J. Neurol. 217, 145—158 (1978)

Journal of
Neurology

Original Investigations

Epilepsy in Children

An Etiological Study Based on Their Obstetrical Records

R. Degen*

The EEG and Outpatient Departments for Epileptic Children (Chief: Prof. Dr. R. Degen) at the v. Bodelschwinghschen Anstalten, Bethel (Direktor: Prof. Dr. V. Alsen)

Summary. Events which might have a causal significance for epilepsy were collected from the obstetrical case reports of 100 epileptic children who were born in four hospitals in a large town. 100 healthy children of the same age, who had been born in the same hospitals, served as a control group. The differences were worked out by means of the Chi square test and where small numbers were involved the Yates theory was used. It indicated that some possibilities of damage (e.g. higher age of the mother at birth, toxemia of pregnancy, premature birth, heavy weight at birth) are important either with respect to all patients or to the different types of attacks, whereas other factors (e.g. abnormal positions, instrumental delivery, coiling of the umbilical cord) whose roles are likewise never usually doubted, can be neglected. Exogenous reactions were found most frequently in the case of patients with grand mal and focal attacks, although, as was expected, they were missing in patients with absences, whose main genetic nature is known. It is pointed out that only with extreme caution may the various possibilities of damage be found responsible for epilepsy in children in general or for the individual types of attacks.

Key words: Epilepsy – Seizures in childhood – Etiology – Obstetrical records in epilepsy.

Zusammenfassung. Es wurden aus den geburtshilflichen Krankengeschichten von 100 epileptischen Kindern, die in vier Kliniken einer Großstadt geboren wurden, die Ereignisse erfaßt, die für das Leiden ursächlich Bedeutung haben könnten. Als Kontrollgruppe dienten 100 gleichaltrige gesunde Kinder, die in denselben Einrichtungen geboren wurden. Die Unterschiede wurden mittels des Chiquadrat-Tests berechnet, bei kleinen Zahlen die Korrektur nach Yates eingeführt. Es zeigte sich, daß einige Schädigungsmöglichkeiten (z. B. höheres Alter bei Geburt, Schwangerschaftstoxikose, Frühgeburt, hohes Geburts-

* *Address for offprint requests:* Prof. Dr. med. R. Degen, Chief of the EEG-department and outpatient department for epileptic children at the v. Bodelschwinghschen Anstalten, Bethel, Postfach 130340, D-4800 Bielefeld 13, Federal Republic of Germany

0340-5354/78/0217/0145/$ 02.80

gewicht) entweder hinsichtlich des Gesamtkrankenguts oder bestimmter Anfallsformen von Bedeutung sind, andere Faktoren jedoch (z. B. Lageanomalien, instrumentelle Geburt, Nabelschnurumschlingung), deren ursächliche Rolle in der Regel ebenfalls nicht angezweifelt wird, per se weitgehend vernachlässigt werden können. Exogene Einwirkungen wurden am häufigsten bei Patienten mit Grand mal und fokalen Anfällen gefunden, fehlten aber erwartungsgemäß völlig bei solchen mit Absencen, deren vorwiegend genetische Natur bekannt ist. Zusammenfassend wird nochmals darauf hingewiesen, daß die verschiedenen Schädigungsmöglichkeiten nur mit aller Vorsicht für die kindlichen Epilepsien insgesamt und die einzelnen Anfallsformen verantwortlich gemacht werden dürfen.

From the etiological point of view a distinction must be made between genetically conditioned and symptomatic epilepsy. The increased occurrence of seizures in the families of epileptics [7, 13, 28, 52, 69], the examination of twins [19, 63, 64], electroencephalographic examinations of families [11, 12, 21, 30, 34—36, 42, 67, 70, 80] as well as the occurrence of epileptic fits in neurometabolic and degenerative diseases of the brain [88, 96] indicate the importance of genetics.

Exogenous factors in the realm of brain damage in infancy and childhood can lead to epilepsy. The damage can be caused during the pre-, peri- or postnatal stages. It is only rarely that the cause of the suffering is explained by laboratory chemical (e.g. phenylketonuria), serological (e.g. toxoplasmosis, listeriosis, zytomegalia), CSF examinations (e.g. meningoencephalitis) or pathological anatomical findings (e.g. neurodegenerative diseases). As a rule we must depend on the anamnesis.

Considering all possible causes of the disorder–the individual types of attacks to varying degrees of frequency—we were able to find factors in from 57% to 87% of the cases (Fig. 1), which might have been responsible for the complaint [28]. One had to realize immediately that not every possibility had any basic connection with the complaint, especially as many children are known to have developed perfectly normally after such disturbances. It was also shown that even in the case of absences, which are predominantly genetically conditioned, factors

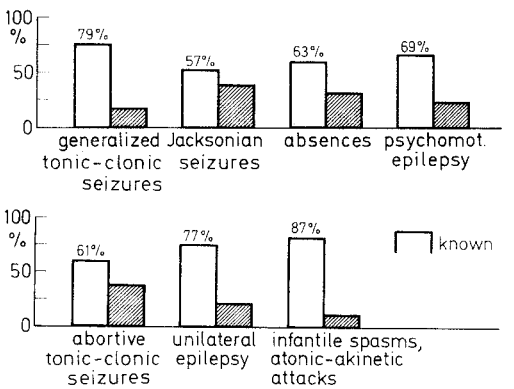

Fig. 1. Exogenous possibilities of brain damage with the different types of seizures

were found in 63% of the cases which only intensified the uncertainty about their etiological importance.

