INDIAN JOURNAL OF PEDIATRICS

March, 1966 Vol. 33 No. 218

PATHOGENESIS OF BRAIN VENTRICLE HAEMORRHAGE IN NEWBORNS*

S. SRSEN

Czechoslovakia

The analysis of autopsy findings of our cases of intracranial haemorrhage (I.H.) in the newborns demonstrated that the bleeding into the brain ventricles formed its principal part—41·91 (32·5—51) per cent and that it should be considered a serious problem in newborn pathology. The hypotheses about its pathogenesis are still rather vague and the studies of various authors show various, often even contradictory, viewpoints. These facts prompted us to study the problem of the pathogenesis of the intraventricular (I.H.) and to attempt to contribute to its solution.

Material

Our study was performed in 1953-1962. At that time the number of live-born newborns at the Obstetrical Clinic in Kosice was 28,003 (excluding 22 who died and in whom the autopsy was not performed due to difficulties of a technical nature).

Of these 412, i.e. 1·47 (1·4-1·5) per cent died within the first 10 days of life. Section findings proved I.H. in altogether 136-4·86 (4-6) per thousand, the intraventricular I.H. being demonstrated in 57 cases—2·07 (2-2·5) per thousand of the total count of the live-born newborns.

Of the infants released from the neonatal department of the Obstetrical Clinic and hospitalized at the Children's Clinic, who died at various ages after the 10th day of life, a further 24 cases of I.H. were found out of which 5 with intraventricular I.H., were identified by autopsy. These cases were also included in our study, so that the whole sample with I.H. consisted of 160 (129 premature and 31 mature) infants, the total count of infants with intraventricular I.H. being 62 (59 premature and 3 mature).

The extent of ventricle system affection is given in Fig. 1 indicating that affection of all the ventricles took place in the majority of cases. In the group

*From the Pediatric Clinic, Medical Faculty, P. J. Safarik University Kosice, Director : Professor MUDr F. Demant, Cathedra of Internal Medicine, Medical Faculty, Komensky University Bratislava, Branch Dept. Martin, external Director Doc. MUDr Vl. Galanda.

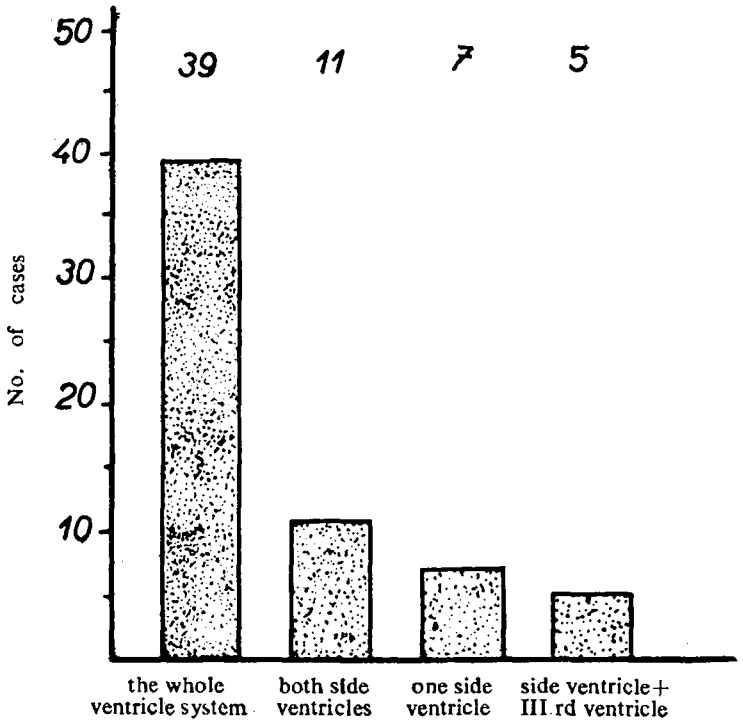

Fig. 1. Extent of bleeding into the ventricular system in different subjects.

of infants with the bleeding into all ventricles, in 4, the blood found in the fossa cerebri posterior, or as far as the spinal canal, had overflowed most probably from the fourth ventricle.

Methods

The study was started in 1953 as a part of the research problem of the Ministry of Health "Birth Traumatism of the Newborn". When the research problem was concluded in 1955, the study was continued using the same method.

