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EARLY DETECTION AND MANAGEMENT OF CEREBRAL PALSY

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To

ANITA LORING

for her dedication to the work of the
International Cerebral Palsy Society

PREFACE

At the end of September 1984 Dr. M. Veličkovič and Prof. H. Prechtl with the help of the International Cerebral Palsy Society organized an international conference on "New developments in the assessment of early brain damage" in Bled, Yugoslavia. I was invited as a speaker at this conference and I went there, curious, but without too much knowledge about the central theme: cerebral palsy.

During the conference and a satellite meeting I became impressed by the quality of various contributions and also by the great variety of problems related to the etiology, early diagnosis, management and psychosocial aspects of cerebral palsy.

Today, in many areas of biology and medicine, progress seems to require concentration on a very narrow field. As a consequence many conferences are highly specialized and most (young) scientists rightly consider this as most useful for their own work.

On the other hand the care of patients and counselling of parents and other close relatives require a multidisciplinary approach. Also, advances in the study of complicated unresolved medical biological problems are often made unexpectedly by using ideas, theories, approaches or methods from other disciplines.

In this context I thought it might be useful to collect a number of updated articles written by distinguished experts in very different areas, present at Bled conference. Once the various contributors agreed it was logical to ask the main organizers as the editors and to dedicate the book to Anita Loring who spends so much of her energy and time as a secretary general of the International Cerebral Palsy Society. Since I had done most of the organizing work for this book the publisher thought I should act as an editor as well: a layman behaving as an expert as is so often the case in society!

Nevertheless I am happy with this book because it contains chapters on the epidemiology and genetic aspects of cerebral palsy, prenatal- and perinatal risks and the early detection of neurological abnormalities, visual impairment and speech and language disorders. But it also provides information about the management and daily handling of a handicapped child and about important aspects of parenting behaviour, mother-child relationships and the attitude of society towards the handicapped. We hope that this compilation will be of interest to general physicians, obstetricians, pediatricians, neurologists, physiotherapists, psychosocial experts and all those others confronted with the problem of cerebral palsy which still influences the life of so many people.

H. Galjaard

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INTRODUCTION

Cerebral palsy (CP) is a term used for a group of chronic neurological conditions seen in children and characterised by impaired motor function with paresis, incoordination or involuntary movement. The classifications are based on clinical findings and not on etiology. Hemiplegia, diplegia or tetraplegia have been observed in 50-60% of the CP syndromes, dyskinetic features (mainly dystonic or athetotic) in 25-30% and ataxia in 10-15% of the patients. Some 30% of the CP children have mental retardation. Most affected children will show improved motor performance with increasing age but as will be mentioned in different chapters of this book, much depends on an early diagnosis, proper management, parenting behaviour and a good interaction between the patient, parents and professional workers.

The prevalence of CP is 1-2 per 1000 among babies born at term with a weight of > 2500 gm. The prevalence in premature babies is higher and amounts 5-6 per 1000 among babies with a weight of < 1500 gm. These figures have been observed in countries with advanced medical and psychosocial care and they are likely to be higher in countries with less facilities. However, also in Sweden with a declining infant mortality and a constant proportion of CP among surviving babies there has recently been an increase again of the number of CP children (see Chapter 2).

Over the years the panorama of patients designated as CP must have changed. During the last few decades several syndromes associated with spasticity, ataxia, athetosis and other features were found to be due to a specific gene mutation. More than a dozen of single gene disorders have ataxia impaired motor function and athetosis as major clinical features. Each time the etiology of such a syndrome had been resolved it was no longer classified as cerebral palsy and consequently the group of CP patients has changed with time and by definition its etiology remained unknown.

One of the challenges for the future is to further reduce the group of CP patients by discovering the causes followed by primary prevention. This is a difficult task because of the etiological heterogeneity. The overall recurrence risk in families with a CP relative is of the order of 1-2% and most evidence points to a multifactorial etiology, i.e. a combination of as yet unknown genetic and exogenous factors. It is, however, likely that there will also be cases which are due to a single gene mutation or a minor chromosomal aberration whereas the birth of other CP patients might be the result of exogenous factors alone.

In order to be able to study in depth the genetic, biochemical, cellular and physiological basis of CP it will be of great help to identify different groups of patients on the basis of their prenatal and perinatal history and the dif-

ferent clinical features.

In Chapter 2 the Hagbergs report results of their epidemiological studies of cerebral palsy, mild and severe mental retardation and a number of other major neurodevelopmental impairments. They also discuss the changes in perinatal mortality, infant mortality, stillbirths and the rate of CP during the period 1959-1978 in Sweden as well as the changing panorama of CP. Among the major neurodevelopmental impairments CP seems to be most strongly related to negative perinatal events. Preterm birth is a risk factor but much more clearly so in CP associated with diplegia than in other forms. Asphyxia at birth seems to be a predominant pathogenetic factor in babies born at term and who develop the dyskinetic form of CP. In preterm births frequent episodes of postpartum hypoxia were found to be characteristic and this could not be related to any specific clinical form of CP. For further studies on the etiology the Hagbergs recommend to separate the different clinical syndromes as well as the groups of preterms and babies born at term since their brain seems to react differently to perinatal damaging factors.

As is evident from a review by Illingworth (1979) the importance of genetic and prenatal factors in the etiology of cerebral palsy has already been mentioned during a period of fifty years. In a study of 43 families with more than one CP patient Gustavson et al. (1969) found 16 families with cases of identical syndromes and a history of a normal pregnancy, delivery and perinatal period. In this group, congenital nonprogressive ataxia and mental retardation were most common and a Mendelian inheritance is likely. In the 24 families with non-identical familial cases the spastic syndromes were most frequent; here the etiology is probably due to a combination of genetic and exogenous factors. More recently also Fiona Stanley (1984,1986) has pointed to the importance of prenatal and genetic factors on the basis of her studies in Australia.

In Chapter 3 a review is given of the recent advances in the early diagnosis and prevention of congenital disorders. At present several dozens of congenital disorders are known to be due to a chromosomal aberration and more than 3600 diseases in man are known to be caused by a single gene mutation. The cytogenetic methods to identify chromosomal aberrations and the biochemical techniques to diagnose a genetic disease at the level of a specific (enzyme) protein have improved constantly during the last decade. The development of DNA technology will further widen the scope of early diagnosis and enables the detection of a gene mutation at the level of the genome. Basic research in cell biology, biochemistry, immunology and molecular genetics will provide more and more opportunities to elucidate the underlying defects in diseases of unknown etiology, including multifactorial abnormalities such as certain forms of cerebral palsy.

Already, the developments described in Chapter 3 offer new perspectives for couples at risk for a handicapped child and in the future such developments may be of importance for CP as well. Early diagnosis of an index patient with a congenital abnormality or timely detection of carriership followed by

genetic counseling enables couples at risk to adapt their reproduction to their specific situation. Various follow-up studies have shown that a considerable proportion of couples at high risk of an affected child are deterred from pregnancy after genetic counseling.

Yet, the decision of not having any (further) children is very difficult especially for couples who do not have a healthy child. The possibility of prenatal monitoring means an important alternative for many parents at risk. At present, all chromosomal aberrations and some 100 single gene disorders can be detected by analysis of chorion tissue at the 10th week of pregnancy or of cultured amniotic fluid cells at 16-18 weeks gestation. When the fetus is found to be affected the couple may decide to interrupt their pregnancy thus preventing the birth of a handicapped child. Due to improving techniques, better information and a variety of social and economic factors the use of prenatal monitoring and selective abortion is increasing rapidly, not only in Western countries but also in other parts of the world.

Another approach towards prenatal detection of congenital anomalies is ultrasonography. In Chapter 4 this technique and some of its applications are being described. The discovery of anatomical and functional fetal abnormalities in early pregnancy offers better opportunities for pregnancy management and treatment of the newborn. If nothing can be done and the abnormalities detected are of a serious nature early prenatal diagnosis may be followed by termination of the pregnancy.

The methods of ultrasonography have improved considerably during the last two decades and more and more information about normal and abnormal fetal development can be obtained. At present the main emphasis is on routine examination of pregnant women, the early detection of fetal anomalies and the use of ultrasound as a guidance during sampling of fetal material (fetal blood sampling, chorion villus sampling, amniocentesis). The development of real-time ultrasound equipment has, however, also made it possible to study fetal movements and behaviour. As in the postnatal period it is hoped that the study of abnormal behaviour will provide an additional tool in the prenatal diagnosis of fetal abnormalities (Prechtl, 1985).

In the future it may well be that more insight in the genetic and prenatal factors involved in CP will enable a better identification of pregnancies at risk. The parallel improvement of prenatal diagnostic methods might then contribute to the prevention and management of this group of disorders.

At the present time the main emphasis in the early diagnosis of CP still is in the postnatal period. In Chapters 5 and 6 a number of prenatal and perinatal risk factors are described which may call for extra attention during the neonatal period. Intrauterine growth retardation and preterm birth as well as neonatal acidemia are risk factors but very rarely is a single obstetrical factor related to neonatal neurological morbidity. Still, the quality of obstetric and pediatric care is directly related to the neonatal neurologi-

cal outcome.

In evaluating the neurological status of the newborn it must be realized that the nervous system of a newborn baby is strikingly different from that of the older child or adult. A design for comprehensive neurological examination of the full term newborn has been described by Prechtl (1977). A neonatal neurological examination is important for the organization of the well-baby care, the prediction of later functioning and in case of neurological abnormalities for a proper treatment including the mother-baby relationship.

In Chapter 6 Touwen describes some results of follow-up studies of neurologically abnormal infants who had been referred to the pediatric neonatal department of a University hospital. Hypertonia and hemisyndromes of central origin were found to have an unfavourable prognosis and the same is true for hyperexcitability lasting longer than 6-8 weeks. The follow-up studies described also showed that after 4-6 years about 10% of unselected neonatally abnormal babies are neurologically severely abnormal. Although a majority of neurologically abnormal newborns recovered, the small minority who developed cerebral palsy originated from the neonatally abnormal group.

Early diagnosis is essential for optimal management and this is also true for visual impairment. In Chapter 7 different methods to evaluate the visual system are discussed. In premature infants this system is capable of some flexibility in response to abnormal structural and/or functional development. Also there are different sensitive periods where the visual system is susceptible to visual deprivation and these periods seem to be different for various anomalies such as cataract, ptosis, corneal insults, strabismus, astigmatism etc. Recently, various methods have been developed which allow quantitative assessment of behavioural visual functions requiring little cooperation and no verbal capacity. The application of such methods in the evaluation of visual functions in normal and neurologically abnormal newborns is described.

Patients with cerebral palsy often have speech and language disorders but unfortunately referral for therapy is often delayed until the child has failed to attain the "developmental norms" for speech production. Early diagnosis and intervention are important factors in prevention as is pointed out in Chapter 8. Feeding problems may be the first sign of disturbances of the fine motor coordination required for intelligible speech. There are different approaches to the management of speech and language disorders in various types of handicap. One of the important tasks of the speech therapist is counseling of parents in the management of sucking, chewing and swallowing. The parents should be considered as partners in the management: on the one hand they should realize that a CP child is in disadvantage in exploring the environment which in turn is necessary for the acquisition of language, on the other hand parents should not over-stimulate their child. The role of the speech therapist is summarized by Ena Davies as: "to ensure the child has something to say, provide a means of saying it and a reason to communicate."

Chapter 9 deals with the importance of early treatment to prevent or minimize the development of abnormal movement patterns. Since cerebral palsy is a heterogenous group of disorders and all patients anyway live in a specific cultural, social and emotional setting, therapy should be provided on an individual basis. Therapy also includes advising the parents about the everyday handling and sufficient time must be available for listening and answering questions. Challenge of the child is necessary but overchallenge should be avoided.

In Chapter 10 a more detailed account is given of the activities of the physiotherapist. Although there has been (too) much attention for differences among therapies there are also common denominators such as the importance of early treatment, the use of developmental motor stages, the use of sensory stimuli to evoke activity or to reduce spasticity, repetition of motor actions and motivation to move. Chapter 10 also emphasizes the importance of assessment and the interaction with the parents and teachers of the CP patient.

The last three chapters (11, 12 and 13) deal with the important psychosocial aspects of CP and handicap in general. Papousek et al. in Chapter 11 point to the importance of maternal behaviour in acquiring good performance of the infant. They provide evidence that early social interactions between the infant and the parents can effectively contribute to an optimal development. Conversely, difficulties in these interactions may lead to problems in the socioemotional, cognitive and behavioural development. The authors describe a model for the early recognition of interaction failure and provide suggestions for improvement.

Frölich in Chapter 12 focusses on the psychological problems of the mother of a handicapped child. He reports about tensions which often exist between the parents and the professional workers mainly because of different aims and methods. The mother often has a subjective, depressive view on reality including the burden of her daily life. Good contact with the mother/parents is essential because they need early psychological relief and often conversational therapy when the child will be institutionalized.

In the last chapter (13) Morris describes how the social attitudes towards the handicapped have changed during the last decades. Because of the remarkable improvements of infant mortality and -morbidity in many countries most young couples put aside and out of mind the possibility of premature birth, stillbirth or congenital abnormality. When it happens it is felt as a great shock which requires adequate approaches of the professional workers involved. In the first contacts with the parents a handicapped baby should not be handled as something special but it should be examined according to the normal routine. In subsequent contacts both parents should be asked to be present and much attention should be given to what they have to say because parents often are the best observers.

For an optimal development of the handicapped child it is essential not to concentrate on the abnormality alone and to describe what the child will not be able to do. Instead, perspectives should be given of all activities that will be

possible. In this respect maybe the most important aspect is the integration of the handicapped child into the ordinary education system since this will prevent the patient and his family to become outsiders in society.

The Editors.

EPIDEMIOLOGY OF CEREBRAL PALSY AND OTHER MAJOR NEURODEVELOPMENTAL IMPAIRMENTS - RELATIONS TO PERINATAL EVENTS

Bengt Hagberg and Gudrun Hagberg

1. INTRODUCTION

The type of epidemiological research referred to in this survey implies detailed mapping and analysis of available data for population-based series of children with neurodevelopmental impairments. The aim of the present survey was to investigate not only prevalence rates and their changes over time, but also the background patterns underlying the possible origin of the conditions and the variations of disability. The studies are retrospective. Their informative value depends firstly on a strict use of defined criteria for inclusion and exclusion of cases, secondly on the existence and reliability of data from obstetric and neonatological records of all cases, and thirdly on the establishment of a homogeneous system for follow-up and for criteria for diagnosis and classification of disabilities. In Sweden there are good opportunities for carrying out such studies, in particular through the structure of the national health service, and especially the conformably organized neuropaediatrics and habilitation of the handicapped child all over the country. The relative facility of ascertainment of cases and follow-up in a sparsely populated country like ours is also of advantage.