We recently compared the case histories of 422 epileptics with those of 150 healthy children of the same age and determined statistically the differences between the individual possibilities of damage [31]. It was found that both in the number of all patients (10.2%) and the various kinds of attacks (5.6%—13.5%) the occurrence of seizures in the families of patients was greater than was in the families of the control group (0.6%), which underlines the importance of genetics. There were also numerous exogenous factors which must be etiologically responsible partly for the number of all patients and also more so for the various kinds of attacks. On the other hand it was concluded that no statistical significance could be secured for some factors whose importance is never normally disputed. Finally it suggested that a definite difference between genetically conditioned and symptomatic epilepsy is no longer true, but rather the exogenous lesions frequently represent the realization factors for genetically conditioned epilepsy.

This article examines the obstetrical case reports about the course of pregnancy and birth in mothers of epileptic children and compares them with those of healthy children of the same age.

Methods

During the years 1964 to 1967 100 children were treated in the outpatient department of a university children's clinic, all of them having been born in one of four gynecological hospitals in a large town. Pre- and perinatal factors which could have had a causal importance on the complaint were collected from the obstetrical case reports of these children. We used as a control group 100 healthy children of the same age from a kindergarten and an elementary school, who had been born at virtually the same time in one of the four hospitals. Any possibility of damage during pregnancy and birth was collected from their case reports.

The frequency of the different exogenous disturbances was presented in the original and as a percent and the differences between the number of patients and the control group were worked out statistically by means of the Chi square method. In the case of small numbers the results were based on the Yates theory. In order to be able to work out the different statistical significances, the following symbols in Table 2 haven been chosen: $P<0.05=$(a), $P<0.025=$(b), $P<0.01=$(c), $P<0.005=$(d), $P<0.001=$(e), $P<0.0005=$(f).

Clinical Material

Of the 100 epileptic children 24 suffered from pure grand mal, 26 from pure abortive grand mal, 11 from typical and abortive grand mal and 13 from each of the following: infantile spasms or atonic-akinetic seizures, absences and focal attacks. Among those suffering from absences there were 5, from infantile spasms or atonic-akinetic seizures there were 3 and from focal attacks there were 4, who also suffered from grand mal, so that of pure and combined attacks together there were 73 patients who suffered from grand mal. It was determined from the case reports of the outpatient department and as far as available from those of the clinic, that seizures were found in 28% (including those suffering from febrile convulsions) of the relatives of the patients and that more than half of the patients (54%) had their first seizure during the first three years of their lives and only 8% after their tenth year (Table 1). 32% of the patients suffered from some mental retardation to varying degrees, 60.6% had become free of attacks because of anti-

Table 1. Age at the time of the first seizure

Age years	1	1—3	3—6	6—10	>10	Totals
All epilepsies	22	32	19	19	8	100
Grand mal	8	16	5	10	4	43
Abortive grand mal	9	13	7	9	3	41
Absences	—	—	3	9	1	13
Infantile spasms, atonic-akinetic seizures	10	2	1	—	—	13
Focal attacks	1	4	4	3	1	13

epileptic treatment. 52% of the patients were registered as having EEG hypersynchronous activity, 17% had unspecific pathological changes (diffuse changes, unspecific foci etc.) and 31% had normal EEG activity. The individual forms of attacks were to be recognized from their different findings as is to be expected.

Results (Table 2)

With regard to the social status of the mothers of epileptic children it is to be noted there were basically fewer intellectuals (4%) and more working women (30%) than in the control group (10% to 25%); however, statistically this difference is of no significance. All other classes (office workers, manual workers) were represented by roughly the same number. The mothers "without a profession" were housewives.

The mothers of the patients were, on the average, older than those of the healthy children. Altogether 4% of the mothers of all epileptic children were over 40 years of age ($P < 0.05$) and among the mothers of children with grand mal 6.6% ($P < 0.05$) were over 40 (control group 0%). Among the children with grand mal there were more mothers between the ages of 30 and 40 ($34.4\% = P < 0.05$) and fewer between the ages of 20 to 30 ($50.8\% = P < 0.05$); in the control group the percentages were 20 and 70% respectively.

In the case of the mothers of the children with grand mal, miscarriages *before the pregnancy in question* occured more often ($21.3\% = P < 0.05$) than in the control group (10%). The preceeding frequency of premature births was roughly the same as for the mothers of the healthy children.

During the course of pregnancy toxemia and eclampsia played a big etiological part in the case of the mothers of children with grand mal ($9.8\% = P < 0.01$), infantile spasms and atonic-akinetic seizures ($15.4\% = P < 0.005$) as well as the number of all patients ($9\% = P < 0.01$; control group 0%). The mothers of children with grand mal ($6.6\% = P < 0.05$) had hemorrhages which are of significance (control group 0%). The differences in the cases of the symptoms of "nausea" (0%—7.7%; control group 1%) and "pyelitis" (0%—7.7%; control group 4%) were not statistically guaranteed. Altogether, difficulties during pregnancy for the mothers of children suffering from any kind of attacks were noticeably

more frequent (7.7%—24.6%; control group 5%), the only statistical certainty being in the case of those suffering from grand mal (24.6% = $P < 0.0005$) and the number of all patients (21% = $P < 0.001$).