Infants with birth weight (B.W.) of 2,501 g or more were designated as mature, and those with B.W. 2,500 g. or less were termed premature. The newborns with B.W. under 1,000 g. who died within the first 24 hours of life, were considered as abortions (according to the intimation of the Ministry of Health valid at that time) and were therefore excluded.

The following causes of death were decided upon as basic : mechanical birth trauma, intrauterine asphyxia, postnatal asphyxia, profound prematurity, other basic causes of death.

Infants with B.W. 1,250 g. or less were included in the group with "profound prematurity". Prematurity is not considered as the basic cause of death in the true sense of this expression. This group was formed because in these infants more than in other cases it was difficult to demonstrate

to what extent mechanical trauma, asphyxia and profound prematurity of the organism participated in the appearance of the I.H. and which cause was decisive in a given case.

The group, "other basic causes of death" included infants with autopsy findings of I.H. or intraventricular I.H. who nevertheless died due to some other cause (infection, inborn developmental defects, nuclear icterus, haemorrhagic diathesis, etc.).

In one of our previous papers (Srsen, 1965) we pointed to the statistically significant differences of the individual questions of the I.H. problem in mature and premature newborns. It is principally important to analyse these separately in the said two groups. As the intraventricular I.H. is found especially in premature infants (in 59 cases from the total count of 62 infants with intraventricular I.H. in our material), a special statistical evaluation was performed in premature newborns, besides the evaluation of the whole sample.

For statistical calculations the formula from the quoted literature was used (Statistical Research group 1947, Cramer, 1954, Janko 1958). 95 per cent reliability intervals for the given percentage (i) was found in Janko's statistical table No. 28, or they were read from the graph (23, p. 333). The statistical sign)(is replaced in the text by the sign x^2 because of technical reasons.

Pathogenesis of Intraventricular Intracranial Haemorrhage

On the basis of our experience and data from the literature we arrived at the following conclusion about the pathogenesis of I.H.

One of the most important factors in the appearance of the I.H. is prematurity. Fig. 2 shows the statistically significant character of the incidence of I.H. in premature infants, as compared with the mature individuals (x^2—4·64, table value—3·84). This difference is still more significant in I.H. (x^2—12·8, table value—3·84).

Our results are in accordance with

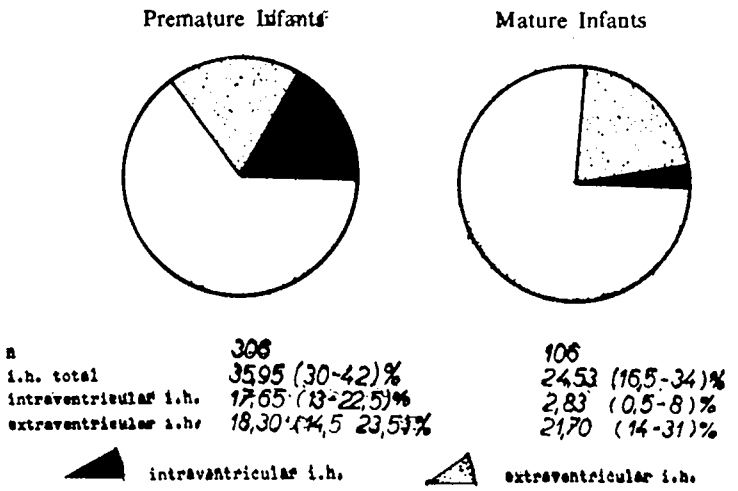

Fig. 2. Total incidence of I.H., incidence of intra- and extra-ventricular I.H. in autopsy findings of mature and premature infants, live-born but dead within the first 10 days of life.

the literature referring to the finding of intraventricular I.H. as "the main", "most common", "frequent" finding in premature infants (Hemsath 1934, Craig 1938, Brachfeld *et al.* 1950, Grontoft 1954, Benesova 1956, Goerttler 1961, Debakan 1962, Larroche 1965).

Fig. 3 (where the weight group up to 1,000 g. is not evaluated because of incompleteness due to the reasons already mentioned) indicates the statistically significant differences in autopsy findings of I.H. in the individual weight groups of infants, live-born but dead within the first 10 days of life (x^2—27·09, table value—9·49). The highest frequency was found in newborns with the lowest B.W. The incidence decreases with the increasing B.W.

In the statistical evaluation of the incidence of extraventricular I.H. (the infants with B.W. lower than 1,000 g. having been eliminated) no significant differences were found (x^2—1·97, table value—9·49).