Epidemiological studies are seldom able to give complete aetiological answers. Nevertheless, they can offer important indications as to major patterns of origin, background factors and potential predisposing negative and interacting events, providing clues to a better understanding and to the best mode of future approach. The outcome of such studies can thus lead to more appropriately directed research and hopefully also in the long run to effective measures for prevention of the impairments in question.

2. PREVALENCE OF MAJOR NEUROPAEDIATRIC IMPAIRMENTS

The current Swedish panorama of major developmental impairments is presented in terms of prevalence in Table 1. A high frequency of multihandicap problems is characteristic of all children with damage within the central nervous system (CNS).

The frequencies of additional disorders in cases of mild and severe mental retardation (MR), cerebral palsy (CP) and infantile hydrocephalus (IH), are given in Table 2. The origin of the conditions within these groups can be more or less

clearly attributed to negative events which have occurred pre-, peri- or postnatally, or to combinations of such events.

TABLE 1.

PREVALENCE OF NEUROPAEDIATRIC IMPAIRMENTS IN SWEDEN 1985

	Prevalence per 1000	Age in years
Mild MR (IQ 50-70)	4	8-12
Severe MR (IQ <50)	3	11-16
Early psychosis	0.2	5-20
Cerebral palsy	2	7-10
Infantile hydrocephalus	0.4	2-17
Myelomeningocele	0.5	5
Epilepsy	4	All ages
Myopathy	(0.2	1-15)[1)]
Polyneuropathy	0.2	5-17
Severe visual failure	(~1	1-15)[1)]
Hearing loss	1.4	2-11

[1)] Current epidemiological data lacking

TABLE 2.

APPROXIMATE FREQUENCIES OF MAJOR ASSOCIATED CNS IMPAIRMENTS

	MR*	CP	IH	Epilepsy	Blindness
Mild mental retardation	-	10%	3%	15%	1%
Severe mental retardation	-	20%	6%	30-35%	10%
Cerebral palsy	30%	-	7%	25%	5-10%
Infantile hydrocephalus	35%	25-30%	-	30%	5-10%

*MR = Mental retardation

For feedback information to perinatologists the groups of disorders with a close pathogenetic association with the perinatal period are of particular epidemiological interest today.

As can be seen from the data in Table 3, CP is most often related to negative events during the perinatal period whatever definition for this period is chosen. IH is also closely related to the perinatal period, particularly in the case of babies who have been born very preterm.

TABLE 3.

RATES OF PERINATAL ORIGIN IN FOUR MAJOR CATEGORIES OF CNS DISORDERS

Type of disorder and period of birth	Definition used for perinatal period: Birth to 7 days postnatally	28 wks gestation to 4 wks postnatally
Mild MR* (IQ 50-70) (1966/70)	~10	15-20
Severe MR* (IQ <50) (1959/70)	~10	15-20
Cerebral palsy (1959/74)	~45	~65
Infantile hydrocephalus (1967/82)	~35	~40
Hearing loss (1970/79)	?	~10

*MR = mental retardation

Other characteristic differences between different categories of handicap are illustrated in Table 4, which shows the distribution by gestational age (GA). The data show relatively low frequencies of preterm children among MR cohorts. In contrast, children born preterm constituted nearly one-third of the groups with CP and IH, and in fact more than half of the whole group with CP diplegia (Table 5).

TABLE 4.

DISTRIBUTION OF FOUR MAJOR CATEGORIES OF CNS IMPAIRMENTS AMONG PRETERM AND TERM BIRTHS

	Gestational age	
	≤36 wks	≥37 wks
Mild mental retardation		
n = 91	11%	89%
Severe mental retardation		
n = 73	14	86
Cerebral Palsy		
n = 681	33	67
Infantile hydrocephalus		
n = 202	30	70
General population Sweden	6	94

TABLE 5.

DISTRIBUTION OF DIFFERENT CP SYNDROMES AMONG PRETERM AND TERM BIRTHS

	Gestational age	
CP syndrome	≤36 wks	≥37 wks
Hemiplegia	23%	77%
Diplegia	55	45
Dyskinetic forms	29	71
Simple ataxia	8	92
All CP	33%	67%

In all discussions of changes, particularly gains and hazards indicated by epidemiological data for CNS handicap, parallel alterations in perinatal mortality have to be taken into account as well. The steadily declining figures in Sweden through the last 20 years are presented in Table 6.

TABLE 6.

PERINATAL MORTALITY RATES IN SWEDEN IN 1940-1983

Year	Promille	Year	Promille
1940	45	1977	10.1
1961-65	22.2	1979	8.5
1966-70	17.7	1981	7.8
1971-75	13.8	1983	6.8

The secular trends in perinatal mortality, infant mortality, stillbirths and CP rates during the period 1959 to 1978 are depicted in Fig. 1.

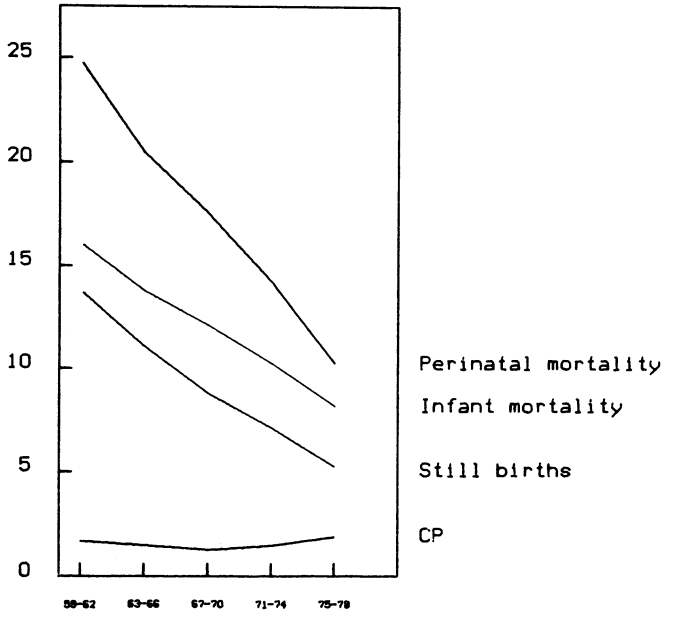


FIGURE 1. Cerebral palsy 1959-1978. Rates of perinatal mortality, infant mortality, stillbirths and cerebral palsy in Sweden.

This presentation deals with three major categories of CNS impairments: mental retardation, infantile hydrocephalus and cerebral palsy. The main emphasis will be upon CP, of which the live-birth prevalence rates and the impairment patterns through the years will be considered in the hope to obtain useful information regarding perinatology.

3. MENTAL RETARDATION

In severe mental retardation (SMR) (IQ <50) biomedical factors are strongly predominant aetiologically (1). Among SMR cases 15-20% originate from factors occurring during late pregnancy, at delivery or during the first weeks of extra-uterine life - i.e. during the period regarded as 'perinatal'. In such SMR cases caused by perinatal damage the presence of an additional CP syndrome is the rule. Small for gestational age and other states of fetal deprivation of supply are important predisposing factors.

On the other hand, preterm infants born with a weight appropriate for gestational age are only exceptionally found among Swedish series from the sixties and early seventies. In the total SMR cohort the aetiology in 70-75% of the cases is more or less referable to the early prenatal period or to preconceptional events (chromosomal 1 40-45%, 'syndromes' 15%, progressive encephalopathies 5-10%, simple familial <5%, untraceable <15%). In some 5-10% SMR has a postnatal aetiology.

To conclude: negative perinatal events are responsible for only a minor proportion of SMR cases. When such events occur, they practically always result in a multihandicap syndrome, a simultaneous CP being particularly characteristic.

The aetiology of mild mental retardation (MMR) (IQ 50-70) was formerly thought to be predominantly of combined constitutional and sociocultural origin. In recent studies, however, a considerable proportion of cases with a biomedical background has been revealed (1,2). This proportion is considered to be larger in populations with a relatively low prevalence of MMR, as in Sweden. The proportion of MMR cases with a perinatal origin was found to be 15-20% in a recent series (1). A high percentage of patients with perinatally derived MMR have other neurodevelopmental abnormalities, but these are usually less severe than those found in SMR. Preterm cases that are appropriate for gestational age are found, but they are relatively rare.

4. INFANTILE HYDROCEPHALUS

In recent years, IH as a sequele of negative perinatal events has gained increasing interest on account of the high percentage of cases of intraventricular bleeding followed by ventriculomegaly among preterm babies. This applies particularly to the rapidly increasing number of surviving babies born at a gestational age of less than 28 weeks (3,4). Ongoing epidemiological studies of IH in Sweden (5,6) have revealed a significant increase in the prevalence of IH among preterm

infants through 1967-1982. The corresponding prevalence rates of IH in term infants have not changed. The total prevalence for the period was 0.53 per 1000 live-born infants.

Aetiologically, at least 70% of cases of IH born preterm can be referred to the perinatal period. In the large majority of them there is proof or an indication of a post-haemorrhagic condition. A minor proportion is secondary to postinfectious arachnoiditis.

Among IH cases born at term, more than two-thirds have indications of a prenatal origin. A broad pattern of different prenatal pathological conditions is known to underly so called 'congenital hydrocephalus'. It is estimated that about 20-25% of cases of IH have a perinatal origin, and again the majority are post-haemorrhagic (6). Some 5% have a postnatal cause.

The frequency of major neurodevelopmental sequelae is high among patients with IH, both those born at term and preterm, in spite of early shunt treatment. Children born at term after negative events during the prenatal period are particularly likely to suffer severe multi-impairment syndromes, usually with combinations of MR, CP and epilepsy.

5. THE CHANGING PANORAMA OF CEREBRAL PALSY AND ITS BACKGROUND

Cerebral palsy (CP) is the nosological group of neuro-developmental impairments in which major changes have occurred during the last 35 years. Aetiologically, perinatal negative events are predominant, irrespective of whether a restricted definition of the term 'perinatal period' (e.g. from delivery to 7th postnatal day as used by us) or a broad one (from a 28 weeks gestation to the 28th day postpartum as used by perinatologists) is applied (see Table 3).

The clinical material studied consisted of three series with a total of 1485 cases of CP during the birth years 1945-1978:

1. An early, nor completely population-based series of 628 cases born in 1945-1953 (7);
2. A population-based series of 560 cases born in 1954-1970 (8);
3. A population-based series of 297 cases born in 1971-1978 (9).

For definitions of pathogenetic periods, causes and risk factors, the reader is referred to previous publications (9, 10). The Swedish classification into syndromes was employed (8). The changing panorama through the three periods 1945-1953, 1954-1970 and 1971-1978 is given period for period below. The prevalence rates in the years 1959-1978, divided into term and preterm births, are illustrated in Fig. 2.

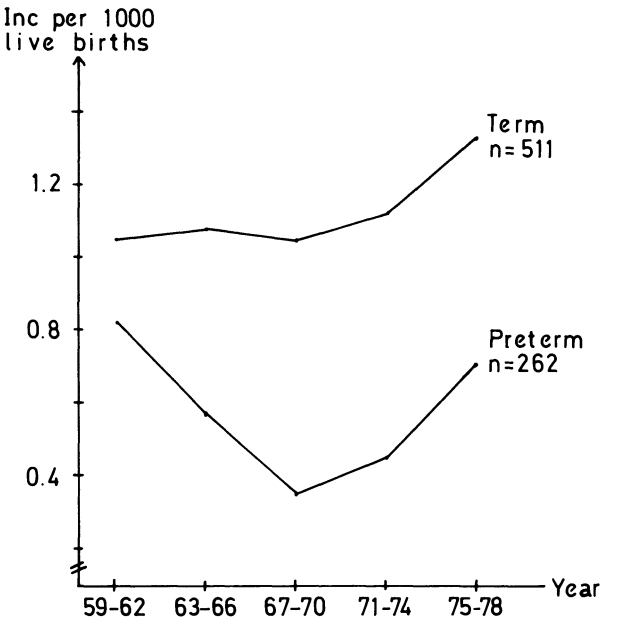


FIGURE 2. Cerebral palsy 1959-1978. Live-birth prevalence of cerebral palsy among term (n = 511) and preterm (n = 262) cases.

a. Period 1945-1953

The most dramatic change through the years is documented from the semi-epidemiological first period. It dates from the early 1950s and occurred parallel to the introduction of a centralized regional organization for exchange transfusion services, providing care for all babies at risk of developing kernicterus from blood group incompatibilities. Severe icterus as the major damaging factor, which it had been in the 1940s, was almost eradicated within a few years. In parallel with this improvement, dyskinetic forms of CP, particularly the classical choreo-athetotic forms, also decreased to a modest fraction. Both term and preterm babies were saved from being impaired.

b. Period 1954-1970

A significantly decreasing prevalence of CP occurred during this period. While the proportion of low birth weight (LBW) infants remained constant (4.3%) through the years, the prevalence of LBW diplegic children decreased significantly, and

this applied particularly to LBW babies weighing ≤ 2.000 g. The decline was considered to have been due not to any particular single factor but more to a combination of systematic efforts on a very basal perinatal care level. Among other improvements compensation for acidosis, hypoxia, hypothermia, hypocaloric states and hypoglcaemia was systematically incorporated into the routines of neonatal care. Such simple measures were thought to have had an essentially positive influence. All this occurred parallel to a progressive centralization of a well developed service in each county for obstetrics and basic neonatology, mainly concentrated to one or two large central hospitals.

c. Period 1971-1978

After the very satisfactory decline in the prevalence of CP through the years 1950-1969, there was a significant increase which began in about 1970 and reached 2.0 per thousand in the years 1975-1978. Like the decrease in the previous period, this increase was mainly referable to spastic/ataxic diplegia in preterm cases of CP. In addition, however, there was also an increase in dyskinetic CP syndromes in infants born at term. Pathogenetically, the rise in the prevalence of CP was mainly accounted for by groups with potential perinatal risk factors (Fig. 3).