Within the sphere of the *course of birth*, the various positions out of which the child was born (vertex, pelvic or transverse presentation) should be without importance. Also the decrease of the child's heart beat as a single symptom, coiling of the cord, as well as manual expression, played no role. Certainly the healthy children were more often born by spontaneous delivery (94%) and rarely by section (1%), forceps delivery (2%) or vacuum extraction (0%), but there were no real differences from the births of epileptic children (88%, 4%, 3%). Among the possibilities of brain damage a lengthy birth must be taken into consideration in the case of focal attacks (38.5% to 8%), of which the occurrence in the case of the children with grand mal (13.1%) and epilepsy in general (13%) in their turn are statistically of no significance. The frequency of premature and small-for-date babies (weight at birth 2500 g and under) is in the case of grand mal (13.1% = $P < 0.05$), focal attacks (7.7% = $P < 0.05$) and also in the number of all patients (9% = $P < 0.05$) greater than in healthy children (4%). Weight at birth over 4000 g of children with infantile spasms and atonic-akinetic seizures (15.4% to 10%) was increased ($P > 0.05$).

Postnatal 95% of the healthy children were completely unremarkable, whereas only 78% of the children later to become epileptic were ($P < 0.0005$); the differences in the cases of grand mal (75.4% = $P < 0.0005$) and infantile spasms and atonic-akinetic seizures (76.9% = $P < 0.025$) were statistically backed up, not those in the cases of absences (84.6%) and focal attacks (84.6%). A delayed established pattern of breathing was often registered in children with grand mal (14.8% = $P < 0.05$) and in those with infantile spasms and atonic-akinetic seizures (15.4%) and epilepsy in general (12%; control group 5%); asphyxia was often noted with grand mal (9.8% = $P < 0.01$), focal attacks (15.4% = $P < 0.05$) and the number of all patients (10% = $P < 0.005$; control group 0%). 86% of the healthy children, but only 77.8% of those with grand mal ($P < 0.05$), 7.7% of those with focal attacks ($P < 0.0005$) and 72.7% ($P < 0.025$) of those with attacks in general were born within the normal date (± 14 days). A premature birth was often found in children with focal attacks (81.8% = $P < 0.0005$; control group 7.5%) and the number of all patients (13.6% = $P < 0.05$) and a late birth was found (control group 6.5%) in grand mal (18.5% = $P < 0.025$), focal attacks (7.7% = $P < 0.05$) and attacks in general (13.6% = $P < 0.05$). As the children at the time of the drawing up of the results (1964—1967) were in different age groups, neither Apgar scores nor exact neurological examinations were used when some of the sick and the healthy children had just been born, so that this parameter could not be referred to, as interesting as its comparison would have been.

Discussion

As regards the methodology is must be made clear that the individual parameters for the case histories of the patients were taken from 4 different gynecological hospitals; nearly the same documentation however was guaranteed because some

Table 2. Exogenous possibilities of brain damage by considering the obstetrical case histories

	Grand mal		Absences		Infantile spasms, atonic-akinetic seizures		Focal attacks, psychomotor seizures		All epilepsies		Control group	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	61		13		13		13		100		100	
Mother's profession												
working woman	16	26.2	4	30.8	4	30.8	6	46.2	30	30	25	25
office worker, manual worker	20	32.8	2	15.4	3	23.1	3	23.1	28	28	28	28
intellectual	4	6.6	—	—	—	—	—	—	4	4	10	10
without profession	21	34.4	7	53.8	6	46.2	4	30.8	38	38	39	39
Mother's age												
< 20	5	8.2	2	15.4	2	15.4	1	7.7	10	10	10	10
20—30	31 (b)	50.8	9	69.2	10	76.9	11	84.6	61	61	70	70
30—40	**21** (a)	34.4	2	15.4	1	7.7	1	7.7	25	25	20	20
>40	**4** (a)	6.6	—	—	—	—	—	—	**4** (a)	4	—	—
Before pregnancy												
miscarriages	**13** (a)	21.3	1	7.7	—	—	2	15.4	16	16	10	10
premature births	1	1.6	—	—	2	15.4	—	—	3	3	5	5
During pregnancy (prenatal)												
gestational toxemia, eclampsia	**6** (c)	9.8	—	—	**2** (d)	15.4	1	7.7	**9** (c)	9	—	—
hemorrhage	**4** (a)	6.6	—	—	—	—	—	—	4	4	—	—
nausea	2	3.3	—	—	1	7.7	—	—	3	3	1	1
pyelitis	3	4.9	1	7.7	—	—	1	7.7	5	5	4	4
troubles during pregnancy altogether	**15** (f)	24.6	1	7.7	3	23.1	2	15.4	**21** (e)	21	5	5
During birth (perinatal)												
Position of the fetus												
vertex presentation	57	93.4	12	92.3	12	92.3	13	100	94	94	97	97
breech presentation	2	3.3	1	7.7	1	7.7	—	—	4	4	3	3
transverse presentation	2	3.3	—	—	—	—	—	—	2	2	—	—
Slowing of the heart beat	5	8.2	—	—	1	7.7	1	7.7	7	7	6	6
	61		13		13		13		100		100	