It is a well-known fact—and it is valid in the case of our material also—that with the increasing B.W., i.e. with the increasing maturity of the newborns, the neonatal mortality (deaths within the first 10 days of life) decreases. Yet, our results (Fig. 3) indicate that whereas the extraventricular I.H. does not show any substantial variations in the section findings of newborns deceased within the first 10 days of life as to the incidence in the individual weight groups, so that consequently this incidence practically decreases proportionally with the neonatal mortality, this is not true in the case of intraventricular I.H. The most frequent findings are observed in infants with the highest degree of prematurity, and the decrease of the frequency with the increasing B.W. is distinctly more rapid as compared with the decrease of neonatal mortality.

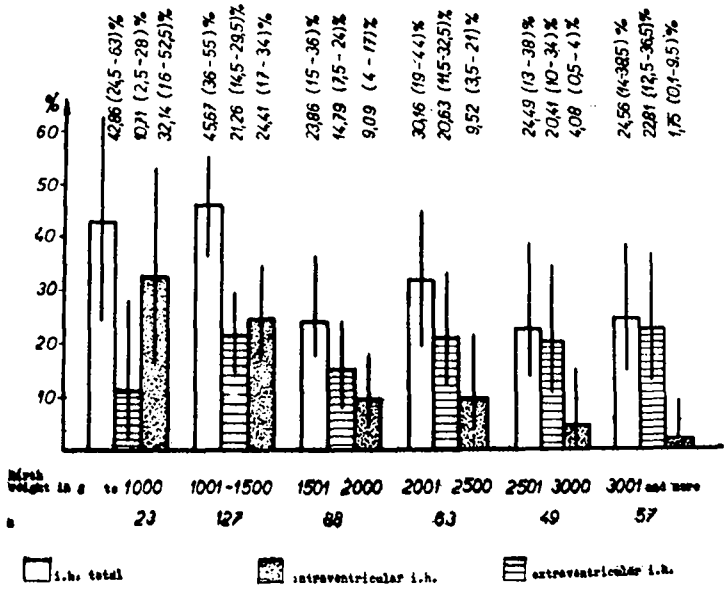

Fig. 3. Total incidence of I.H., incidence of intraventricular and extraventricular I.H. in the individual weight groups of infants, live-born, but dead within the first 10 days of life.

Fig. 4 shows that the ratio of intraventricular I.H. to the total number of cases of I.H. in the individual weight groups is indirectly proportional to the B.W. It is the highest up to the weight of 1,000 g. (3/4 of the total number of infants with I.H.); between 1,001—1,750 g. B.W. it represents approximately one half of the cases, in weight groups from 1,751—2,750 g. it makes one quarter, whereas it is quite exceptional in the higher weight groups.

A similarly performed statistical evaluation of the incidence of the intraventricular and extraventricular I.H. in relation to the B.W. was not found in the available literature, yet the literary data are in principal accordance with our results concerning the most frequent findings of the intraventricular I.H. in infants with the most pronounced prematurity (Brachfeld *et al.* 1950, Gruenwald 1951, Lelong and Laumonier 1953, Potter 1953, Grontoft 1954, Janko 1958, Goerttler 1961).

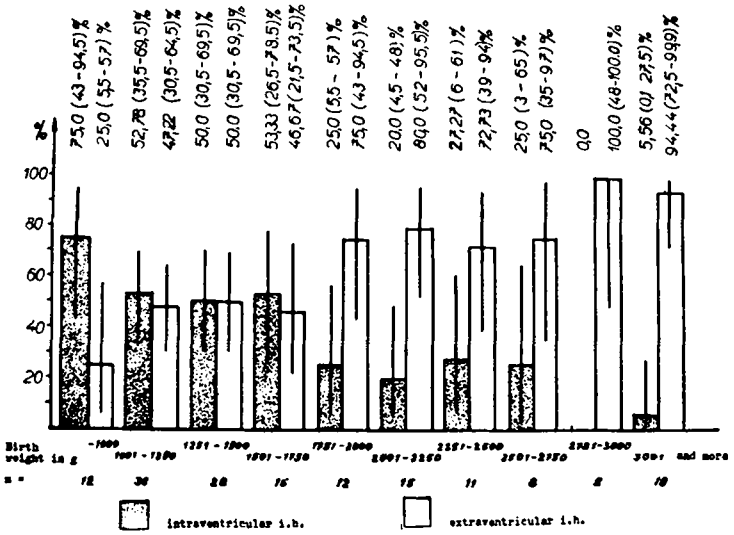

Fig. 4. Incidence of intra- and extra-ventricular I.H. in live-born infants who died of I.H., according to weight groups.