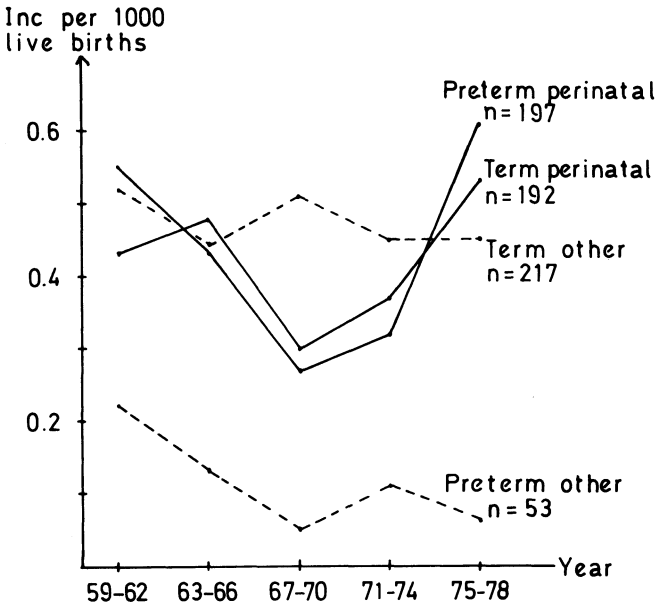


FIGURE 3. Cerebral palsy 1959-1978. Live-birth prevalence of cerebral palsy distributed by origin (obvious pre- and postnatal cases excluded).

When analysed on the basis of surviving babies in birth-specific groups, the prevalence of CP in 1963-1978 was found to have increased in all groups, but the increase was only statistically significant in the low birth weight group of 2000-2500 g (Fig. 4).

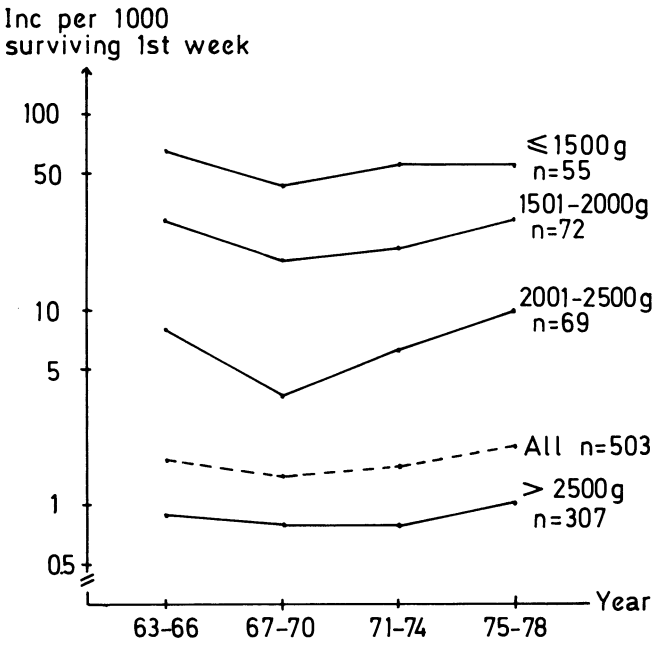


FIGURE 4. Cerebral palsy 1963-1978. Birth-weight-specific prevalence per 1000 infants surviving the first week of life.

Time trends of associated disorders were analysed, and particularly for mental retardation (MR), defined as an IQ level of $\leq$ 70. Marked differences in this respect between preterm and term CP were found (Fig. 5). In spite of the significant increase in the prevalence of all preterm CP, the proportion of children with MR tended to decline gradually through the two latest periods also. In contrast, the prevalence of term CP children with simultaneous MR had increased.

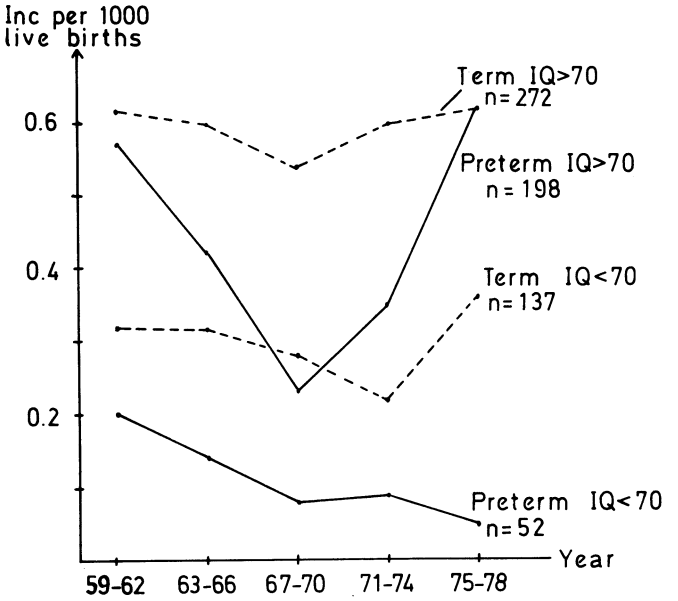


FIGURE 5. Cerebral palsy 1959-1978. Live-birth prevalence of cerebral palsy by IQ among term and preterm children (obvious pre- and postnatal cases excluded).

FIGURE 6. A slightly disabled girl, birth weight 1550 g, with spastic diplegia and normal intellectual development.

Thus three-quarters of the increase in later birth years was characterized by a preterm, mildly motor-disabled, spastic diplegic child with a well preserved intellectual capacity (Fig. 6). One-fourth represented a term, severely multi-handicapped child, usually with a primitive dyskinetic (dystonic) condition combined with MR and often epilepsy (Fig. 7 A and B).

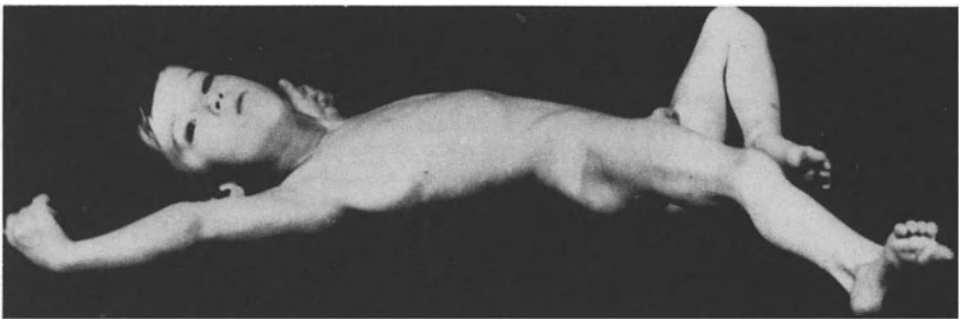
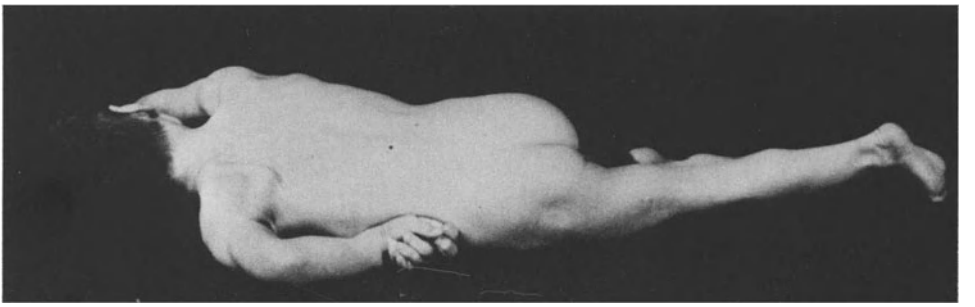


FIGURE 7. A boy born at term with severe birth asphyxia severely disabled by a dyskinetic syndrome with positionally released variations in dystonic posturing.



d. Sequelae from birth asphyxia and postpartum hypoxia

Analyses of the whole CP series (1954-1978) indicated that birth asphyxia in babies born at term was the predominant pathogenetic factor underlying dyskinetic CP. Asphyxia was proportionately less prevalent among cases of spastic CP and only exceptionally noted in patients with congenital ataxia (Table 7).

TABLE 7.

PERCENTAGE SEVERELY ASPHYXIATED* PATIENTS WITH CEREBRAL PALSY BORN AT TERM 1959-1978)

Different CP syndromes		
Dyskinetic	40/69	58%
Spastic	56/388	14%
- Diplegic	29/149	19%
- Tetraplegic	7/32	22%
- Hemiplegic	20/207	10%
Ataxic ("cong.ataxia")	2/54	4%
Total	98/511	20%

*Severe asphyxia defined as: "Respiration not established after 1 minute. Correlation to Apgar score ≤3 at 1 minute".

Characteristic of preterm cases were frequent episodes of postpartum hypoxia independent of the type of clinical CP syndrome. Spastic diplegia was the predominant syndrome among preterms and comprised more than half of the whole spastic diplegic group. There was generally a clustering of associated pre- and perinatal risk factors in the whole CP series.

The data clearly support the concept that the brain of the term infant reacts differently from the preterm brain as the target organ for perinatal brain-damaging factors which lead to CP. Cases born at term should therefore be analysed separately from those born preterm when considering the origin of brain damage related to birth asphyxia and/or postpartum hypoxia. In very recent studies we have analysed in more detail the appearance and impact of birth asphyxia and

postpartum hypoxia in 128 CP children born in 1975-1978 (11, 12). The series was population-based and cases of obvious pre- and postnatal origin were excluded. The series was divided into three gestational age (GA) groups:

Group I (GA $\geq$ 37 completed weeks; n = 76). Birth asphyxia defined as an Apgar Score of < 7 at any time had been present in 30 infants (39%) of whom more than two-thirds had had Apgar scores of $\leq$ 3 at one minute. The corresponding proportions in a control group of 215 non-CP babies were 1.4 and 0% respectively. Postpartum hypoxia had been present in 24 infants (32%), of whom four had been ventilated in a respirator. Postpartum hypoxia among controls had been present in 0.9%. In over 90%, the birth asphyxia had been preceded by signs of fetal deprivation of supply, leanness (birth weights to birth lenghts $\leq$ -1 SD) or intrauterine asphyxia and in 60% it had been followed by postpartal hypoxia. In only two cases was the birth asphyxia the only risk factor noted. Leanness, intrauterine asphyxia and postpartum hypoxia were strongly correlated to the Apgar score. The proportions of these negative items increased progressively with decreasing Apgar scores. Leanness was present, for example in two-thirds of cases with an Apgar score of 0 but only in 4% of those with an Apgar score of 10. The majority of cases with dyskinetic CP syndromes manifested as a severe dystonia had had Apgar scores of $\leq$ 3. Congenital ataxia and atactic diplegia were the only two syndromes with a rather weak association with birth asphyxia.

Group II (GA 32-36 weeks; n = 29). Birth asphyxia had been present in nearly half of the cases and near two-thirds of these had had an Apgar score of $\leq$ 3. Postpartum hypoxia had been present in two-thirds of the cases, of whom slightly fewer than half had been ventilated in a respirator. Spastic diplegia and spastic hemiplegia were the predominant CP syndromes - about 60 and 30% respectively.

Group III (GA $\leq$ 31 weeks; n = 23). Birth asphyxia had been present in half of the infants, of whom 40% had had Apgar scores of $\leq$ 3. Postpartum hypoxia was present in more than 95%, of whom nearly half had been ventilated in a respirator. All infants with birth asphyxia had also had other perinatal risk factors. Fetal deprivation of supply, intrauterine asphyxia, and leanness were relatively less frequent than in the more mature groups. Spastic diplegia and hemiplegia were the dominating CP syndromes, as in group II.

Findings from this series, added to our previous data, emphasize the multifactorial background underlying the brain damage in CP. The proportion of cases with birth asphyxia increased with decreasing GA. The severity was most pronounced, however, in term birth CP infants, of whom more than 2/3 had had an Apgar score of $\leq$ 3. The proportion of cases with postpartum hypoxia increased with decreasing GA, as did the severity. More than 2/5 of the infants born preterm had

needed respirator treatment. Regarding the different CP syndromes, dyskinetic patients born at term and all CP patients born preterm are the ones showing the closest association with asphyxia-hypoxia. Thus attention should particularly be focused on these categories when penetrating factors of importance for perinatal brain damage in future research (9).

e. Epidemiological aspects of gains and hazards

The increasing prevalence of CP in Sweden since the beginning of the 1970s began in spite of a continued and successive decline in the perinatal mortality, infant mortality and stillbirth rates (Fig. 1). This ongoing trend is embarassing but not really surprising. A decreasing birth prevalence of CP - as occurred during the periods before 1970 - can only be achieved if there is a simultaneous substantial decrease in the rate of CP among survivors. If the rate of CP among neonatal survivors is constant, the prevalence of CP per live birth will be bound to rise with a steadily increasing survival rate. This is illustrated for very low birth weight babies in Fig. 8.

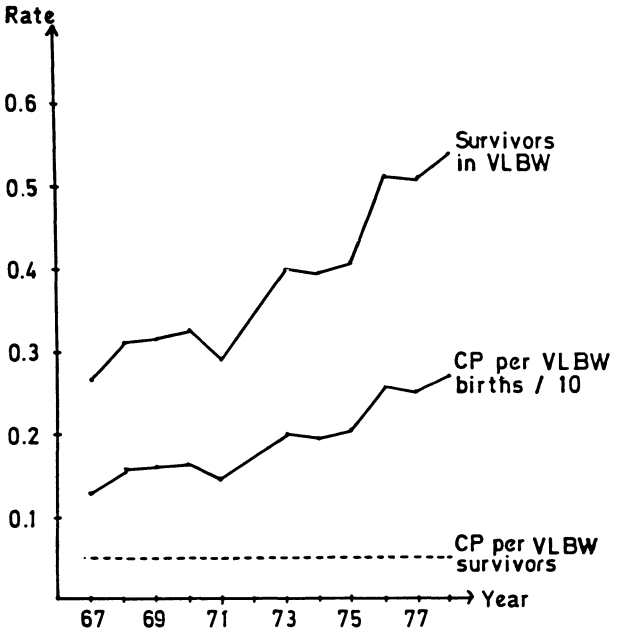


FIGURE 8. Illustration of the logically rising prevalence of cerebral palsy among very low birth weight infants when calculated on the basis of live-births, given a constant rate of cerebral palsy among survivors.