Coiling of the umbilical cord	3	4.9	2	15.4	2	15.4	1	7.7	8	8	11	11
Course of labor												
spontaneous	55	90.2	12	92.3	10	76.9	11	84.6	88	88	94	94
section	3	4.9	—	—	—	—	1	7.7	4	4	1	1
forceps	1	1.6	—	—	1	7.7	1	7.7	3	3	2	2
vacuum extraction	—	—	—	—	1	7.7	—	—	1	1	—	—
manual expression	2	3.3	1	7.7	1	7.7	—	—	4	4	3	3
Duration of labor												
< 20 hours	53	86.9	13	100	13	100	8 (f)	61.5	87	87	92	92
> 20 hours	8	13.1	—	—	—	—	**5** (d)	38.5	13	13	8	8
Birth weight												
< 2500 g	**8** (a)	13.1	—	—	—	—	1	7.7	9	9	4	4
2500—4000 g	46	75.4	12	92.3	11	84.6	11	84.6	80	80	86	86
> 4000 g	7	11.5	1	7.7	2	15.4	1	7.7	11	11	10	10
Condition of the newborn (postnatal)												
normal	46 (f)	75.4	11	84.6	10 (b)	76.9	11	84.6	78 (f)	78	95	95
delayed start of breathing	**9** (a)	14.8	1	7.7	2	15.4	—	—	12	12	5	5
asphyxia	**6** (c)	9.8	1	7.7	1	7.7	**2** (a)	15.4	**10** (d)	10	—	—
	54		13		10		11		88		93	
Date of birth												
normal ± 14 days	42	77.8	11	84.6	10	100	1 (f)	7.7	64 (b)	72.7	80	86.0
earlier	2	3.7	1	7.7	—	—	**9** (f)	81.8	12	13.6	7	7.5
later	**10** (b)	18.5	1	7.7	—	—	1	7.7	12	13.6	6	6.5

Explanation of symbols: (a) = $P < 0.05$; (b) = $P < 0.025$; (c) = $P < 0.01$; (d) = $P < 0.005$; (e) = $P < 0.001$; (f) = $P < 0.0005$

of the medical superintendents and assistents who worked with them had come from the university gynecological hospital. In the control group importance was stressed only with regard to the same age; other points worth noting (sex, social position etc.) were not referred to especially as a choice would have had to have been made. From this it is to be assumed that the healthy children represent the average of a normal population.

With regard to the social status, we had to concern ourselves with the mother's profession because the father's was not always given. The known experience [2, 19] is confirmed, although it was not statistically proven that there were more mothers of epileptic children who were workers (30% to 25%) than there were intellectuals (4% to 10%). Unfortunately there was never any distinction made between skilled and unskilled workers, which would doubtless have shown some interesting differences.

The mothers of epileptic children are on the average older than those of healthy children, a fact which was proven partly by the number of all patients, but above all by cases of grand mal. While mothers between the ages of 20 and 30 were more often to be found among healthy children, such differences did not exist with regard to mothers younger than 20 years of age. Thus the obstetrical experience is confirmed, that multipara of 35 or more years of age and primipara over 30 years of age have an essentially higher risk [39, 56]. This could be attributed partly to the smaller elasticity of the soft parts at parturition and partly also to the increasing rate of premature or dysmature children accompanied with and without insufficiency of the after birth [56]. In several cases one could also think of an increased rate of malformations including chromosome anomalies. It has been reported that a certain number of children suffering from infantile spasms [33] and absences [67] were born to older primipara and in both cases the greater age of the mother at birth was seen to be very important [52, 67].

Since toxemia of pregnancy and eclampsia occurred in 9% of the mothers of all patients studied, in 9.8% of those with grand mal and in 15.4% of those with infantile spasms and atonic-akinetic seizures, which is far more frequently than in the control group (0%), this would appear to be of essential causal importance. They not only lead to increased intrauterine [17] and perinatal mortality [4, 81], but they also cause and even increase the possibility of brain hemorrhage and asphyxia [10]. Through the added birth of babies, premature because of toxemia [14, 54], additional damage may also develop. In the literature on epilepsy there are reports, without control groups as a rule, on the increased occurrence of nephropathy and pre-eclampsia in mothers of children with infantile spasms [53, 82, 99], atonic-akinetic seizures [60], grand mal [27] and absences [25].

Of the hemorrhages during pregnancy, those due to placenta previa shortly before birth should be of great importance as this could lead to brain damage as a result of anemia and shock [56, 92]. Hemorrhages during the whole pregnancy experienced by mothers of children with grand mal (6.6%) were far more frequent than in the control group (0%). In the literature one can also read of hemorrhage during pregnancy in mothers of children with grand mal [27], infantile spasms [53, 82] and absences [25, 52].

Even if increased abnormalities are described after hyperemesis [74, 85], this does not lead to epilepsy. The cases which are mentioned in the literature [25—27, 51] should occur only within the range of normal frequency.

Even pyelitis and cystopyelitis, which are mentioned by some authors as occuring in mothers of children with absences [25, 52], play no role etiologically. In our patients they occured in 5% of the cases and in the control group in 4%.

Complications of pregnancy altogether were increasingly found in the mothers of children with all kinds of attacks (7.7%—24.6%; control group 5%), but the statistics could only be proven in the number of total patients and grand mal. Very rarely were they found as reported by other authors [7, 37, 43, 67] in patients suffering from absences (7.7%). Prenatal damage was found by us in all epilepsies in 21% and by Bamberger and Matthes [7] in 16% of the cases. In the case of infantile spasms various authors [26, 51, 53] found they occured with greater frequency.