Comparing the findings of intraventricular and extraventricular I.H. in the individual weight groups we found that up to the B.W. of 1,000 g. the intraventricular I.H. prevails; in the range of 1,001—1,750 g. both types of I.H. are approximately of the same importance, while in the higher weight groups the extraventricular prevails over the intraventricular I.H. This difference is statistically significant (x^2—57·53, table value—16·9).

The results unequivocally indicate that the intraventricular I.H. appears especially in premature infants and that there is a direct dependence between the degree of prematurity (grossly expressed by the birth weight), and the incidence of the intraventricular I.H.

Our further studies were aimed at the problem whether there are differences in the relation to the degree of prematurity in the samples in which

the autopsy finding of bleeding into the brain ventricles was unaccompanied with other localization of the I.H. (isolated intraventricular I.H.) and where it was combined with other type or types of I.H. (combined I.H.).

The polygon of weight distribution (Fig. 5) shows that both types of intraventricular I.H. are most frequent in groups with the lowest weight (infants with B.W. to 1,000 g. have not been considered due to incompleteness of data), after that, a decrease follows in both, getting more pronounced and ceasing in the sample with isolated intraventricular I.H. in the weight group of 1,501—1,750 g.; in the sample with combined intraventricular I.H. in the weight group 1,751—2,000 g. The milestone after which the isolated intraventricular I.H. appears only rarely is the B.W. of 1,500 g. whereas in the case of combined intraventricular I.H. it is the B.W. of 1,750 g. The data presented indicate a certain shift to the lower B.W. (i.e. to the higher degree of prematurity) for the isolated I.H., as compared with the combined intraventricular I.H.

This is confirmed also by Table I indicating a lower average B.W. in a sample of infants with isolated intraventricular I.H., as compared with the sample with combined I.H. This

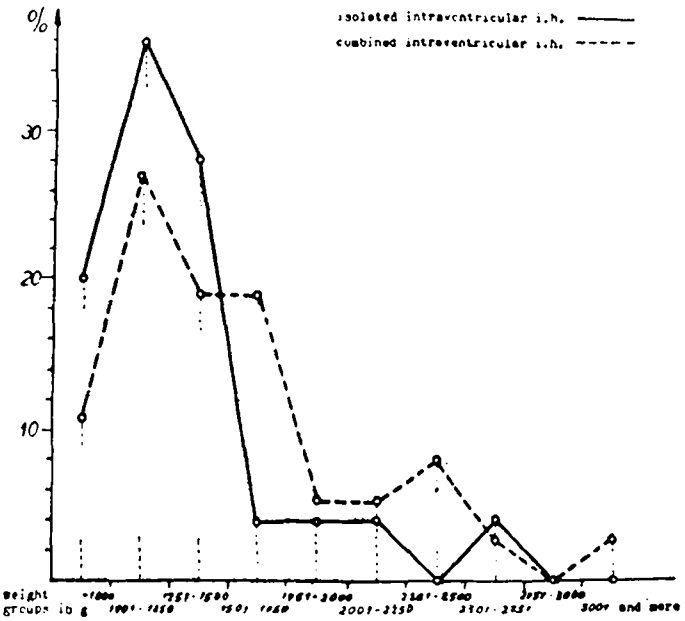

Fig. 5. Polygon of weight distribution in the sample of isolated and combined intraventricular I.H.

difference is statistically significant (t—2·18, critical test value—2·02).

Thus we can say that a more pronounced degree of prematurity is more important for the appearance of isolated intraventricular I.H. than for the appearance of the combined intraventricular I.H.