It would therefore be more correct to express the CP prevalence on the basis of neonatal survivors than of liveborns and also to document the data in relation to specified birth

weight categories. This demands access to national statistics on live births and neonatal mortality by birth weight. Such statistics have been available in Sweden since the mid-1960s. Fig. 4 shows the birth weight specific CP prevalence per 1000 babies surviving the first week. The crude CP prevalence shows a significantly rising trend. This rise is predominantly due to the contribution by the birht weight group 2000-2500 g. All the other groups display small secular rising trends and this is particularly alarming with respect to full-term babies with normal birth weights. They constitute the large majority, 94% of all births. Even minor increases in the prevalence of CP will affect a large number of children. These children are mostly severely disabled, and a high proportion are mentally retarded.

TABLE 8.

"GAINS AND HAZARDS" OF PREVENTIVE EFFORTS*

	Gains	Hazards
	additional surviving non-CP children	additional CP children
period 1971-1974	n = 1228	n = 52
period 1975-1978	n = 2668	n = 212

*Based on Swedish epidemiological data for cerebral palsy, in the periods 1971-1974 and 1975-1978 compared with 1967-1970 (calculations per 100 000 births/year).

The impact of the progressively declining perinatal mortality is twofold, with a gain in terms of surviving non-CP children and a cost in the increased number of CP cases (13). These have been calculated for the last two four-year periods of our studies and compared with the figures for 1967-1970 (Table 8). The 'silent' cohort of now surviving and 'healthy' children is impressive - but often forgotten. However, the 'costs' are increasing, the occurrence of additional severely damaged infants born at term being a new and particularly challenging problem for preventive research.

ACKNOWLEDGEMENTS

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EARLY DIAGNOSIS AND PREVENTION OF GENETIC DISEASE

H. Galjaard

1. INTRODUCTION

In chapter 1 the Hagberg's conclude that out of four major neurodevelopmental impairments cerebral palsy is most closely related to negative perinatal events. Yet, genetic factors and disturbances during organogenesis and in later pregnancy have also been mentioned as a possible etiology (1). These observations need not be contradictory since many perinatal events have their origin during the prenatal period; also disturbances during embryonic development may be caused by genetic or environmental factors alone or by a combination of both. Studies on the (genetic) etiology of cerebral palsy (CP) are, however, especially difficult because it represents a rather heterogeneous group of chronic neurological conditions rather than a well defined clinical syndrome (2).

Recently, Bobrow (3) suggested that the group of CP patients may have changed with time because of the exclusion of syndromes associated with spastic paralysis, ataxia and/or dyskinesia each time a chromosomal, genetic or other cause has been discovered for such a syndrome. The remaining patients with unexplained CP, however, still remain a heterogeneous group where yet undetected chromosomal anomalies, gene mutations, multifactorial developmental abnormalities and perinatal complications each may play a role in the different syndromes presently grouped together as CP.

The heterogeneity is not only reflected in the types and severity of physical handicaps and the presence or absence of mental retardation and/or sensory functions, but also in the familial predisposition and recurrence risk. Whereas the overall incidence of CP among babies with a normal birth weight is 1-2 per 1000 liveborns (see also chapter 1) a recurrence risk after the birth of an affected child of 2% has been reported (4,5). Such figures are also found for some common single congenital malformations which are believed to be caused by a combination of genetic and environmental factors such as neural tube defects and cleft lip/palate (6). There are, however, differences among the various CP syndromes. Those associated with ataxia are most often familial and Gustavson et al. (4) estimated that in Sweden 50% of the congenital ataxias with mental retardation are familial compared with a 10% family history of all cerebral palsies (7). Barraitser and Winter (8) mention a 1% recurrence risk for sibs of a patient with CP associated with (double) hemiplegia, diplegia or asymmetric quadriplegia and a 10% recurrence risk

in case of CP with ataxia, dyskinesia or symmetric spastic paraplegia; unfortunately these authors do not provide information about the background of these data.

In cases with a high familial prevalence the involvement of a single gene mutation must be considered as the cause of CP. According to Gustavson et al. (4) about 1.5% of all CP cases in Sweden were autosomal-recessive conditions, but the diagnosis of such conditions very much depends on the diagnostic methods used (9,10). Several congenital disorders of Mendelian inheritance are known to be associated with spastic paralysis, ataxia and dyskinetic features and undoubtedly there will be several more which have remained undetected so far. The elucidation of the exact molecular etiology in congenital disorders of Mendelian inheritance is especially important since the parents are not only confronted with the birth of a handicapped child but also with a very high (25% or 50%) risk of recurrence in each subsequent pregnancy.

During the last decade quite impressive advances have been made in the study of molecular nature of genetic diseases and new methods of early diagnosis and prevention have been developed. Progress has also been made in basic research, diagnosis and prevention of congenital anomalies caused by a chromosomal aberration and the application of some of the modern cytogenetic techniques might be useful in the study of certain groups of patients with CP. In the area of congenital malformation supposed to have a multifactorial etiology, much less advances have been made. Yet, delineation of the recurrence risk, proper genetic counseling and in an increasing number of instances early fetal diagnosis by ultrasound may contribute to a reduction of the number of liveborns with serious multifactorial congenital handicap. It is the purpose of this chapter to review the main possibilities and developments in the early diagnosis and prevention of genetic diseases and related handicaps with the hope that some of these approaches will also be useful in the prevention of cerebral palsy.

2. DIFFERENT TYPES OF GENETIC DEFECTS.

Since Garrod's first description of an "inborn error of metabolism" in 1908 some 3500 conditions in man have been ascribed to the mutation of a single gene (9). Their overall incidence among liveborns is assumed to be between 0.6 and 1.4% (10). Yet, there are still many abnormalities of Mendelian inheritance to be discovered since the human genome is believed to contain between 50,000 and 100,000 structural genes and within one gene many different mutations may occur.

The change of a single gene may have different effects as far as metabolic processes, cell and organ function, clinical symptoms and course of a disease are concerned. Some gene mutations will always remain undiscovered since they are not compatible with early embryonic development and life. Others may result in such severe, generalized abnormalities of essential metabolic processes that death occurs before or shortly after birth. Still other mutations may affect the function of

various organs and may result in physical and/or mental handicaps which may either progress rapidly and fatal in early childhood or have a gradual, milder course. Finally, there are gene mutations which alter the structure of a protein in such a way that its function is affected only after certain environmental challenges (for instance the use of particular drugs or nutrients). Sometimes the function of a genetically altered protein is not affected at all and such mutations will be discovered accidently or in screening programmes (for comprehensive reviews on Mendelian disorders see 9-11).

In over 90% of the 3500 conditions in man known to be of Mendelian inheritance the involvement of a gene mutation has been established on the basis of clinical and pathological features, family studies and more extensive pedigrees. About 55% of the conditions are inherited as autosomal-dominant traits, 38% as autosomal-recessives and 7% are X-linked (9).

In about 10% of the Mendelian disorders a genetically determined protein defect has been discovered. Some 210 of these are enzyme deficiencies, the others concern proteins essential for the cell's structure or for the intercellular space (such as the collagens) or hormones, receptors, circulating proteins, hemoglobins or immunoglobulins.

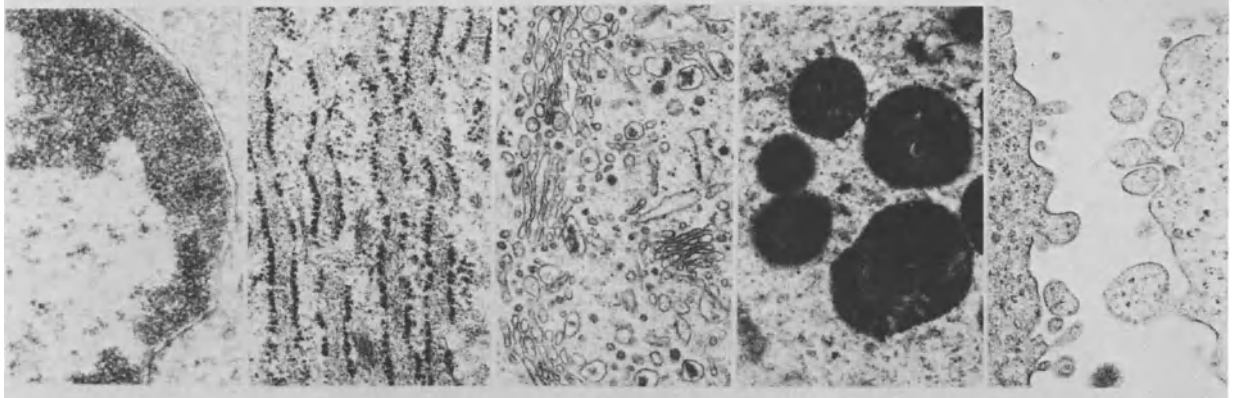
In the majority of these (enzyme) protein defects the existence of a gene mutation has been indirectly demonstrated via an alteration of the structure and/or function of the particular protein in body fluids or cell material from the patient and sometimes the heterozygous parent(s).

Only in relatively few instances, such as in some hemoglobinopathies, studies of the gene sequence in human mutant cells have been performed and have revealed the exact nature of the mutation at the level of DNA itself. The development of recombinant DNA techniques will enable such studies for a much larger number of human genetic diseases in the future.

2.1. Mutations at the level of the gene

Basic research has already revealed the existence of different types of mutations at the level of the gene, but future studies will undoubtedly reveal additional types. Deletion or insertion of a single base will result in an alteration of the reading frame of the genetic code so that every triplet distal to the mutation is changed (frame shift mutation). Another type of mutation is the replacement of one base by another (point mutation). In about 75% of the cases this implies the change of the codon for one aminoacid to another. A third type of mutation is the deletion of larger portions of a gene which often results in the absence of the translation product (protein) of that particular gene. Because of the complex gene regulation mechanism in cells from higher organisms the mutation in one (part of a) gene may affect the expression of other (parts of a) gene(s) (see references 11,16,17,27,42).

FIGURE 1
DIFFERENT TYPES OF GENETICALLY DETERMINED (ENZYME) PROTEIN DEFECTS



NUCLEUS

- no or erroneous transcription

ENDOPLASMIC RETICULUM

- no protein synthesis
- enhanced degradation of newly synthesized protein
- no segregation from E.R.

GOLGI

- impaired glycosylation
- impaired phosphorylation
- wrong compart-mentalization
- secretion or enhanced degradation

LYSOSOMES or other organelles

- no uptake of protein
- no binding to other proteins
- enhanced degradation
- impaired binding to substrate
- impaired enzymatic activity

CELL SURFACE

- absence of receptor
- functional inactive receptor

2.2. Mutations at the level of proteins

Also at the level of proteins the effects of a gene mutation may be very different. In Fig. 1 some major categories of protein defects are summarized mainly derived from experimental work on genetic defects of lysosomal enzymes. Most of these lysosomal storage diseases are associated with mental retardation and physical handicaps often including spastic paralysis, ataxia, dyskinesia and impairment of hearing, vision and speech.

These clinical features are based on cellular disfunction because of the intracellular storage of certain cellular and extracellular constituents which cannot be degraded in the lysosome as a result of a deficiency of one or more lysosomal enzymes normally involved in the breakdown of these constituents (10-13).

During the last few years basic research on the various steps involved in the posttranslational modification and intracellular routing has revealed that a lysosomal enzyme deficiency may be the result of a genetically determined impairment at many different levels (14,15) (Fig. 1). As described above there are certain gene mutations where no immunologically detectable enzyme protein is synthesized. Other mutations affect the structure of the protein in such a way that it is rapidly degraded after its synthesis at the endoplasmic reticulum or that the polypeptide cannot seggregate from its site of synthesis. It is also possible that a mutation alters the primary, secondary or tertiary structure of the polypeptide which in turn may interfere with the correct intracellular routing of the protein. Since many other (enzyme) proteins are involved in the various posttranslational modification steps a genetically determined defect of each of such proteins may also result in the deficiency of one or more other (enzyme) proteins.

For the functioning of a protein it is also essential that the protein is properly located within the cell. Therefore, mutations interfering with processes needed for a correct subcellular routing (for instance specific receptors) will also lead to the deficiency of one or more enzyme proteins; the structure of the latter proteins is not altered.

Finally, the function of an (enzyme) protein may be impaired by mutations interfering with its catalytic activity or its binding properties to substrate or other proteins or cell constituents.

The examples illustrated in Fig. 1 apply mainly to the category of lysosomal proteins but in the context of this chapter a further description of various other types of protein defects resulting from a single gene mutation seems inappropriate; the interested reader is referred to more specialized articles to be found in references 9-11. The number of genetic diseases where the exact nature of the molecular defect has been elucidated at the level of the primary, sec-

ondary or tertiary structure of the protein is as yet rather limited.

Since cerebral palsy is clinically and etiologically very heterogeneous some of the cases known or supposed to be of Mendelian inheritance may be based on different types of molecular defects as described above. The elucidation of such defects usually follows the detection of particular metabolic disturbances and/or the demonstration of a specific gene/protein defect. By using a combination of techniques such as protein purification, radioimmunological analysis of protein biosynthesis and immunoelectronmicroscopical studies on the subcellular routing, the defect may be further identified (14,15). The primary structure of the (mutant) protein can be obtained via protein sequencing or, presently more rapidly via gene sequencing once the coding gene has been cloned (for review see 17). From the primary structure it is sometimes possible to obtain insight in the tertiary structure of a protein and hence in a possible disturbance as a result of the mutation. There are, of course, a number of other, physical and chemical techniques which have been successfully used in the study of (abnormal) protein structure and function.

2.3. Chromosomal aberrations

The description so far has focussed on different types of genetic defects involving a single gene. There are, however, several dozens of congenital disorders which are now known to be caused by an abnormal number and/or localization of microscopically visible chromosomes or parts of these (18,19). The epidemiology of the chromosomal aberrations is well known and the overall incidence among liveborns is about 1 in 170. The majority are aberrations and some 30% are balanced structural rearrangements where the total amount of genetic material is normal but where chromosomes or parts of these have an erroneous localization.

