0	0	
Cesarean section		70	8.6	6		1.4	1		4.3	3		14.3	10	
Vertex presentation	35–37	465												
Spontaneous delivery		318	2.8	9		1.3	4		0.3	1		4.4	14	
Vacuum extraction		40	2.5	1		0.0	0		0.0	0		2.5	1	
Cesarean section		107	4.7	5		3.7	4		1.9	2		11.2	11	*
Vertex presentation	38–43	4203												
Spontaneous delivery		3444	0.9	32		0.4	12		0.1	3		1.4	47	
Vacuum extraction		425	1.7	7		1.2	5		0.0	0		2.8	12	
Cesarean section		334	1.2	4		0.9	3		0.0	0		2.1	7	(*)
Breech presentation	24–43	380												
Spontaneous delivery		156	1.9	3		1.3	2		3.2	5		6.4	10	
Cesarean section		224	4.0	9		5.8	13	(*)	4.9	11		14.7	33	*
Breech presentation	24–30	38												
Spontaneous delivery		7	14.3	1		14.3	1		71.4	5		100.0	7	
Cesarean section		31	9.7	3		16.1	5		29.0	9	(*)	54.8	17	(*)
Breech presentation	31–34	56												
Spontaneous delivery		2	50.0	1		0.0	0		0.0	0		50.0	1	
Cesarean section		54	7.4	4		11.1	6		3.7	2		22.2	12	
Breech presentation	35–37	61												
Spontaneous delivery		19	5.3	1		0.0	0		0.0	0		5.3	1	
Cesarean section		42	4.8	2		0.0	0		0.0	0		4.8	2	
Breech presentation	38–43	225												
Spontaneous delivery		128	0.0	0		0.8	1		0.0	0		0.8	1	
Cesarean section		97	0.0	0		2.1	2		0.0	0		2.1	2	

The significance of differences in the incidence of peri/intraventricular haemorrhage depending on mode of delivery was established for each grade of PIVH as well as for the total group of PIVH. Significant differences are indicated by (*)$P<0.10$; *$P<0.05$; **$P<0.01$; ***$P<0.001$. Due to their low number women delivered by vacuum extraction below 35 weeks of gestation were not included into the statistical analysis.

were born from a breech presentation (Table 10). Taking an expectant management of the mature newborns, i.e. those born in the 38th to 43rd gestational week, that presented in a breech position ($n=225$), 56.9% ($n=128$) were delivered vaginally, regardless of parity. In these cases the incidence of PIVH (0.8%, $n=1$) was no higher than in the infants delivered from a breech presentation by cesarean section (2.1%, $n=2$) or those born spontaneously from a vertex presentation (1.4%) (Table 10). The three cases of PIVH observed in this group were all second grade haemorrhages. Among infants delivered between the 35th and 37th gestational weeks, either by cesarean section or vaginally with assistance from a breech presentation, the haemorrhages observed were all first grade (Table 10). Before the 35th week of pregnancy, breech presentations were delivered vaginally only in exceptional cases (Table 10).

4. Discussion

The prospective cranial ultrasound study presented here is an example of successful collaboration between obstetricians and paediatricians to investigate the incidence and severity of PIVH and other pathological findings in neonates in a large, unselected population and to relate these findings to risk factors arising during pregnancy and delivery.

4.1. Does immaturity raise the risk of cerebral haemorrhage?

The most important risk factor associated with PIVH is immaturity at birth [6,10]. One reason for this resides in the germinal matrix [11], an extremely vulnerable glioblastic tissue that is subependymal and, up to the 33rd week of

pregnancy, covers the head and body of the caudate nucleus. Approximately 80% of subependymal, intra- and periventricular haemorrhages in preterm neonates originates from there [12,13]. Secondly, insufficient autoregulation of the cerebral circulation is thought to contribute to haemorrhage in preterm babies [14]. Extremely preterm neonates, born before the 30th week of pregnancy, are further endangered by the fact that, at this stage of development, the parenchymal cerebral vessels consist solely of an endothelial layer without any smooth muscle, collagen or elastin [15]. The incidence of vessel rupturing is therefore much higher, particularly if due to a lack of autoregulation cerebral blood flow changes with systemic blood pressure [12]. It is these disadvantageous structural and circulatory features of the premature neonate brain that render it so vulnerable to asphyxia and fluctuations in blood pressure and raise the risk of brain damage [16].

The incidences of PIVH observed in this study agree in part with those noted in the literature [16–18], although some of ours are higher [3,6]. The only group who found a markedly higher incidence were Wille et al. [2] who, for infants with a birth weight of less than 1500 g, measured a rate of 82% compared with our 41%. When the incidence of PIVH in our study is calculated separately for each year, a steady decrease can be observed from 1984 to 1988. Furthermore, discrepancies between studies can well be explained by the variable powers of resolution of the ultrasound equipment used by different groups, or by the fact that the data in some studies was obtained by computer tomography [1,18–20].