Although abnormal positions are an added risk [62, 83, 86, 91] which increases even more in the three times higher rate of premature births among those born with a pelvic presentation [44, 93], they occured no more frequently among the epileptic children than among the healthy children (4% to 3%). One suggestion about the increased occurrence of breech presentation for epilepsy in general [7] and absences [20], could not be confirmed by Doose [37] and Janz [52] with regard to absences. We worked out the result of 4% for the occurrence of breeches in the number of all patients and 0%—7.7% for the various types of attacks (control group 3%). Position anomalies today probably no longer play any role, etiologically speaking, because if difficulties are expected or develop at birth, the baby will usually be born by cesarean section.

Although hypoxia is considered the chief cause of the birth "trauma" [22, 23, 32, 56, 94], a slowing of the baby's heart at birth occured no more frequently than in the control group (7% to 6%). However there was asphyxia, which in the opinion of numerous authors [40, 55, 56, 68, 69, 78, 87, 90] can lead to severe cerebral damage, more often in those who have any sort of attacks, especially those with grand mal (9.8%), focal attacks (15.4%) and epilepsy in general (10%; control group 0%). Epileptologists also describe asphyxia as more frequent [26, 52, 53, 60].

Brain damage and pathological EEG findings are said to follow forceps deliveries [47, 48, 59, 72, 73] as well as vacuum extraction [6, 16, 41, 47, 48, 66]. Bajard and Huber [6] have noticed that babies born by vacuum extraction develop convulsions in 2.6% of cases. However there were no control groups to compare with in their investigations. It indicates [8, 75] that forceps is relatively harmless when used as outlet forceps. Toxic brain hemorrhages are not at all rare after secondary cesarian sections [56], and after primary sections only quite isolated, traumatic cases of cerebral hemorrhage are seen [15, 57]. It is therefore no wonder that the individual authors write about instrumental deliveries as causing the various kinds of attacks [7, 25, 26]. However, from our present investigations we are able to report that statistically these occur no more often than in the control group. And manual expression, which has been replaced by other methods in modern obstetrics, plays no role either.

A lengthy birth has been noted often in the case of epilepsy in general as well as with grand mal and focal epilepsy, although differences between them and the control group (8%) can only be statistically backed up in the latter cases (38.5%). Brain damage is said to occur not only after too quick a birth [8, 98], but also after a very long one [24] and even after a birth has been artificially prolonged [18, 50]. Not only infantile spasms [26, 53] and grand mal [27] but also epilepsy in general [7] were noted to occur after prolonged births.

Cerebral damage after premature and low birth weight births is not at all rare [1, 3, 46, 49, 58, 61, 65, 76, 77, 89, 97]. The more underweight the children are, the worse the damage [45, 58, 61]. Various authors [9, 68, 71] have pointed out, however, that it is not just the immaturity that leads to brain damage, but birth injury must have occured. Premature babies are therefore often noted to suffer from various epileptic attacks later on [5, 26, 27, 37, 52, 53]. In the examinations under consideration we found the birth weight 2500 g, or less, more frequent in children with grand mal (13.1%) and in the number of all patients (9%) than in the control group (4%). However, the differences are only statistically proven in the cases of grand mal. Considering the problem from the point of view of the date of birth, it seems that focal attacks occur because of a premature birth (81.8%; control group 7.5%) and grand mal because of a late birth (18.5%; control group 6.5%). A normal birth date ($\pm$ 14 days) was registered far less frequently in the number of all patients (72.7%) and in those suffering from focal attacks (7.7%) than in the healthy children (86%).

95% of the healthy children had no postnatal problems, whereas only 75.4% of the children with grand mal, 76.9% with infantile spasms and atonic-akinetic attacks and 78% of the number of all patients had no such problems. The difference between the children with absences and focal attacks (at present 84.6%) and those in the control group is statistically of no significance.

From Table 2 it appears that some possibilities of damage (e.g. the age of the mother at birth, toxemia of pregnancy, asphyxia, premature birth) are in actual fact responsible for the complaint, whereas we have found no connection with other possibilities (e.g. intrumental delivery, coiling of the umbilical cord, abnormal positions) which have been said to have had a causal significance. In any case almost all authors [7, 25—28, 31, 37, 52, 53, 67] have, as a rule, spoken only of possibilities of damage since, on the grounds of the anamnesis, it is only possible to indicate with certainty the cause of the complaint in individual cases (e.g. severe asphyxia, meningoencephalitis, or serious cranial injury).

In addition one must realize that certain factors are true for all patients, whereas others are true only for certain types of attacks. Absolutely no possibility of damage could be found to be responsible for the complaint in the case of absences, as it is generally accepted that the complaint is predominantly genetically conditioned. Perinatal factors were relatively frequently found for grand mal and focal attacks. Rather surprisingly they were rarely found to have any bearing on infantile spasms; however, as in the case of absences and focal attacks, it was a matter of 13 patients, who certainly can not be taken as representative.

The parallel existence of a familial occurrence of epilepsy along with exogenous possibilities of brain damage in the same patient finally indicates that a difinite

separation between symptomatic and genetically conditioned epilepsy is no longer acceptable. Moreover, it must be agreed that exogenous reactions frequently represent only the realization factor for a genetic complaint.