The excess or deletion of chromosomal material nearly always results in severe physical and mental handicap except in the case of a sex chromosome. This is not surprising since a chromosome anomaly involves an excess or deletion of a large number of genes. Even when modern staining techniques are being used (20) the resolution of the microscope sets a practical limit to the detection of chromosomal aberrations of about 0.5 microns. This implies that anomalies involving smaller chromosome parts containing an average of less than 50-100 genes cannot be detected with the present methods. Yet, there may be patients with unexplained physical and/or mental handicaps which are based on an excess or deletion of chromosome parts containing a few genes up to several dozens of genes. Some of the cerebral palsy syndromes might be among them and new techniques enabling the detection of large DNA fragments (21) may yield useful information in the future.

3. METHODS OF EARLY DIAGNOSIS

In all instances of congenital disorders, including genetic disease where the responsible molecular defect has not been

identified, the clinical and pathological manifestations form the basis for the diagnosis. As has been pointed out in the previous section this is the case for about 90% of the diseases of Mendelian inheritance. In the 10% of Mendelian disorders where the primary defect is known the demonstration of specific metabolic abnormalities, an abnormal structure or function of a particular (enzyme) protein or the gene mutation itself enables a diagnosis directly after birth and often far before birth, independent of any clinical features. In such instances there must, of course, be a reason for performing such biochemical analyses and the same is true for chromosome studies. The following paragraphs will summarize the main indications and results of early diagnosis using cytogenetic and biochemical methods.

The establishment of an early diagnosis is in some cases of great importance for the patient since early treatment may avoid or diminish the occurence of physical and/or mental handicap. As will be described in several other chapters of this book an early diagnosis nearly always offers the best perspectives for medical and psychosocial management of the patient and the family in instances where no real treatment can be accomplished. Finally, an early diagnosis of a congenital disorder is essential for genetic counseling of the parents and/or other close relatives of a patient and this in turn may contribute to the prevention of the birth of subsequent affected children in the family. The main aspects of genetic counseling and prenatal diagnosis will be described in section 4.

3.1. Diagnosis of chromosomal aberrations.

The postnatal diagnosis of most chromosomal aberrations requires not more than a few milliliter of heparinized venous blood which can be sent to a cytogenetic laboratory. There, the lymphocytes will be cultured for a few days after phytohaemaglutinin stimulation of their cell division. The chromosome pattern can then be analyzed using one or several of the available staining techniques which enable the identification of each individual chromosome and even of small parts of them by their specific banding pattern (20). The detection of numerical chromosome abnormalities is quite simple, the diagnosis of some structural anomalies, where very small parts of a chromosome are deleted, translocated or inversed, requires more experience. Sometimes, especially in the case of mosaicism (cells with different chromosome patterns within one individual) cytogenetic analysis of other cell types such as cultured skin fibroblasts may be required.

The main indications for cytogenetic analysis are:

- multiple congenital malformation and unexplained mental retardation.
- suspicion on a clinical basis of a syndrome known to be caused by a chromosome anomaly such as Down syndrome.
- X-linked mental retardation.
- abnormal sexual development.

- syndromes associated with chromosome breakage such as Bloom syndrome or Fanconi anemia.
- possible carriership of a balanced chromosome translocation because of the presence of a hereditary chromosome anomaly in one or more relative(s).
- recurrent (⩾2) spontaneous abortions because in these instances 5-10% of one of the parents is a carrier of a balanced chromosome translocation or another chromosome anomaly (22).

A special category of indications are the leucemias and other myeloproliferative disorders where chromosome analysis of bone marrow cells may be important for an exact classification of the disease and for the prognosis and treatment. This category falls outside the scope of this chapter on prevention of congenital disorders.

Depending on the clinical selection chromosome studies in regional laboratories reveal an average of 10-25% abnormalities with the indications mentioned above.

The discovery of a chromosomal anomaly has no therapeutic consequences for the patient but it provides a definite diagnosis and it forms the basis for information about the recurrence risk in subsequent pregnancies of the parents of a patient. In the case of a non hereditary chromosome anomaly this recurrence risk is usually of the order of 1-2% but the age of the mother has to be taken into account as well. In pregnancies at maternal age less than 35 years the population risk of offspring with a chromosomal anomaly is less than 0.5%, but this risk increases to 1-2%, up to age 40 and becomes as high as 10% over 45 years (23).

When an unbalanced chromosome translocation is found in a patient, cytogenetic analysis of the parents should be performed in order to establish whether one of them is a carrier of a balanced chromosome abnormality. If this is so the recurrence risk will vary from a few percent up to 15% and even 100% dependent on the type of chromosome translocation and the question whether the father or mother is a carrier. By further family studies other carriers may be detected before reproduction and timely genetic counseling may then enable prevention of a first affected child in such couples. In the case of cytogenetic studies of (healthy) relatives of a patient thorough information about the reasons for the chromosome analysis and about the possible consequences of carriership is mandatory to avoid unnecessary confusion or anxiety.

In some instances of cerebral palsy, especially when associated with multiple congenital malformations and unexplained mental retardation, cytogenetic studies may be useful. In the (near?) future new techniques, using DNA analysis and/or in situ hybridization with probes capable of demonstrating large DNA fragments (21) it may become feasible to detect chromosome anomalies which presently remain undiagnozed because they fall below the resolution of the microscope (see also section 2).

3.2. Early diagnosis of genetic metabolic disease.

The number of genetic diseases and the clinical heterogeneity within many of these diseases is too large to enable even a summary of the clinical and pathological manifestations. There are, however, a number of symptoms which by themselves are not specific for any single disease, but which might point to the existence of a genetic metabolic disease. In the neonatal period such symptoms are:

- feeding problems and growth retardation
- vomiting
- diarrhea
- dehydration
- metabolic acidosis
- icterus
- hepatosplenomegaly
- convulsions
- hypo/hypertonia
- hyperventilation

In addition to accurate clinical investigation, biochemical analysis of blood, urine and sometimes cerebrospinal fluid may be valuable to direct further diagnostic analyses. More than 100 genetic diseases are associated with abnormalities of the quantity or characteristics of metabolites in body fluids (10,11,24,25). The most frequent biochemical abnormalities in the neonatal period are (hereditary) aminoacidopathies and organic acidemias but also inborn errors of nucleic acid metabolism, mucopolysaccharidoses or oligosaccharidurias will be detected by chromatographic and electrophoretic methods (25). For further identification of certain compounds gas chromatography and mass spectrometry are sometimes needed and also high-performance liquid chromatography is being used by more and more laboratories in the biochemical diagnosis of genetic disease.

During the later development in childhood a number of other clinical features may be indicative for the presence of a genetic disease and especially a combination of several abnormalities is suspicious:

- delayed psychomotor development
- coarsening of facial features
- skeletal abnormalities
- ataxia, dyskinesia
- muscular weakness
- impairment of speech, vision and hearing
- loss of acquired functions
- hydrocephaly
- hepatosplenomegaly
- hyper- or hypotonia
- skin and hair abnormalities
- peculiar odour and aversion towards certain nutrients

Again, extensive clinical, pathological and biochemical investigations are required for a correct diagnosis. Both in the case that metabolite abnormalities are found and when the urine/blood does not show such abnormalities the ultimate diagnosis of a genetic (metabolic) disease should be based on the demonstration of the responsible (enzyme) protein defect. Depending on the type of defect erythrocytes, white blood cells, serum, cultured skin fibroblasts or organ biopsies can be used as a source of diagnostic material. This material can

be sent to a specialized laboratory which should be contacted about the type of material required and the optimal conditions for transport. Also it is essential that diagnosttic material (urine, blood, skin biopsy/cultured fibroblasts) is stored in time when the condition of the patient deteriorates rapidly. A diagnosis may be useful even after the death of a patient because it will provide the basis for genetic counseling and preventive measures in case of an increased genetic risk of the parents in subsequent pregnancies (see next section).

In most instances the demonstration of a genetically determined protein defect involves assays of enzyme activities with either artificial or natural substrates, using colorometric-, fluorometric- or radiometric procedures. For the demonstration of structural/functional abnormalities of other proteins chromatographic, electrophoretic or other methods are used. Once the responsible protein defect has been established it is useful to store cultured skin fibroblasts from the patient and from the heterozygous parents in liquid nitrogen or send them to a cell bank*. This cell material is essential in cases where prenatal diagnosis will be performed in subsequent pregnancies of the parents or other close relatives.

Sometimes it is possible to demonstrate carriership in (healthy) adults and if both partners turn out to be a carrier of the same autosomal-recessive mutation, they can take preventive measures before reproduction. One example of screening for carriership among population at high risk for certain genetic diseases are the programmes for the ganglioside storage disease G_{M2}-gangliosidosis of Tay-Sachs (associated with severe multiple handicaps and early death) among Ashkenazy jews, where about 1 in 30 people is a carrier of this mutation (26). Also, in an increasing number of countries with a high incidence of hereditary anemias (sickle-cell anemia, various forms of thalassemia), screening programmes for carriers followed by genetic counseling and prenatal monitoring of pregnancies at risk have been successful in preventing these diseases (27,28).

Just to illustrate what kind of results are being obtained in biochemical diagnosis the combined results of 6 centres for clinical genetics in The Netherlands are summarized in Table 1. It appears that studies on metabolites in blood, urine and other body fluids reveal a genetic metabolic disease in 4-5% of the children investigated. Enzyme (protein) assays are usually performed on a more selected group of patients and this is reflected in a higher percentage of diagnoses of inborn errors of metabolism.

*Central repositories are available in Canada, the USA and in Europe. One of the latter is located at Dept. Cell Biology and Genetics, Erasmus University, P.O.Box 1738, Rotterdam; Prof. Dr. M.F. Niermeijer tel. (10) 4634307.

Table 1.

Biochemical diagnosis of genetic disease

	Metabolites in blood and urine	enzyme deficiency in leucocytes, fibroblasts or organ biopsy
total number of patients studied	5000	1500
total number affected	225	200
percentage different categories of disease		
carbohydrate abn.	11%	22%
mucopolysaccharidoses	14%	16%
(muco)lipidoses	2%	20%
aminoacidopathies	55%	
organic acidemias	13%	14%
nucleic acid abn.		3%
others	5%	25%

*Data obtained in 1982 by six university laboratories for metabolic diseases covering the 14 million inhabitants of The Netherlands and 180,000 livebirths.

In the case of X-linked diseases with a known molecular defect an early diagnosis of a male patient should be followed by cell biological/biochemical studies of cell material from the mother in order to establish whether she carries the X-linked mutation. Theoretically, in the case of one single patient in a family one third is caused by a new mutation of the germ cells of the mother and the recurrence risk is then usually low. If, however, the mother is a carrier, the risk is 25% and further family studies have to be performed to detect

whether other female relatives are also heterozygous. In such instances timely carrier detection and genetic counseling may prevent the birth of other affected children (for reviews see 10,11,29,31).

In a few instances the biochemical diagnostic methods have been simplified to such an extent that their large scale application at relatively low costs is possible. This has enabled newborn screening for a number of congenital/genetic disorders by analysis of small blood spots dried on filter paper which are sent to specialized laboratories (30). An increasing number of regions and countries have large screening programmes for phenylketonuria (microbiological assay for phenylalanine) and congenital hypothyroidism (TSH and/or T_4 hormone assays) where the occurrence of mental and physical handicaps can be prevented by early treatment following biochemical diagnosis in the neonatal period.

In the group of cerebral palsy patients with clinical features as reported in this section, cytogenetic studies or biochemical assays on body fluids and/or cell material may be useful in some categories of patients. In others, where no chromosomal anomaly or known biochemical abnormality is found, further research must be attempted, of course in addition to the management of the patient and close relatives. An important part of the management is genetic counseling in order to inform parents of a handicapped child about the possible cause, the recurrence risk and preventive measures in next pregnancies.

4. GENETIC COUNSELING AND PRENATAL DIAGNOSIS

4.1. Genetic counseling

Some congenital malformations can be corrected by surgery, and in a few others such as congenital hypothyroidism and a number of genetic metabolic diseases physical and mental handicaps can be prevented by early treatment with hormones, drugs, coenzymes or a specific diet. Unfortunately, most congenital disorders cannot be treated successfully and the emphasis has therefore been on genetic counseling and prevention of the birth of subsequent affected children in one family. Population screening for carriers of a particular gene mutation and prevention of a first affected child is possible to a limited extent as mentioned in the previous section.

The major groups of people in need for genetic counseling are parents who have already given birth to a handicapped child and couples who have one or more affected relative(s) but who do not yet have children themselves. Other reasons for asking genetic advice are the presence of a congenital disorder in one of the partners, consanguinity, higher age and exposure to possible harmful environmental factors such as X-radiation, chemicals, infections, the use of certain drugs and other risk factors during pregnancy like diabetes, inborn error of metabolism, hypertension or blood group antagonism.

Genetic counseling implies information about the severity

and course of the disease, the possibilities of treatment or management, the involvement of hereditary factors, the (recurrence) risk of affected offspring and the possibilities of preventing the birth of a (next) handicapped child. For many counselees this type of information is difficult to understand (most people do for instance not think in terms of statistics like 25% or 1 in 4) and the subjects are often highly emotional. Difficult decisions have to be taken about refraining from pregnancy or accepting the risk of a(nother) handicapped child, fertilization with donor eggs or sperm in case one of the parents is a carrier of a chromosome translocation or gene mutation, or prenatal monitoring and termination of the pregnancy if the fetus will be found to be affected (for review on practical genetic counseling see 31).

The kind of decisions about progeny in case of an increased risk of an affected child depend on a combination of factors: experience with handicaps, the presence of healthy children, the age of the parents, their socioeconomic situation, the severity of the handicap involved, the possibilities of treatment/management, the magnitude of the risk, the availability of preventive methods and the ethical/religious background of the counselees.

Various follow-up studies after genetic counseling indicate that a substantial proportion of parents with a handicapped child and a high recurrence risk are deterred from further procreation. More than 50% of couples with a child suffering of Duchenne progressive muscular dystrophy did not dare a next pregnancy after having been informed about their 25% recurrence risk (Emery, personal communication). Kaback et al. (32), investigating the reproductive behaviour after counseling of couples with a child with the genetic disease cystic fibrosis, found that 60% of them had no further children and 36% had fewer children than they wanted. In the same study more than 80% of the parents said they would favour the availability of a prenatal test and that such a test would encourage them to have more children.