The analysis of the results in Fig. 3 indicates that with respect to pre-

Table 1. *Average birth weight of infants with isolated and combined intraventricular I.H.*

Infants with intraventricular I.H.	Number of cases	Average weight in g	Mean error in g	Single observation error in g	95% reliability interval for the mean
Isolated	25	1288·00	79·35	396·77	1124·57 1451·43
Combined	37	1570·27	101·94	620·07	1364·15 1776·39

maturity, the factors of general character, responsible for the total neonatal mortality in the individual prematurity degrees, are not decisive for the appearance and incidence of the intraventricular I.H., but that the principal importance lies in the specific factors which are especially distinctly pronounced in small premature infants and which lose their importance with the increasing B.W. They must logically concern the areas of the brain ventricle region, since there is a rich and early developing blood supply of the ventricle wall which contrasts with the poor supply of the brain cortex and centrum ovale (Lelong and Laumonier, 1953), thinness of the vein-walls in the subependymal region is conspicuously different from the thickness of the vein-walls in the brain cortex and in the centrum ovale regions (Gruenwald 1951, Banker & Larroche 1962, Debakan 1962), and finally, the specificities of the composition of the subependymal tissue which due to its cell richness and lack of supporting elements does not afford a sufficient support for the arteries situated there and enables an easy diffusion of the bleeding which arose in it (Hemsath 1934, Gruenwald 1951, Lelong and Laumonier 1953, Znamenacek 1961, Debakan 1962).

For the appearance of intraventricular I.H. circulatory disturbances in the vena cerebri magna system are of importance. The anatomic condition of the respective blood drainage system acts supportingly in this respect.

Larroche (1965) emphasizes that stasis, ruptures of arteries and thromboses appear most frequently at the sites of the strongest blood stream (on the head of the nucleus caudatus and at the foramen of Monroe level), i.e. at the site where the veins draining the white brain matter (vena septalis, chorioidealis and terminalis) unite in the vena cerebri interna.

Other authors mention in this respect the anatomic condition along the vena terminalis (Grontoft 1954) and the position and character of sinus rectus (Schwartz 1961). Of the veins in the vena cerebri magna region the vena terminalis is in pathogenetic connection with the intraventricular I.H. (Rydberg 1932, Hemsath 1934, Lelong and Laumonier 1953, Grontoft, 1954, Benesova 1956, Banker 1962). Plexus chorioideus can be also the source of bleeding into the ventricles (Giraud 1958).

Which, then, are the causes leading to circulatory disturbances in the v. cerebri magna system ?

Most authors are of the opinion that asphyxia is responsible for the appearance of arterial congestion in the vena cerebri magna region and of the subsequent bleeding (Gruenwald 1951, Grontoft 1954, Benesova 1956, Blanc *et al.* 1957, Nesbitt 1957, Znamenacek 1958). In this respect all states enhancing or participating in the appearance of asphyxia act supportingly.

Of the other factors causing the intracranial venous congestion, forces of mechanical character must be taken into account. For this reason an analysis of the types of delivery in infants with intra- and extra-ventricular I.H. was performed. Table 2 (interleaf) shows that in two-thirds of infants with the autopsy finding of intraventricular I.H. a spontaneous birth with head presentation took place (in more than a half of these cases without complications), in one-fourth there was a spontaneous breech delivery and only in a small number of cases—8·06 (2·5—19) per cent the other types of delivery were recorded. (Into the last group the following types were included : transverse position corrected by internal version into breech presentation and terminated by extraction by the leg, extraction by the leg in the breech presentation, collision of twins, deflection positions, caesarean section and forceps delivery.)

When comparing the type of delivery in infants with intra- and extra-ventricular I.H. it can be seen that there are more deliveries with head presentations in the sample with intraventricular I.H. (this is caused by the higher number of deliveries with head presentations without complications), a little less frequent is the incidence of breech deliveries and distinctly less frequent are the deliveries grouped under the head "other types of delivery" where the traumatizing influence of the delivery was the most pronounced.

Although this difference is statistically significant in the evaluation of the whole samples (x^2—9·92, table value-9·49), it ceases to be significant when evaluating the prematures with intra- or extra-ventricular I.H., after the elimination of the mature infants (x^2—7·11, table value—9·49).

Further, the basic causes of the deaths were analysed. We are aware of the fact that death in this period is often a state resulting sometimes from several, mutually connected reasons and consequences and that it is therefore rather difficult to determine which of these was the primary and substantial one. Besides that we know the works of various authors (Rydberg 1932, Nesbitt 1957, Goerttler, 1961, Goerttler and Draisbach 1963) mentioning the difficulties of differentiating the affection of the C.N.S. due to asphyxia or mechanical factors, according to section findings. Nevertheless, we consider the above analysis useful, as it is not based on a merely static and mechanical classification of the autopsy findings according to certain criteria, but on a detailed and complex evaluation of the dynamically followed course of pregnancy and delivery and on the confrontation of these with the autopsy findings.