References

1. Alm, J.: The longterm prognosis for premature born children. Acta paediat. (Uppsala) **42**, Suppl. 9 (1953)
2. Alström, C. H.: A study of epilepsy in its clinical, social and genetic aspects. Acta Psychiat. Neurol., Suppl. 63. Copenhagen: Munksgaard 1950
3. Asher, C., Roberts, J. A. F.: A study on birth weight and intelligence. Brit. J. soc. Med. **3**, 56 (1949)
4. Baird, D., Billewicz, W. Z.: Birth weights and placental weights in preeclampsia. J. Obstet. Gynaec. Brit. Emp. **64**, 370 (1957)
5. Baird, H. W., Borowsky, L. G.: Infantile myoclonic seizures. J. Pediat. **50**, 332 (1957)
6. Bajardi, F., Huber, K.: Erfahrungen mit der Vakuumextraktion unter besonderer Berücksichtigung kindlicher Spätschädigungen. Arch. Gynäk. **198**, 566 (1963)
7. Bamberger, P., Matthes, A.: Anfälle im Kindesalter. Basel, New York: Karger 1959
8. Benaron, H. B. W., Brown, M., Tucker, B. E., Wentz, V., Yagorzynski, G. K.: The remote effects of prolonged labor with forceps delivery, precipitate labor with spontanous delivery and natural labor with spontanous delivery in the child. Amer. J. Obstet. Gynec. **66**, 551 (1953)
9. Beskow, B.: Mental disturbances in premature children at school age. Acta paediat. (Uppsala) **37**, 125 (1949)
10. Brash, A. A.: The effect of toxemia of pregnancy upon the foetus and newborn child. Arch. Dis. Child **24**, 107 (1949)
11. Bray, P. F.: Temporal lobe syndrom in children. A longitudinal review. Pediatrics **29**, 617 (1962)
12. Bray, P. F., Wiser, W. C.: The relation of focal to diffuse epileptiform EEG discharges in genetic epilepsy. Arch. Neurol. (Minneap.) **13**, 223 (1965)
13. Bridge, E. M.: Epilepsy and Convulsive Disorders in Children. New York, Toronto, London: McGraw-Hill 1949
14. Brown, E. W., Lyon, R. A., Anderson, N. A.: Causes of prematurity: Influence of toxemia on the incidence of prematurity. Amer. J. Dis. Child **71**, 378 (1946)
15. Buxton, B. H.: Perinatal mortality in cesarean section. Trans. New Engl. obstet. gynec. Soc. **17**, 87 (1963)
16. Cacara, K. V.: EEG in newborn infants after normal delivery and after forceps and vacuum extraction. Čs. Gynek. **43**, 725 (1964)
17. Carey, H. M., Liley, A. W.: The assessment of the risk intrauterine death in pre-eclampsia. N.Z. med. J. **58**, 450 (1939)
18. Carter, C. H.: The hold-back maneuver as an obstetrical hazard. Obstet. and Gynec. **25**, 710 (1965)
19. Churchill, J. A.: The relationship of epilepsy to breech delivery. Electroenceph. clin. Neurophysiol. **7**, 161 (1955)
20. Conrad, K.: Die erbliche Fallsucht. In: Hb. Erbkrankh. III., 103. Leipzig: Thieme 1940
21. Davidson, S., Watson, C. W.: Hereditary light sensitive epilepsy. Neurology (Minneap.) **6**, 235 (1956)
22. Davis, J. A.: The effect of anoxia in newborn rabbits. J. Physiol. (Lond.) **155**, 56 (1961)
23. Davis, J. A., Tizard, J.-P. M.: Practical problems of neonatal pediatrics considered in relation to animal physiology. Brit. med. Bull. **17**, 168 (1961)
24. Dayton, N. A.: Abnormal labor as an etiological factor in mental deficiency and other associated conditions. Analysis of 20.473 cases. New Engl. J. Med. **203**, 398 (1930)
25. Degen, R.: Klinische und elektroenzephalographische Untersuchungen bei Absencen. Pädiatrie u. Grenzgeb. **1**, 236 (1962)