It is clear that also parents of children with cerebral palsy need genetic counseling. This is especially important in those syndromes which are of Mendelian inheritance (1,4) with a very high recurrence risk. But also in cases which seem to be multifactorial and where the recurrence risk is probably of the order of a few percent it is important to inform parents about this. What seems to be a low risk to the doctor, physiotherapist or psychosocial expert may be experienced as an unacceptable high risk to couples who have personal experience with a severily handicapped child in daily life.

Proper genetic counseling should be based on exact information about the type of handicap, its cause and its pattern of inheritance. Ample time must be available to provide the information to the counselees and in most instances two sessions are necessary as well as some written information which can be of help for the counselees to understand and/or to

formulate new questions. Doctors who are closely involved in the care of specific groups of patients may also be best suited to provide genetic counseling if they are sufficiently knowledgeable and have enough time. In complex situations as far as the diagnosis, family history and possible genetic factors are concerned, it is to be recommended to refer the parents and/or other relatives to a specialized centre of clinical genetics.

4.2. Prenatal diagnosis of congenital disorders.

For an increasing number of congenital disorders, fetal diagnosis in early pregnancy has become possible which offers an important perspective for parents at increased risk of a handicapped child. In some instances the diagnosis of a fetal malformation enables the obstetrician to adapt the management of the pregnancy and delivery in such a way that the chances for the baby improve significantly. Especially the improvement of ultrasound methods have had a major impact on fetal monitoring. Close cooperation between obstetrician/ultrasound expert on the one hand and the pediatrician/neonatologist, pediatric neurologist and (neuro)surgeon on the other hand, may lead to timely intervention preventing permanent damage as a result of fetal malformation (33,34) (see also chapter in this book by Kurjak).

Again, most fetal abnormalities cannot be adequately treated and in those instances early prenatal diagnosis can be followed by interruption of the pregnancy thereby preventing the birth of a handicapped baby. Early fetal diagnosis is presently possible for all chromosomal aberrations, some 80 genetic metabolic diseases, open neural tube defects and a variety of other structural malformations (for reviews see 10,28,33-35).

At 16 weeks of pregnancy transabdominal amniocentesis can be performed and in experienced hands 10-20 ml of amniotic fluid can be aspirated with hardly any risk for mother and fetus. The viable cells from the fetal skin and mucous membranes can be cultivated and usually after 10-14 days there are enough cell divisions to enable reliable cytogenetic analysis. In this way fetal chromosomal anomalies such as trisomy 21 (Down syndrome) and others can be detected and also the fetal sex which is important in pregnancies at risk for X-linked diseases where the responsible molecular defect is not known. In case of a female fetus the parents can be reassured, if a male fetus is found there is a 50% risk that it will be affected and parents may want to interrupt their pregnancy thus avoiding the birth of a handicapped boy. The ethical disadvantage of this approach is that in 50% of the cases a non affected male fetus is being aborted.

Fetal open neural tube defects can easily be detected by an elevated level of the fetal protein alphafetoprotein in the amniotic fluid supernatant and ultrasound examination will provide additional diagnostic information.

The prenatal detection of genetic metabolic diseases is more complex and requires (micro) biochemical analyses of cultured amniotic fluid cells and comparison of the results with those from analyses on amniotic fluid cells from controls and skin fibroblasts from an index patient, the heterozygous parents and controls (see also section 3). About 80 genetic (enzyme) protein defects are expressed in cultured fibroblasts and amniotic fluid cells and for these diseases a prenatal diagnosis in early pregnancy is possible usually 2-3 weeks after amniocentesis when proper techniques are being used (10). This implies that in cases of an affected fetus the pregnancy cannot be terminated before 18-19 weeks gestation.

In Table 2 the results are summarized of more than 10,000 second trimester fetal diagnoses performed in our centre at Erasmus University. The overall percentage of fetal abnormalities is 4.6% and in nearly all of these cases the parents decided to ask for interruption of their pregnancy. About 95% of the couples at risk could be reassured on the basis of the analytical results. These couples now have a healthy baby whereas many of them would otherwise not have dared a pregnancy because of their increased genetic risk. Follow-up studies have not shown any adverse effects on the development of the fetus and child after amniocentesis (10,35) although a recent Danish study suggests a somewhat higher incidence of respiratory problems (36).

TABLE 2.

EXPERIENCE WITH PRENATAL DIAGNOSIS IN ROTTERDAM

(up to 1-6-1985)

Indication	No.pregnancies tested	no. and % fetal abnormality	
Maternal age ≥38 Yr.	4213	121	2.9%
Previous chromosome abnormality	1030	13	1.3%
Parental chromosome translocation	227	29 (unbalanced)	13%
Risk X-linked disorder	240	111	
Risk open neural tube defect	3347	1 chrom.abn. 36 NTD	1.1%
Risk genetic metabolic disease	525	19 chrom.abn. 98	19%
Other indications	643	42	6.5%
Total	10.225	469	(4.6%)

During the last few years an important new approach towards prenatal diagnosis has been introduced: chorionic villus analysis (for reviews see 28,37,38). At 10 weeks gestation it is possible to aspirate some chorionic tissue using a thin (1 mm diameter) flexible, polythene catheter which is introduced through the cervical canal under ultrasound control. Methods have been developed which enable direct chromosome pregnancies and direct biochemical diagnoses of nearly all genetic metabolic diseases which are also detectable in cultured amniotic fluid cells (37,38). In the latter case chorionic villi from control pregnancies and skin fibroblasts from an index patient and the heterozygous parents serve as comparative cell material (38).

The main advantages of chorionic villus analysis are the early stage of pregnancy, the painless procedure, the rapid diagnosis (one to few days after sampling) and the possibility of abortion by vacuum aspiration as an outpatient procedure if the embryo is found to be affected. Although from an ethical point of view it still means the termination of embryonic life, the psychological burden for the couple, especially the mother, is much less than in the case of late termination at 18-20 weeks after a 2-3 weeks waiting period.

The risk of chorionic villus sampling has not yet been sufficiently evaluated but the data from large series (28,37) and those from a small matched-control series (39) are promising.

Table 3.

DNA ANALYSIS IN EARLY DIAGNOSIS OF GENETIC DISEASE

Direct demonstration of gene mutation	Via linked polymorphisms	
Sickle-cell anemia	Some β-thalassemias	Adrenoleucodystrophy
α-Thalassemia	Phenylketonuria	Polycystic kidneys disease
Some β-Thalassemias	Haemophilia fact.III	Retinitis pigmentos.
α_1 -anti trypsin deficiency	Haemophilia fact.IX	Cystic fibrosis
OTC deficiency	Duchenne musc.dystr.	Huntington chorea?
Chron.granulomatous disease	Becker mucs.dystr.	Adrenal hyperplasia

The scope of fetal diagnosis will be further widened in the future by the application of recombinant DNA technology. In

this case the gene mutation is demonstrated either directly, like in sickle-cell anemia, or indirectly by the demonstration of restriction fragment length polymorphisms closely linked to the mutation (16,28,40,41). Table 3 summarizes the present potential of DNA analyses in fetal diagnosis of genetic disease. The advantage of this approach is that it is not necessary that the protein defect responsible for a genetic disease is expressed in the available fetal cells nor is it required that this defect is known as exemplified by the prenatal diagnosis of Duchenne muscular dystrophy (40).

Disadvantages of DNA analyses based on linked polymorphisms are the necessity of extensive family studies in order to investigate whether the available DNA probes are informative either for a reliable diagnosis of an affected fetus or for excluding that it is affected. Also there is always the possibility of misdiagnosis because of recombination; the chance for this to occur increases with the distance between the gene mutation (not demonstrated) and the linked polymorphism(s) which is demonstrated by using one or several DNA probes. Finally, non paternity may cause a false interpretation of DNA analysis in family studies.

Despite these limitations the (in)direct demonstration of gene mutations by DNA analysis has already contributed to prenatal diagnosis and is likely to do so more in the future (41). It is possible that studies on certain categories of patients with cerebral palsy will also reveal linkages with specific DNA sequences. It is, however, apparent from other contributions in this book, that attention must also be given to exogeneous factors which in combination with a certain genetic constitution may result in CP.

Another development which in the future may contribute to the prenatal diagnosis of syndromes associated with cerebral palsy is the detection of abnormal fetal motor behaviour by ultrasound techniques (42).

Because of the considerable heterogeneity of cerebral palsy and the fact that many of the syndromes seem to be of multifactorial etiology, much basic research will, however, be required before the molecular basis of the different syndromes will be understood. This chapter was meant to summarize the various approaches towards research, early diagnosis and prevention of congenital disorders. Some of these disorders like CP now were not understood in the past but can presently be prevented to a certain extent in individual families and in some instances even at a larger (population) scale.

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ULTRASONOGRAPHY OF THE NORMAL AND ABNORMAL FETAL NEUROANATOMY

A.KURJAK, V.LATIN, Ž.ALFIREVIĆ, M.BILJAN

1. INTRODUCTION

The lack of any yet proven deleterious effects to the mother or fetus has made ultrasound a unique and powerful tool for evaluation and management of the obstetric patient. Up to now ultrasound has been used predominantly to identify placental location, fetal position, number of fetuses and gestational age. Recent improvements in ultrasound technology, particularly the introduction of new high-resolution real-time instrumentation, favour the detection of subtle differences in fetal soft tissue structures. This has increased our knowledge and awareness of normal fetal anatomy which is very important, especially if one is to make a confident diagnosis of a congenital anomaly.

The ultrasonic analysis of the normal intracranial anatomy by physicians involved in obstetric sonography gives not only the possibility of choosing the exact scanning plane for cephalometry, but also allows an accurate and early diagnosis of pathological intracranial conditions. This paper reviews recent experiences in the ultrasonic evaluation of normal and abnormal fetal developmental neuroanatomy.

2. NORMAL NEUROANATOMY

It is essential to understand the normal sonographic appearance of the brain in order to avoid confusion between the normal structures or variations of anatomy and pathological states.

The fetal head can be visualised by means of ultrasound from the 9th gestational week. The main part of solid brain tissue is made up of the primordia of thalamus and corpus striatum at this time(1). The large fluid-filled cerebral vesicles can also be seen, but clear visibility of cerebral ventricles is possible only after the 13th week. (Fig. 1).

The cerebral subarachnoid space in the fetus can be seen as early as 13 weeks. This space, measuring 1 to 3 mm, surrounds the brain parenchyma and contains varying amounts of fluid. After 30 weeks of pregnancy this can be seen rarely, probably because of increasing size of the temporal and parietal lobes (2).

At the 13th week of pregnancy the lateral ventricles are large in comparison with the size of cerebral hemispheres. They occupy more than 50% of the hemispheres and are not yet differentiated into the central parts, anterior, posterior and inferior horns. The lateral walls of the anterior third of the lateral ventricles are demonstrated as two lateral echoes

running parallel to the midline echo complex (Fig. 2).

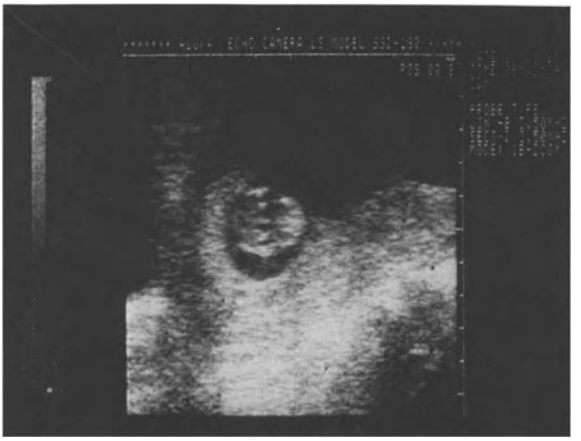

FIGURE 1. Fetal head at the 12th week of pregnancy. Echogenic choroid plexi filling lateral ventricles are demonstrated.

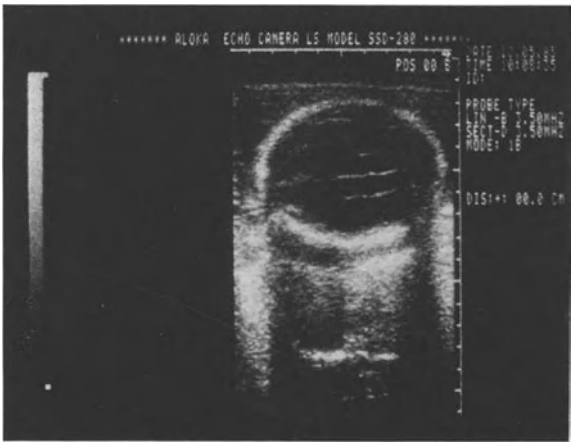

FIGURE 2. The bodies of the lateral ventricles at the 21st week of pregnancy.

The lateral walls of the middle and posterior thirds of the ventricles diverge from the midline echo almost reaching the skull posteriorly (Fig. 3).

Finally, by the 25th week of pregnancy the lateral ventricles take on the characteristic pattern which will be recognized

throughout the remainder of pregnancy. The lateral ventricular size in relation to the transverse intracranial dimension (lateral ventricular width/hemispheric width ratio, LVW/HV ratio) reach almost constant value of 0.29. This value remains unchanged until term, except from another slight decrease during the last two weeks of pregnancy (4).

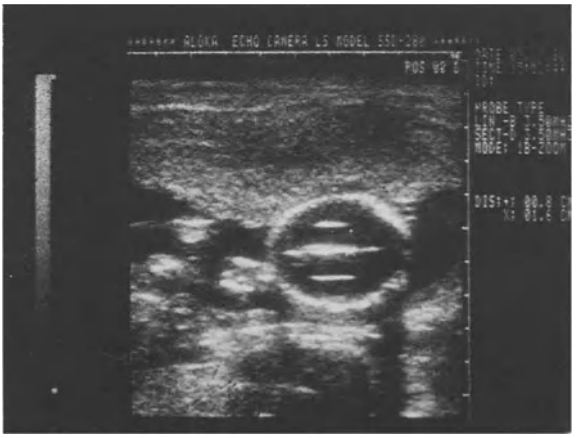

FIGURE 3. Anterior horns of the lateral ventricles at the 17th week of pregnancy. The lateral borders appear as echogenic limes parallel to the falx.