Our results are summarized in Table 3. When statistically evaluating the basic causes of death in the whole samples of infants with intra- and extra-ventricular I.H. a statistically significant difference is found (x^2—21.

Table 2. *Type of delivery in infants with intraventricular and extraventricular I.H.*

Types of delivery			Head presentation									Breech presentation									Other			Total	
			without complications			with complications			altogether			without complications			with complications			altogether								
			count	%	i	count	%	i	count	%	i	count	%	i	count	%	i	count	%	i	count	%	i	count	%
Intracranial haemorrhage	Intraventricular	Premature	22	37·29	25 52	18	30·51	18·5 44·5	40	67·80	54·5 79·5	8	13·6	6 25	7	11·86	5 23·5	15	25·42	15 38	4	6·78	2 16·5	59	100
		Mature	1			1			2												1			3	
		Total	23	37·10	25 51·5	19	30·64	17 46·5	42	67·74	54 79·5	8	12·9	4·5 26	7	11·29	4 22·5	15	24·19	13·5 37·5	5	8·06	2·5 19	62	100
	Extraventricular	Premature	18	25·71	15·5 37·5	16	22·86	13 35	34	48·57	36 61	10	14·28	7 25	11	15·71	7·5 27	21	30·0	19·5 42·5	15	21·43	12 33	70	100
		Mature	1			12			13			3			5			8			7			28	
		Total	19	19·39	12 28·5	28	28·57	20 38	47	47·96	37·5 58	13	13·26	7 22	16	16·33	9 25	29	29·59	21 39	22	22·45	14·5 32·5	98	100

Table 3. *Basic cause of death in infants with intra- and extra-ventricular I.H.*

Infants with I.H		Basic cause of death	Mechanical birth trauma			Intrauterine asphyxia			Postnatal asphyxia			Profound prematurity			Other			Total	
			count	%	i	count	%	i	count	%	i	count	%	i	count	%	i	count	%
	Intraventricular	Premature	6	10·17	4 21	9	15·25	7 27	8	13·56	6 25	26	44·07	30·5 58	10	16·95	8·5 29·5	59	100
		Mature	1						2									3	
		Total	7	11·29	4 22·5	9	14·52	5·5 28	10	16·13	7·5 28·5	26	41·93	29 56	10	16·13	7·5 28·5	62	100
	Extraventricular	Premature	16	22·86	18 35	14	20·0	11·5 32	5	7·14	2·5 16·5	18	25·71	15·5 37·5	17	24·28	14 36·5	70	100
		Mature	17	60·71	40·5 78·5	5									6			28	
		Total	33	33·67	24 44	19	19·39	12 28·5	5	5·10	2 12	18	18·37	11·5 27·5	23	23·47	15 33	98	100

71, table value—9·49). This difference is most pronounced in the "mechanical birth trauma" (for the intraventicular I.H. in the minus sense) and in the "postnatal asphyxia" and "profound prematurity" (for the intraventricular I.H. this time in the plus sense).

These differences persist even after the elimination of the mature newborns and on evaluating only the samples of prematures with the two types of I.H., yet they are no more statistically significant ($x^2=8·72$; table value—9·49).

Similarly performed analysis of the basic death causes in the newborns with isolated and combined intraventricular I.H. (Table 4) demonstrates that in no case of isolated intraventricular I.H. the mechanical birth trauma could be considered the basic cause of death, whereas in the sample of infants with combined intraventricular I.H. it appears in 18·92 per cent of cases. In the participation of the "intrauterine asphyxia" and "other basic death cause" no marked difference was recorded in our two samples, but in the isolated intraventricular I.H. the participation of "profound prematurity" and "postnatal asphyxia" is greater. These differences could not be, nevertheless, statistically evaluated due to the small number of cases.

Although the analysis of the type of delivery and of the basic death causes in the whole samples with intraventricular and extraventricular I.H. indicates a statistically significant difference implying that the mechanical birth trauma is less important for the appearance of the intraventricular I.H., we cannot state this so unambiguously after the precision of the statistical evaluation and limiting the analysis to the samples of premature newborns only.

The relative underpressure in the vagina in the head presentation, referred to by Schwartz, or the pressure differences in the uteroplacental region (Schwartz 1961) certainly play a role.