26. Degen, R.: Klinische und elektroenzephalographische Befunde bei Blitz-, Nick- und Salaamkrämpfen. Psychiatr. Neurol. med. Psychol. **14**, 326 (1962)
27. Degen, R.: Klinische und elektroenzephalographische Untersuchungsergebnisse beim großen epileptischen Anfall im Kindesalter und ihre Beziehungen zueinander. Habil.-Schrift, Leipzig 1963
28. Degen, R.: Klinik und Elektroenzephalographie der Anfallsleiden im Kindesalter. Dtsch. med. Wschr. **92**, 204 (1967)
29. Degen, R.: Die kindlichen Anfallsleiden. Stuttgart: Hippokrates 1976
30. Degen, R., Arnold, H., Bruhn, B., Daute, K. H., Kirsten, G., Külz, J., Klust, E., Läßker, G., Müller, K., Munde, B., Petermann, H.-D., Rohmann, E., Schmidt, G., Schütze, J.: Zur Genetik der Blitz-Nick-Salaam-Krämpfe aufgrund anamnestischer Erhebungen und elektroenzephalographischer Familienuntersuchungen. Schweiz. Arch. Neurol. **110**, 80 (1972)
31. Degen, R.: Die Ätiologie der kindlichen Epilepsien aufgrund anamnestischer Erhebungen im Vergleich mit einer Kontrollgruppe. Fortschr. Neurol. (im Druck)
32. Desmond, M. M., Moore, J., Lindley, J. E., Brown, C. A.: Meconium staining of the amnion fluid. Obstet. and Gynec. **9**, 91 (1957)
33. Doose, H.: Zur Nosologie der Blitz-Nick-Salaam-Krämpfe. Arch. Psychiat. **206**, 28 (1964)
34. Doose, H., Gerken, H.: On the genetics of EEG-anomalies in childhood IV. Photoconvulsive reaction. Neuropädiatrie **4**, 162 (1973)
35. Doose, H., Gerken, H., Hien-Völpel, K. F., Völzke, E.: Genetics of photosensitive epilepsy. Neuropädiatrie **1**, 56 (1969)
36. Doose, H., Gerken, H., Völzke, E.: Genetics of centrencephalic epilepsy in childhood. Epilepsia **9**, 107 (1968)
37. Doose, H., Völzke, E., Scheffner, D.: Verlaufsformen kindlicher Epilepsien mit Spike-wave-Absencen. Arch. Psychiat. **207**, 394 (1965)
38. Drillien, C. M.: Handicaps at school age after very low birth weight. Pediatrics **39**, 238 (1967)
39. Feldstein, M. S.: Analysis of factors affecting perinatal mortality. Brit. J. prev. soc. Med. **19**, 128 (1965)
40. Ford, F. R.: Cerebral birth injuries and their results. Medicine (Baltimore) **5**, 121 (1926)
41. Fulst, W.: Über Einwirkungen des Vakuumextraktor am kindlichen Schädel und Gehirn. Zbl. Gynäk. **82**, 321 (1960)
42. Gerken, H., Doose, H.: On the genetics of EEG-anomalies in childhood III. Spike and waves. Neuropädiatrie **4**, 88 (1973)
43. Gibbs, F. A., Gibbs, E. L.: Atlas of Electroencephalography. Cambridge, Mass.: Addison-Wesley 1952
44. Hall, J. E., Kohl, S. G., O'Brien, F., Ginsberg, M.: Breech presentation and perinatal mortality a study of 6044 cases. Amer. J. Obstet. Gynec. **91**, 665 (1965)
45. Harpers, P. A., Fischer, L. K., Rider, R. V.: Neurological and intellectual status of prematures at three to five years of age. J. Pediat. **55**, 679 (1959)
46. Heimer, C. B., Cutter, R., Freedman, A. F.: Neurological sequelae of premature birth. Amer. J. Dis. Child. **108**, 122 (1964)
47. Heiss, H.: Neue Gesichtspunkte zur perinatalen Gehirnschädigung des Kindes nach geburtshilflichen Operationen. Geburtsh. u. Frauenheilk. **22**, 1305 (1962)
48. Heiss, H., Lechner, H.: Zur Frage der Gehirnschädigung bei Zangenentbindung. Geburtsh. u. Frauenheilk. **15**, 425 (1955)
49. Heiss, I. H., Lundeen, E.C.: The Premature Infant, its Medical and Nursing care. Philadelphia: Lippincott 1941
50. Hughes, J. C.: The study of the epileptic child. Pediat. Clin. N. Amer. **4**, 1061 (1957)
51. Hunt, J. R.: On the occurence of static seizures in epilepsy. J. nerv. ment. Dis. **56**, 351 (1922)
52. Janz, D.: Die Epilepsien. Stuttgart: Thieme 1969
53. Janz, D., Matthes, A.: Die Propulsiv-Petit Mal-Epilepsie. Klinik und Verlauf der sog. Blitz-, Nick- und Salaamkrämpfe. Basel: Karger 1955
54. Jarvinen, P. A., Pankamaa, P., Kinnunen, O.: The full-term underdevelopt liveborn infant. Étud. néonatal. **6**, 1 (1957)
55. Jensen, G.: On the etiological importance of birth injury in children with congenital spastic paraplegia. Acta obstet. gynec. scand. **6**, 392 (1927)