Before the advent of imaging techniques, brain damage in newborn babies was very difficult to detect. The use of computer tomography, which meanwhile is widely prohibited owing to unacceptable levels of radiation exposure, and that of sonography enabled physicians to detect PIVH and other pathological events or features which had been partly overlooked in routine clinical examinations. It should be added that there is a danger of over-emphasizing the importance of certain minor cerebral lesions in newborns, since their influence on the subsequent neurological and psychomotor development of individual children is impossible to predict, being as it is, so critically dependent on social factors [21]. Preliminary evaluation of a controlled follow-up examination of the studied children has shown retarded psychomotor development (Kramer Test, labyrinth test) and a higher incidence of neurological abnormalities (Touwen's method of neurological examination) in those who were born prematurely and suffered PIVH compared with controls ('matched pairs') (unpublished results). These initial results underline the preventative value of cranial ultrasound screening of neonates, since early detection of brain damage allows speedy commencement of remedial training and treatment and can help to minimize subsequent handicaps. In view of the well-known ability of children to overcome developmental retardation, no final assessment of the relationship of PIVH to psychomotor retardation will be obtainable until these children have been reexamined during their school years or as adults.

4.2. Apgar score

One of the most important findings in our study was that the Apgar score, representing the clinical condition and degree of circulatory centralisation of the infant 1, 5 and 10 min after birth, has more prognostic value than an ante-partum cardiotocogram or arterial cord blood-pH for predicting the likelihood of PIVH. Although active resuscitation may have altered Apgar scores in immature babies, the incidence and severity of PIVH also increased dramatically with decreasing Apgar scores in these subgroups. These findings, some of which have been confirmed by other authors [5,22], contradict the doubts, so often expressed but not supported by any concrete evidence about the value of the scoring system of V. Apgar in clinical practice. In this context, it is particularly noteworthy that even among infants born before the 30th week of pregnancy, there were practically no severe PIVH in those whose clinical condition at birth was good enough to merit Apgar scores of 8 points or more.

Furthermore, it is noted that it is not only the 5-min Apgar score but in particular the 1-min score that appears to be closely related to the incidence of PIVH. Hence, the 1-min Apgar score is a highly sensitive parameter with prognostic value in relation to PIVH. Previous preferential use of the 5-min Apgar score as a prognostic factor for psychomotor development rests on data obtained at a time when severe asphyxia was more common in neonates. With optimal obstetric management and neonatal care, babies experiencing severe circulatory centralization and achieving very low 5-min Apgar scores are rare. For these reasons, proposals to drop the 1-min Apgar score from routine neonatal records should be reconsidered.

From a physiological point of view, the close correlation between Apgar scores and the incidence of PIVH in preterm neonates is not surprising, since a lower Apgar score denotes a condition of shock [23]. The brains of preterm babies are extremely vulnerable and the ability of these infants to effectively centralise their circulation is limited, because their sympathetic nervous system is not fully developed. When oxygen deficiency arises they are, therefore, more prone to a severe reduction in oxygen transport to the brain than mature neonates. Furthermore, the loss of autoregulation in preterm fetuses may lead to rupture of the fragile cerebral vessels when the arterial blood pressure is high or ischemic lesions when the pressure is too low. Babies born at full-term, in contrast, have fully developed circulatory protective mechanisms. Their brains are therefore more resistant as evidenced by a marked tolerance to asphyxia and a lower incidence and severity of PIVH. Therefore, the overall incidence of PIVH in mature neonates with Apgar scores of 5–7 points is no

higher than in those with Apgar scores of 8–10. However, it rises in those neonates with Apgar values as low as 0–4 points.

4.3. Cardiotocography and acid-base status

This study has shown that although cardiotocographic monitoring and measurement of umbilical arterial blood-pH during birth are useful means of detecting conditions of acute or chronic oxygen deficiency, they appear to be less suitable for risk assessment of PIVH at a certain gestational age. Furthermore, the data obtained from these two well-established monitoring techniques, cardiotocography and pH-measurement, correlates only weakly with neonatal clinical condition as represented by the Apgar score while the latter parameter provides the most direct indication, when low, that vital physiological systems are affected in the asphyxiated newborn infant.