At the beginning of the second trimester the ventricular cavities are not completely anechoic, but contain the echogenic choroid plexus. The choroid plexus is formed in the region where the ependymal wall is thin, i.e. roofs of the 3rd and 4th ventricles and internal portion of lateral ventricles. The leptomeninges push this wall into the ventricles forming the primordia of the choroid plexi (3). By the 13th week this richly vascularized meningeal axis is the easiest structure to be recognized by ultrasound because of its high echogenicity, probably due to the rich glycogen content. The central and posterior portions of the lateral ventricles are almost completely filled with choroid plexus tissue which than subsequently decreases in relative size and recedes into a more central location in the ventricles (Figs. 4 and 5).

The benign, developmental cysts of the choroid plexus may sometimes be seen from the 16th week onwards. In all described cases the cysts have disappeared, so it has been suggested that repeated examinations to observe them disappear is all that is needed.

The midline echo complex, which appears as a continuous echogenic line bisecting cranium, is rather thick at the beginning of the second trimester and consists of three very close parallel lines, the external ones represent the medial walls of the lateral ventricle, while the middle line

represents the falx and the fornix (4).

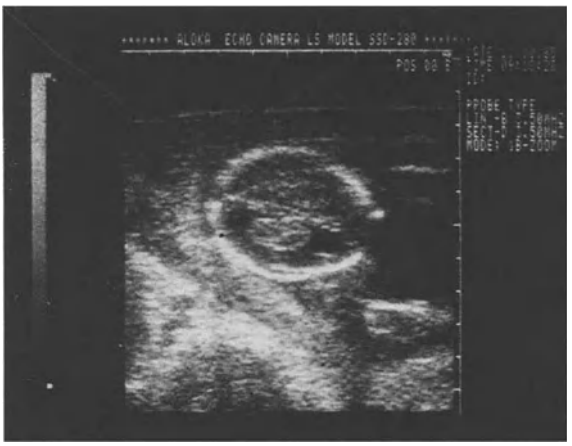

FIGURE 4. Choroid plexus filling the body of the lateral ventricle at the 18th week of pregnancy. Anterior and posterior horns are devoid of choroid at this stage of pregnancy.

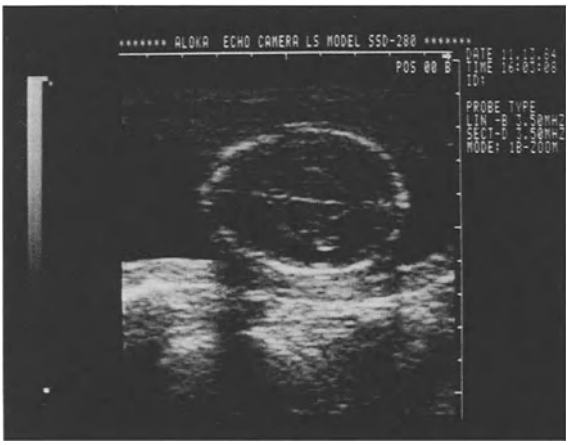

FIGURE 5. Transverse section of the head of a 21 week old fetus. Midline echo and cavum septi pellucidi are shown.

The cavum septi pellucidi is well-defined, small anechoic area interrupting the midline echo at the junction of its anterior and middle thirds. It can be seen as early as the beginning of the second trimester and should not be mistaken

for the third ventricle. The true third ventricle is slightly posterior and caudal to the septum pellucidum. Since it is a very narrow cavity, not wider than 2-3 mm, it is somewhat difficult to visualize it before the 28th week of pregnancy. It appeares as two thin linear echoes which are parallel and very close, and located between the anechoic thalamus. This plane which demonstrates both cavum septi pellucidi and third ventricle is recommended for measuring the biparietal diameter (Fig. 6).

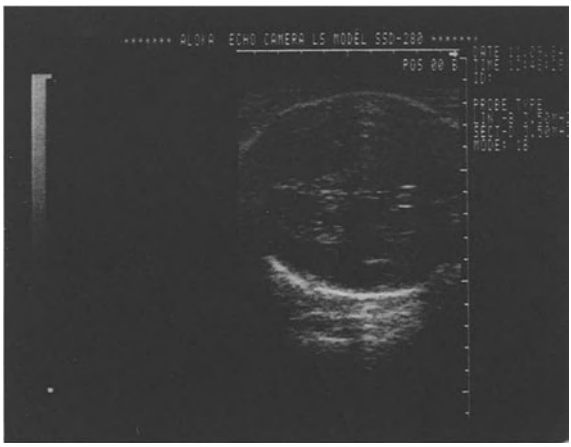

FIGURE 6. Fetal head at the 27th week of pregnancy at transverse section. Cavum septi pellucidi, 3rd ventricle, the talami and Sylvian fissura are demonstrated.

The developing cerebral hemispheres are cellular, made of relatively homogenous, but probably due to lack of myelination, rather anechoic tissue. It is therefore, very difficult to identify a demarcation between lateral ventricles and cerebral mantle until the 15th week, when walls of the lateral ventricles become progressively more visible (1).

Scans caudal to the lateral ventricles demonstrate the thalamus as an oval hypoechoic structure on either side of the linear echo representing the third ventricle. Hypoechoic area located posteriorly and laterally to the thalamus is the hypocampus. Strong echoes between the thalamus and hypocampus are ambient cysterns. The lateral border of the hypocampus is formed by the trigone of the lateral ventricle, where two lines can occasionally be seen, corresponding to the medical and lateral borders of the trigone (Fig. 7).

At the same level, around the 21st to 22nd week insula with overlying Sylvian fissure is first seen. It can be easily identified while the pulsating middle cerebral artery branches demarcate its surface.

Moving caudally from the level of the thalamus the cerebral

peduncles are seen demarcating the region of the midbrain and brain stem. The midbrain is imaged as heart-shaped structure and the pulsation from the basilar artery is easily visualized anterior to the brain stem.

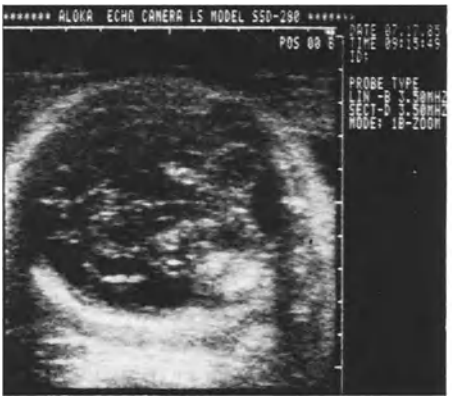

FIGURE 7. Suboccipitobregmatic view of the fetal head showing the cerebellum, cellebral peduncles and echogenic ambient cysterns.

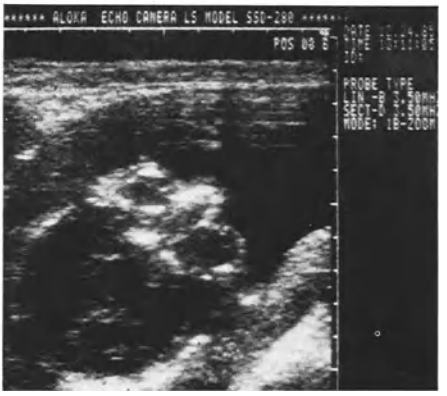

FIGURE 8. Fetal orbites at the 16th week of pregnancy.

On the lowest section through the brain stem image of the base of the skull may be seen demonstrating the typical X-shaped appearance secondary to the greater wing of the sphenoid and the upper portion of the petrous pyramids.

Interest should be turned also to the cerebellum and the posterior fossa. The posterior fossa is well visualized by performing oblique or coronal scans and its lateral regions are occupied by the moderately echogenic cerebellar hemispheres. Often the small fluid space representing the cisterna magna is demonstrated at the base of the posterior fossa. Strongly echogenic tentorium on its superior margin and vermis immediately beneath it can be easily visualized, especially in coronal scans (2, 5).

The fetal orbis can be identified allowing the measurement of the orbital diameters and binocular distance (21). This parameters can be usefull in diagnosing microcephaly and other forebrain developmental disorders (Fig. 8).

3. CRANIAL DEFECTS

Precise ultrasonic visualization of normal and pathologic fetal intracranial structures, enabled experienced investigators to diagnose with almost 100% accuracy the most frequently encountered cranial defects such as anencephaly, hydrocephaly and microcephaly. Early diagnosis of these abnormalities, described below, is still the most successful application of ultrasound.

3.1. Anencephaly

Anencephaly results from an arrest of neural groove closure in the brain. It is thus a disorder of early embriogenesis, caused by defective induction of the prechordal place, the parachordal mesoderm, or poor receptivity of the competent neural plate (3). The incomplete closure of the neural tube at its cephalic end is covered by a thick membrane of angiomatous stroma, but never a bone or normal skin. Absence of the cranial vault is a constant finding, although portions of the cranial bones, especially the occipital bones and the orbites, are usually present (1).

Ultrasound seems to have solved the problem of antenatal diagnosis of this serious defect. A diagnosis of anencephaly is made when the normally ovoid and regular outline of the fetal head is replaced by an irregular mass of the fetal skull and facial bones. The visualization can be made as at the 12th week of pregnancy, although a definitive judgement and decision to terminate pregnancy should be delayed until the 14th or 16th week (Fig.9).

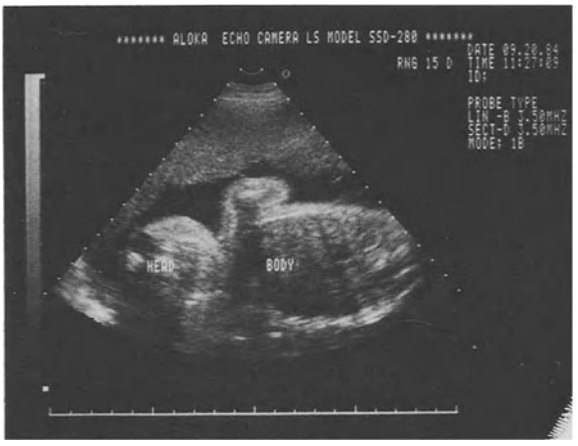

FIGURE 9. Anencephaly at the 24th week of pregnancy.

It is important to remember that due to flexion, the fetal head is often in a different linear plane to that of the body and early engagement of the fetal head can sometimes give a false impression of anencephaly (6).

Most anencephalic pregnancies are nowdays picked up early enough for the pregnancy to be terminated. Retrospective results in Scotland show that from 1971 to 1982 the birth prevalence of anencephaly fell 36%, which is at least partly result of continuous ultrasonic screening, detection and early termination of this condition (7). Carrying a fetus with a known congenital abnormality incompatibile with life, exposes the pregnant woman to unnecessary psychological, social and

physical risk if the pregnancy can be safely terminated (8). According to our experience the use of ultrasonically guided intraamniotic injections of Prostaglandine F_2 alpha is the method of choice in such cases.

3.2. Hydrocephaly

Hydrocephaly is characterized by abnormal accumulation of cerebrospinal fluid in the ventricles or, in case of external hydrocephaly, in the subarachnoidal spaces. There are at least three possible causes of hydrocephaly:

1. Excess production of the cerebrospinal fluid
2. obstruction of circulation
3. defective resorption of the cerebrospinal fluid (9).

Traditional criteria for the diagnosis of intrauterine hydrocephaly are based on findings of a biparietal diameter greater than 11 cm, or a head to abdomen circumference ratio greater than 2. By the time these signs are present the hydrocephalic process is well installed and damage to the brain has already occured. However, during the second trimester of pregnancy, biparietal diameter and head circumference measurements are usually within normal limits for the gestational age. This means that the diagnosis of hydrocephaly should not be made on the basis of increased head size.

Recent improvements in ultrasound technology have now made it possible to differentiate the fine structural details within the fetal cranium allowing the earlier recognition of intracranial pathological conditions (10). Assessment of the new criteria for early recognition of the hydrocephalic fetus is extremely important, since prognosis and treatment directly depend on the time at which the diagnosis has been made.

Recently, it has been suggested that the first recognizable aberration in fetal hydrocephaly is a relative shrinkage of the normally prominent choroid plexus within the body of the lateral ventricles. As long as choroid plexus can be seen filling the lateral ventricular body in its transverse dimension, hydrocephaly is not likely present (1).

Some authors claim that the first manifestation of lateral ventricular dilatation (beginning at approximately 22 weeks and beyond) is medial displacement of the medial wall of the lateral ventricle toward the midline (10) (Fig. 10).

According to our experience, to obtain an early and definitive diagnosis of hydrocephaly, the most useful measurement is the lateral ventricle width/hemispheric width ratio. The lateral wall of the frontal horn is undoubtedly the most easily identifiable part of the lateral ventricles; for this reason the ventricular measurement is to be taken at this point, or in the most anterior part of the lateral wall of the ventricular body. The distance between this lateral wall of the lateral ventricle and the midline echo is then measured. This distance is slightly greater than the true frontal horn width, because the medial wall of the frontal horn lies just laterally to the midline echo. The midline echo is always identifiable, so it is prefered as a landmark instead of the medial wall of the frontal horn. (Fig. 11)

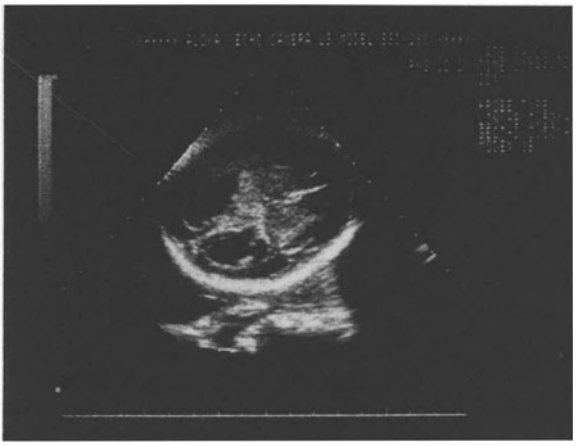

FIGURE 10. The posterior horns of the lateral ventricles at the 27th week of pregnancy. In that gestational age posterior horns may appear unusually dilated but it still represents a normal finding.