56. Joppich, G., Schulte, F.J.: Neurologie des Neugeborenen. Heidelberg, New York: Springer 1968
57. Kansy, J.: Skull depression in a newborn infant delivered by cesarean section. Pediat. pol. **40**, 305 (1965)
58. Knobloch, H., Pasamanick, B.: Complications of pregnancy and mental deficiency. In: Mental retardation. New York-London 1960
59. Krukenberg, H.: Spätschäden bei Kindern mit Zangengeburt und Wendung. Med. Klin. **32**, 1186 (1930)
60. Kruse, R.: Das myoklonisch-astatische Petit Mal. Heidelberg, New York: Springer 1968
61. Kunstadter, R. H.: Premature infants surviving intracranial hemorrhage at birth. In: J. H. Hess, G. J. Mohr, P. F. Bartelsme "The physical and mental growth of prematurely born children". Chicago: Chicago University Press 1934
62. Lazarow, A.: Fetal injuries in cases of breech presentation. Ginek. pol. **36**, 183 (1965)
63. Lennox, W. G.: Sixty-six twin pairs affected by seizures. Ass. Res. nerv. Dis. Proc. **26**, 11 (1946)
64. Lennox, W. G.: The hereditary of epilepsy as told by relatives and twins. J. Amer. med. Ass. **146**, 529 (1951)
65. Little, W. J.: The influence of abnormal parturition, difficult labours, premature birth and asphyxia neonatorum on the mental and physical condition of the child. Trans. obstet. Soc. Lond. **3**, 293 (1861)
66. Mapelli, G., Pecovari, D.: Clinical and EEG findings in a group of newborn infants after use of the vacuum extractor. Acta neurol. (Napoli) **19**, 552 (1964)
67. Matthes, A., Weber, H.: Klinische und elektroenzephalographische Familienuntersuchungen bei Pyknolepsien. Dtsch. med. Wschr. **93**, 429 (1968)
68. McDonald, A. D.: Intelligence in children of very low birth weight. Develop. Med. Child. Neurol. **6**, 144 (1964)
69. McDonald, A. L.: The aetiology of spastic diplegia. Develop. Med. Child. Neurol. **6**, 277 (1964)
70. Metrakos, J. D., Metrakos, K.: Genetics of convulsive disorders. Neurology (Minneap.) **10**, 228 (1960), **11**, 464 (1961)
71. Mohr, G. J., Bartelsme, P. F.: Developmental studies of prematurely born children. In: J. H. Hess, G. J. Mohr, P. F. Bartelsme "The physical and mental growth of prematurely born children". Chicago: Chicago University Press 1934
72. Müller, D., Treiber, A.: Der Einfluß der Zangenentbindung auf das Zentralnervensystem und auf die psychosomatische Entwicklung des Kindes. Zbl. Gynäk. **82**, 1009 (1960)
73. Müller, K.: Zur Beurteilung von Hirnschäden durch Zangengeburt. Münch. med. Wschr. **100**, 321 (1957)
74. Noack, H.-D.: Stören antiemetische Medikamente und/oder das Erbrechen der Schwangeren die Embryogenese? Zbl. Gynäk. **85**, 938 (1963)
75. Nyirjesy, I., Hawks, B. L., Falls, H. C., Munsat, T. L., Pierce, W. E.: A comparative clinical study of the vacuum extractor and forceps. Amer. J. Obstet. Gynec. **85**, 1071 (1963)
76. Peiper, A.: Krankheiten des Neugeborenen. Leipzig: Thieme 1958
77. Peiper, A., Essbach, H.: Warum sterben die Frühgeburten? Z. Kinderheilk. **73**, 188(1953)
78. Preston, M. J.: Late behavioural aspects found in cases of prenatal, natal and postnatal anoxia. J. Pediat. **26**, 353 (1945)
79. Reiss, H.: Foetal asphyxia associated with umbilical cord around the neck. Ber. ges. Gynäk. Geburtsh. **66**, 84 (1959)
80. Rodin, E. A., Gonzales, S.: Hereditary components in epileptic patients. J. Amer. med. Ass. **198**, 221 (1966)
81. Röttger, H.: Die perinatale Sterblichkeit der Neugeborenen bei Spätgestosen. Geburtsh. u. Frauenheilk. **17**, 783 (1957)
82. Roger, A., Foirier, F.: Les encéphalopathies myocloniques infantiles avec hypsarrhythmie. 9e Réunion européenne d'information électroencéphalographique. Rapport précirculé, Marseille 1960
83. Schmitz, H. E., Smith, C. J., Clumpner, E. R.: End results of breech deliveries. Amer. J. Obstet. Gynec. **69**, 984 (1955)

84. Schreiber, M. S.: Posterior fossa haematoma in the newborn. Med. J. Aust. **2**, 713 (1963)
85. Schreier, K.: Die angeborenen Stoffwechselanomalien. Stuttgart: Thieme 1963
86. Seeley, W. F.: Fetal mortality in breech deliveries. Amer. J. Obstet. Gynec. **57**, 113 (1949)
87. Siegert, F.: Tentoriumriß und intrakranielle Blutung bei Kaiserschnitt. Zbl. Gynäk. **51**, 1649 (1927)
88. Soergel, W.: Über die Zunahme von Extremitäten- und Ohrmuschelmißbildungen seit 1960 im Hinblick auf exogene Faktoren. Geburtsh. u. Frauenheilk. **11**, 1473 (1962)
89. Staemmler, H.-G.: Probleme der Frühgeburt. Med. Klin. **56**, 1529 (1961)
90. Stevenson, S. S.: Paranatal factors affecting adjustment in childhood. Pediatrics **2**, 154 (1948)
91. Stoeckel, W.: Mißlungene geburtshilfliche Eingriffe. Mschr. Geburtsh. Gynäk. **75**, 7 (1926)
92. Thalhammer, O.: Pränatale Erkrankungen des Menschen. Stuttgart: Thieme 1967
93. Thompson, J. F.: Perinatal mortality in breech presentation. Obstet. and Gynec. **15**, 415 (1960)
94. Tizard, J. P. M.: Indications for oxygen therapy in the newborn. Pediatrics **34**, 771 (1964)
95. Töndury, G.: Embryopathien. Berlin, Göttingen, Heidelberg: Springer 1962
96. Ulrich, J.: Die cerebralen Entmarkungskrankheiten. Berlin, Heidelberg, New York: Springer 1971
97. Yllpö, A.: Zur Physiologie, Klinik und zum Schicksal der Frühgeborenen. Z. Kinderheilk. **24**, 1 (1919)
98. Yllpö, A.: Das Schädeltrauma bei der Geburt. Mschr. Kinderheilk. **34**, 502 (1926)
99. Zellweger, H.: Blitz-, Nick- und Salaamkrämpfe (Grusskrämpfe). In: Krämpfe im Kindesalter. Helvet. paediat. Acta, Suppl. V. (1948)

Received April 2, 1977