It should, however, be emphasized that although the weak correlation between a pathological cardiotocogram or pH-metry and the risk of neonatal PIVH has also been observed by other investigators [5,24], this by no means detracts from the obstetric value of these two monitoring techniques. In fact, it is thanks to protective obstetric management, including careful cardiotocographic analysis that the pathologic changes in heart rate observed in mature neonates still did not lead to PIVH and other forms of damage. To be consistent, one should add that in premature births where there is a significant correlation between pathological changes in heart rate and/or pathological pH-values and the occurrence of PIVH, analysis of the cardiotocogram may not sufficiently take into account the vulnerable constitution of preterms, so that essential obstetric decisions are taken too late. For premature births where an ultimately protective obstetrical management is called for, the operating team must intervene as soon as possible when a high risk situation develops, and must select the most gentle mode of delivery. There is patho-anatomical proof as well as evidence from animal experiments to support this proposal [23,25]. Thus, apart from the considerable vulnerability of the subependymal germinal matrix, circulatory regulation especially centralization in response to asphyxia are also quite different and more limited in preterm than in mature neonates [23,25]. Among other things, without a fully developed sympathetic nervous system neither the circulatory centralization nor the oxygen transport to the brain can be maintained adequately [23]. The critical problem encountered in cardiotocographic monitoring during birth is that the heart rate response to oxygen deficiency is not different in preterm and mature neonates, and it is impossible to tell from an observed deceleration whether the circulatory centralization has been sufficient or insufficient. Thus it would seem that the only obstetric option for lowering PIVH in premature births is by prompt intervention when high-risk situations arise.

4.4. Risk factors during pregnancy and birth

The present study has clarified the evaluation of risk factors in pregnancy and birth in ways that will help to improve assessment of risk to the child, consultation of the parents and obstetric management. It is important to know that it is not premature rupture of the membranes, prolonged labour or gestosis per se that raise the risk of PIVH in the child, but rather associated secondary complications such as infection of the amnion, growth retardation and others. These, in combination with premature birth and asphyxia, create the real predisposition to PIVH.

The pathological mechanisms underlying such PIVH can be demonstrated best in cases of amnionitis which has been shown here and in other studies to raise the risk of PIVH considerably [12]. The amnion infection syndrome is mostly caused by endotoxin-producing, gram-negative bacteria. Animal experiments have demonstrated that these bacteria disturb the circulatory autoregulation and hinder the centralisation of blood flow during asphyxia [26]. This means that fetal endotoxinaemia can lead to a reduction of the blood flow to the brain even when oxygenation is still sufficient. If the oxygen supply is also curtailed, inadequate centralisation of the fetal circulation will allow cerebral oxygen deficiency to develop [26].

The regulation of blood flow in growth-retarded fetuses differs from that in eutrophic ones. Blood pressure and heart rate responses to oxygen deficiency, for instance, are much less pronounced [27]. Given that, even in eutrophic mature fetuses, acidaemia resulting from moderate oxygen deficiency is accompanied by a reduction in cardiac output [23], it is easy to see how the combination of fetal growth retardation and acidaemia can increase the risk of brain haemorrhage.

4.5. Mode of delivery

Another interesting finding emerging from this study is that the incidence of PIVH in mature newborns is only minimally affected by fetal presentation at birth or by the mode of delivery. This confirms the results of other studies [28]. The observation applies especially to assisted vaginal breech deliveries, which in a total of 128 cases led to only one, second-grade brain haemorrhage (Table 10). The expectant obstetrical management taken in our clinic allows 50–60% of term neonates to be delivered vaginally, regardless of parity, with a minimal incidence of cerebral defects. We, therefore, maintain that the demand, put forward in the 1970s, that all primiparae with breech presentations should be delivered by primary cesarean section can no longer be justified [29]. This is of forensic significance. On the other hand, there is no doubt that premature breech presentations can be delivered more successfully by cesarean section [30]. Where exactly the line should be drawn between vaginal delivery and cesarean section is hard to say. This depends on obstetric

factors as well as the experience of the obstetrician. Although in our study only one, first grade brain haemorrhage was observed among the breech presentations born between the 35th and 37th weeks of pregnancy, vaginal delivery in this gestational age bracket should still be undertaken with caution. Even marginally preterm children are more vulnerable to lesions from traumatic-asphyxia [30–32].

For preoperative consultation of the expectant mother the finding that for vertex presentations at term, the incidence of PIVH in infants delivered by vacuum extraction is not significantly different from that observed after cesarean section, is very important. This finding is also important from a forensic point of view. All too often, when vacuum extraction is indicated, the skin oedema and traction on the child's head lead parents and sometimes even legal medical officers to assert that brain damage was caused by this mode of delivery. The present study shows clearly that this is not the case. On the contrary, when applied correctly, the method of vacuum extraction first introduced to Germany and developed by Evelbauer [33] is particularly advantageous for infants requiring this form of assistance at birth and scores well in terms of cerebral morbidity. Comparable data for forceps deliveries are not available at present.

From the present study we conclude that the incidence of PIVH especially in immature neonates is closely related to the Apgar score at birth. Since the Apgar score represents the clinical condition and degree of circulatory centralisation of neonates that is influenced by various ante- and intranatal risk factors, a protective obstetrical management is necessary to reduce the incidence of PIVH in neonates.

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