Table 4. *Basic cause of death in infants with isolated and combined intraventricular I.H.*

Basic cause of death			Mechanical birth trauma	Intra-uterine asphyxia	Postnatal asphyxia	Profound prema-turity	Other	Total
Intraventricular I.H.	Isolated	Count		3	6	13	3	25
		%		12·0	24·0	52·0	12·0	100
		i		2·5-31	9·5-45	31·5-72	2·5-31	
	Combined	Count	7	6	4	13	7	37
		%	18·92	16·22	10·81	35·13	18·92	100
		i	8·35	6·33	3·26	20-52·5	8·35	

We must not omit to mention the passive congestion of the brain in breech deliveries, caused by the transfer of blood by the pressure of the birth canal to the abdomen and thorax during the presentation of these and by the pressure on the great cervical veins during delivery of the head.

Active participation in the appearance of the circulatory disturbances is attributed also to the vasomotor nerves which cause vasoconstriction and vasodilatation occurring on reflex irritation of the sensitive endings by stimuli of either mechanical or anoxic-metabolic character.

The action of the above-mentioned factors must be understood as a complex, a chain of agents mutually influencing one another. The resulting action—intraventricular I.H.—appears in the premature and therefore especially well-predisposed medium as a result of the summation of all influences of noxious or supporting character (e.g. disturbance of haemocoagulation in the newborn), exerting their activities during pregnancy, delivery and afterbirth. According to the period when they act, the intraventricular I.H. appears in the course of the delivery, but it may appear even before it (Grontoft 1954, Ward 1954, Goerttler 1961, Goerttler and Draisbach 1963), and it is very important that it can appear after birth (Grontoft 1954, Benesova 1956, Blanc *et al.* 1957, Znamenacek 1958).

In the appearance of the intraventricular I.H. due to circulatory disturbances in the *v. terminalis* region three stages can be distinguished : appearance of the circulatory disturbances, appearance of the subependymal haemorrhage, and bursting of the subependymal haematoma into the ventricles.

The appearance of the intraventricular I.H. does not take place in all cases, but according to the intensity and duration of the action of the noxious factors the development can stop at the individual stages mentioned, which was also observed in the material studied.

Summary

On the basis of personal experience during a period of 10 years' research and of the data in the literature, it is attempted to submit, as far as possible, a complex view on the appearance of intraventricular intracranial haemorrhage.

One of the most important factors in the pathogenesis of this type of intracranial haemorrhage (I.H.) is first of all prematurity which is more pronounced in its isolated incidence than in the combination with other types of I.H.

In this connection the specific factors concerning the region in the immediate proximity of the ventricles are principally important, their significance decreases with increasing birth weight.

The appearance of circulatory disturbances in the *vena cerebri magna* system is favourably influenced by the anatomic condition.

The action of asphyxia and mechanical birth trauma exerted either directly or indirectly through the mediation of vasomot or nerves must be understood as a complex, a chain of agents mutually influencing one another.

Intraventricular I.H. appears in the premature and hence an especially well-disposed medium as a result of

the summation of all influences of noxious or supporting character acting during pregnancy, delivery and afterbirth. According to the period when they act, the I.H. appears during the delivery, but it may appear even before it. It is very important to note that it can appear after the birth.

The author is indebted to MUDr M. Stopekova and the members of the staff of the Institute of Pathological Anatomy and of the Obstetrical Clinic in Kosice, as well as to the directors of the mentioned institutions Doc. MUDr I. Kutlik and Professor T. Schwarc for their kind assistance. At the same time the author expresses his thanks to *ing*. J. Vondracek from the Institute of Mathematics, Czechoslovak Academy of Sciences, for the methodic hints in statistical evaluation.

References

Banker, B. Q. and Larroche, J. C. (1962). Periventricular leukomalacia of infancy. *Arch. neurol.* **7**, 386.

Benesova, D. (1956). Damage to the central nervous system of the fetus at the birth recorded in the picture of section findings. (Czech) In *Sbirka ved. praci* 8. p. 57. *Stat. zdrav. nakl.*, Praha.

Blanc, W. A., Brown, R., Silverman, W. A. (1957). Relationship between hematocrit and intraventricular hemorrhage in premature infants. *Amer. J. Dis. Child.* **93**, 63.

Brachfeld, K., Brachffeldova, J., Houstek, J. and Svaty, J. (1950). The occurrence and diagnosis of intracranial haemorrhage in the newborns. (Czech) *Csl. Gynaek.* **15**, 814.

Craig, W. S. (1938). Intracranial hemorrhage in the new-born. A study of diagnosis and differential diagnosis based upon pathological and clinical findings in 126 cases. *Arch. Dis. Childh.* **13**, 89.

Cramer, H. (1954). Mathematical Methods of Statistics. *Princeton Univ. Press*, Princeton, 6th printing.

Debakan, A. (1962). Cerebral birth injury pathology of hemorrhagic lesions. *Res. Publ. Ass. nerv. ment. Dis.* **39**, 196.

Giraud, P. (1958). Les hemorragies meningees des debiles et prematures. Nouvelles recherches anatomo—*cliniques*. *Sem. hop.* (Paris), **34**, 309.

Goerttler, K. L. (1961). Zur Pathogenese der sogen. geburts-traumatischen Blutungen im Zuflussgebiet der Tentorium—Venen. In Verhandlungen der Deutschen Gesellschaft fur Pathologie. 45. Tagung gehalten in Munster vom 23—27, May 1961. p. 362. *G. Fischer Verlag*, Stuttgart.

Goerttler, K. L. and Draisbach, F. J. (1963). On the genesis of tentorium ruptures and intracranial hemorrhages. *Biol. Neonat.* **5**, 59.

Grontoft, O. (1954). Intracranial haemorrhage and blood-brain barrier problems in the newborn. *Acta path. microbiol. scand.* **34**, Suppl. C.

Gruenwald, P. (1951). Subependymal cerebral haemorrhage in premature infants and its relation to various injurious influences at birth. *Amer. J. Obstet. Gynec.* **61**, 1285.

Hemsath, F. A. (1934). Ventricular haemorrhage in the newborn infant. *Amer. J. Obstet. Gynec.* **28**, 343.

Janko, J. (1958). Statistical Tables. (Czech) *Nakl. Csl. akad. ved*, Praha.

Larroche, J. C. (1965). Hemorragies cerebrales intra-ventriculaires chez le premature. I^e partie : Anatomie et physiopathologie. *Biol. Neonat.* **7**, 26.

Lelong, M, Laumonier, R. (1953). L hemorragie massive intraventriculaire du premature. *Sem. hop.* Paris, **36**, 1812.

Nesbitt, R. F. L. Jr. (1957). Perinatal loss in modern obstetrics. *Obstet. and Gynec.* A series. *F. A. Davis Co. Publ.*, Philadelphia.

Potter, E. (1953). Pathology of the Fetus and the Newborn. *The Year Book Publ.*, Chicago.

Rydberg, E. (1932). Cerebral injury in newborn children consequent on birth trauma ; with an inquiry into the normal and pathologic anatomy of the neuroglia. *Acta path. Microbiol. Scand.* Suppl. X.

Schwartz, Ph. (1961). Birth injuries of the newborn. Morphology, Pathogenesis, Clinical Pathology and Prevention. *S. Karger*, Basel.

Srsen, S. (1964). Intraventricular Brain Haemorrhage in the Newborn. Its Significance, Pathogenesis and Clinic in the Relationship to the Other Intracranial Haemorrhage. Slovak. Inaugural Dissertation. Medical Faculty of the J. A. Komensky Univ. Bratislava.

Srsen, S. (1965). The Analyses of Cases with Intracranial Haemorrhage in Relationship to the Maturity or Immaturity. Slovak. *In the press, Bratisl. lek. isty.*

Statistical Research Group, Columbia University (1947). Selected Techniques of Statistical Analysis. *McGraw-Hill Co. Inc.* New York.

Sikl, H. (1961). Pathological-Anatomical Section Techniques and the Principles of the Diagnostics. II ed edition. Czech.

Ward, O. C. (1954). Ventricular haemorrhage in the newborn. *J. Obstet. Gynaec.* **61**, 380.

Znamenacek, K. (1958). The hypothesis on the origin of the late anoxic syndrome and haematocephalus. (Czech.) In Sborn. 9. *pediat. sjezdu*. p. 30. *Stat. pedagog. nakl.* Praha.

Znamenacek, K. (1961). The beginning of the respiration of man. / Czech / *Stat. zdrav. nakl.*, Praha,