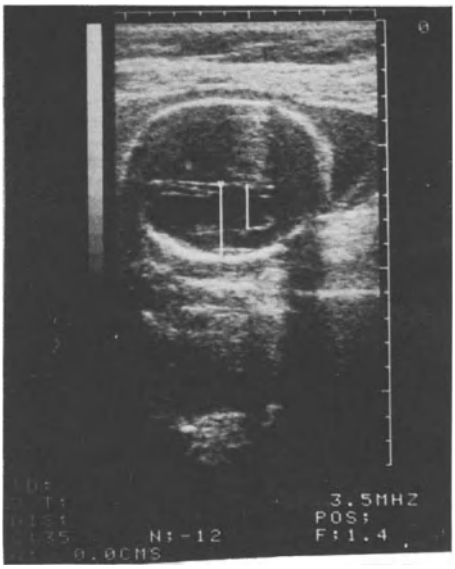

FIGURE 11. Hydrocephalic fetus at the 22nd week of pregnancy. Note dilatation of the lateral ventricle which occupies most of the cerebral hemispheres. Technique of lateral ventricle - hemispheric ratio measurement is illustrated.

The greatest hemispheric width is also measured at the same level as the ventricular width. These measurements should be taken from the inner edge of the midline echo to the inner edge of the distal parietal bone respectively.

A potential pitfall in determing the lateral ventricle width/ hemispheric width ratio (LVW/HW) lies in mistaking the Sylvian fissure for the lateral wall of the ventricular body; such a mistake could be the cause of erroneus diagnosis of hydrocephaly. The Sylvian fissure can be distinguished easily from the ventricular wall because it lies more laterally at a slightly lower level. Furthermore, real-time examination will demonstrate pulsations of the middle cerebral artery within this area, identifying it as the Sylvian fissure.

A higher value of the LVW/HW ratio is the clear evidence of a pathological dilatation of fetal ventricles (11), but one must be very careful when making the diagnosis prior to 20 weeks because the lateral ventricles are usually disproportionately large at this time. Moreover, the ratio measurement accuracy suffers from a wide standard deviations which renders it insensivity to identification of an early dilatation. For this reason it is useful to repeat the ultrasound examination after one week; if the ratio increases, the diagnosis of hydrocephaly can be made without any doubt.

The dilatatation of the posterior horns with borderline dilatation of the anterior horns has recently been recognized, so nomograms of the posterior horn are also now available (12). The lateral wall of posterior horn is sometimes difficult to see and in that case the lateral edge of the choroid plexus is taken as the point of reference.

As the pregnancy proceeds and the ventricular dilatation increases, the ultrasound diagnosis is hydrocephaly becomes much easier: The lateral ventricles are extremely dilated and the LVW/HW ratio is much higher than it normally is. Furthermore, real-time examination makes it possible to recognize the midline echo floating the two dilated ventricles and the choroid plexi hanging in the cerebrospinal fluid inside the dilated ventricular cavities. (Fig. 12, 13)

If the diagnosis of hydrocephaly, has been established, delivery by Cesarean section after the fetus attains pulmonary maturity may be of benefit.

However, some recent reports emphasise that the adverse effects of prematurity may be worse than those of hydrocephalus especially in infants of low birth weight. To reach a right decision consultation with neurosurgent and repetitous examination of fetal intracranial anatomy by perinatologist experienced in ultrasonic diagnosis is recommended (13).

We have treated fourteen newborns with antenataly detected internal hyperthensive hydrocephaly (16, 26). In all our patients ventriculo-atrial or ventriculo-peritoneal shunting was performed. The Pudenz ventriculo-atrial shunt was done in ten cases, and the Hakim ventriculo-atrial shunt in two, while the Pudenz ventriculo-peritoneal shunt was performed in two babies with porencephalic arachnoidal cyst. During postoperative care all the babies presented satisfactory physical developments. In four cases cranial circumference was, three

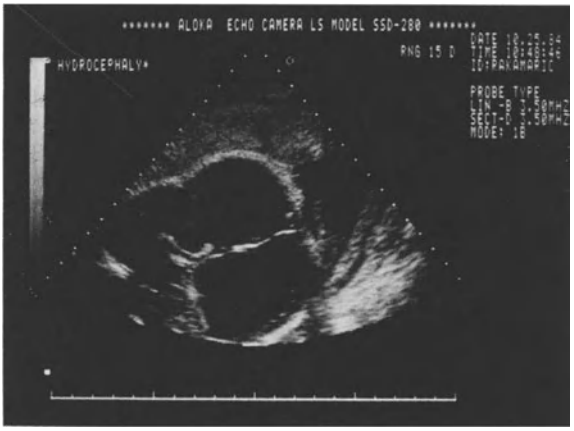

FIGURE 12. Hydrocephalus at the 33th week of pregnancy

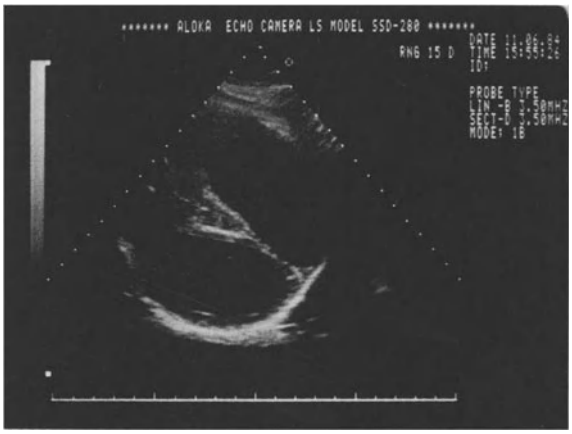

FIGURE 13. Head of the hydrocephalic fetus at the 40th week of pregnancy

months after the operation, slightly enlarged. The physical and mental development of seven hydrocephalic babies was normal six month after the surgery; in four it was slightly retarded and in three cases severe psychomotoric retardation was discovered. Complications observed during the liquor shunting were: sudden decrease of intracranial pressure with consequent intracranial hemorrhage, most frequently presented as subdural hematoma. Postoperative intracranial hemorrhage was registered in two cases, but there was no need for neurosurgical intervention. In the case of one child, Pudenz ventricular catether was occluded by arachnoidal plexus, and it had to be substituted for Hakim ventricular catether.

Selected hydrocephalic fetuses whose condition is detected early in pregnancy and whose condition does not appear to be complicated by other anomalies, should be good candidates for intrauterine treatment. A recent publication by Clewell et al. reported the successful implatation of a fetal intraventricular shunt in a 26-week fetus (14). The use of this technique has been described by several authors, but the benefits of such procedure are not yet satisfactory. It has been stated that the reason for the mixed success has been the fact that various procedures have been attempted without the benefit of testing in a relevant animal model(15). Some failed attempts resulted from poor patient selection. Nevertheless preliminary follow-up evaluations have suggested that operated infants benefited from the intrauterine therapy (16). However until now, there have been too few fetuses treated with shunt placement to assess the value of ventricular decompression with respect to ultimate prognosis.

3.3. Microcephaly

In microcephaly there is a small brain inside a small cranium. It can result from various and heterogenous causes (chromosomal abnormalities, X-irradiation of the mother during pregnancy, rubeolla, toxoplasmosis, cytomegalic inclusion disease, IUGR) (17). Whatever the cause, true microcephaly is always due to reduced growth of the brain and not to smallnes of the skull or premature obliteration of the cranial sutures.

Since many woman are not sure of their menstrual dates, and others are sure but in error, the degree of confidence in diagnosing microcephaly is really limited. There is, also, no universally accepted antrophomorphic definition of microcephaly. Some authors classify those infants with a head perimeter 2 SDs bellow the mean as having microcephaly (18). However, when this standard is used, the association with mental retardation is inconsistent.

Kurtz et al (19) have proposed three definition of microce phaly: Pseudomicrocephaly - an abnormally small biparietal diametar secondary to an unusually shaped fetal head (the head area and circumference measurement are normal); Relative microcephaly - an abnormally small head, between one and three standard deviations bellow the norm; True microcephaly - an abnormally small head having a biparietal diametar more than 3 standard deviation bellow the mean. Other helpfull indicator in diagnosing the true microcephaly is an abnormal head to body ratio associated with normal body growth.

Three standard deviations bellow the mean for the sex and age would appear to be the best single criterion for the definition of microcephaly, as the correlation with mental retardation is stronger than with previously suggested criteria (1). However, it seems that multiple diagnostic tests would be neccessary to optimize diagnostic accuracy in the prediction of microcephaly.

3.4. Posterior fossa and cerebellar anomalies

In order to demonstrate possible anomalies of the posterior fossa and cerebellum an oblique transverse view (sub-occipito-bregnatic) of the fetal cranium should be obtained. Although abnormalities of this area are rare, they should not be overlooked as they usually produce spastic diplegia or other motor disorders (12). These anomalies are often cystic in nature and they may easily be identified sonographically.

Dandy-Walker malformation is a syndrome of unknown etiology which consists of cystic dilatation of the fourth ventricle and agenesis of displasia of the cerebellar vermis.

In the Arnold-Chiari malformation the posterior fossa is reduced in size since a portion of the brain stem and cerebellum are displaced downward into the upper portion of the spinal canal.

In primary cerebellar hypoplasia the cisterna magna enlarges to fill out posterior fossa which remains normal in volume.

The enlarged cisterna magna and the echo-free space between the cerebellar hemispheres allow the antenatal diagnosis of Joubert syndrome to be made (12)

Campbell and Pearce have recently suggested the usefull criteria in ultrasound diagnosis of these anomalies (12). According to them the measurement of each cerebellar hemisphere should be compared to each other in order to exclude unilateral hypoplasia, and then measure the distance from the posterior aspect of the cerebellum to the inner table of the skull.

3.5. Iniencephaly

The severely deformed fetus show the extreme retroflexion of the head with fusion of the occiput to the cervical vertebrae. Rachishisis exists in most cases, but the defective spinal cord and column usually are covered dorsally by brain, cerebellum and skin, so that the open neural plate and vertebral through are not seen on the surface (17).

We have recently diagnosed a case of iniencephaly with associated omphalocele in 18th week of pregnancy.

3.6. Holoprosencephaly

Holoprosencephaly includes several different cerebral abnormalities resulting from incomplete cleavage of primitive prosencephalon of forebrain. Failure in sagital division of these structures can result in appearance of a common ventricle, fused thalamus and a cortex with neither lobes nor an interhemisphere fissura. Absent olfactory tracts and bulbes as well as midline facial anomalies such as varying degrees of hypotelorism, clef lip and palate and nasal malformations are frequently seen in this disorder.

Holoprosencephaly is divided into alobar, semilobar, and

lobar categories based on the degree of separation of the cerebral hemispheres (20).

The characteristic absence of the falx cerebri and the interhemispheric structure which are responsible for the midline echo provides a marker for ultrasound diagnosis of alobar holoprosencephaly. The absence of midline echo is not pathognomonic whilst porencephalic or arachnoidal cysts may cause a pattern similar to midline echo. But, when hypotelorism is found in conjunction with absence of the midline echo the antenatal diagnosis of alobar holoprosencephaly is almost certain (22).

In lobar and semilobar holoprosencephaly the falx cerebri may be present and binocular distance and facial structures may be normal making the sonographic diagnosis difficult or even impossible.

3.7. Hydranencephaly

It is congenital absence of the cerebral hemispheres, probably due to internal carotid artery occlusion in development with resultant necrosis and liquefaction of the cerebral hemispheres (23).

The cerebral hemispheres are almost completely absent, only basal ganglia and remanants of mesencephalon can be visualized. Lateral and third ventricles cannot be visualized, but the choroid plexus can be sometimes identified floating in the supratentorial fluid space.

3.8. Clover leaf skull

Clover leaf skull or Kleblattschädel is an unusual and rare form of distortion of the fetal head due to premature fusion of the coronal and lambdoidal sutures. Compression of the brain as result of small cranial fossa or foramen magnum may be the cause of the obstructive hydrocephalus (24). The increased intracranial prassure causes formation of a grotesque trilobed skull.

3.9. Encephalocele

Encephalocelae are the hernias of the brain protruding through a congenital defect in some part of the cranium. They occur occasionally in the parietal, frontal, nasal or nasopharyngeal region, but the majority - abot 70% - are found in the occipital area (17).

Encephalocelae are recognized sonographically as brain filled sacs extending out of the calvarium. One must always take care not to mistake fetal small parts for herniated brain (25) (Fig. 14).

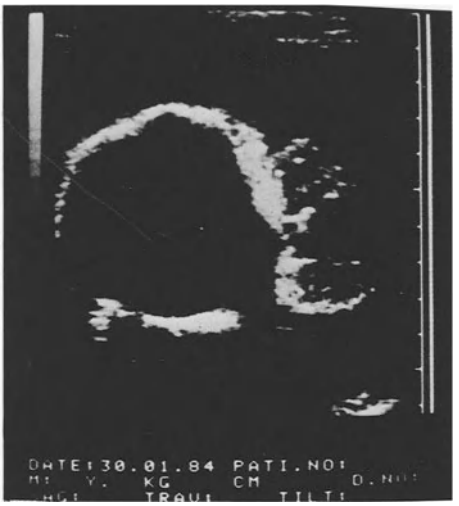

FIGURE 14. Fetus at the 26th week of pregnancy. Encephalomeningocelae located at the occipital region and the complete brain herniation are visible.

4. CONCLUSION

Ultrasound has proved to be a powerful technique for visualisation of normal and malformed intracerebral anatomy. Early diagnosis give an opportunity to prevent the birth of significantly malformed babies. If this is not achieved in early pregnancy, the knowledge that the fetus is or may be abnormal at the end of pregnancy can still be valuable since the manegement of patient before and during labour could be radically altered. Finally, preliminary results indicate that surgical intervention in utero of hydrocephalus in selected cases may not only ameliorate but even entirely prevent the devasting consequences of that cranial malformation. Perinatal diagnosis of fetal malformations and consecutive intrauterine therapy has arised many moral, ethical and legal problems which are yet to be resolved (27, 28, 29). However, the guiding criterion in every action has to be the benefit of mother and unborn child.

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PRE- AND PERINATAL FACTORS AND NEUROLOGICAL DYSFUNCTION

HENDRIK J. HUISJES

In the majority of cases, serious motor handicap and developmental retardation have their origin in the prae- and perinatal period (Hagberg, 1975; Holm, 1982). Among 3162 consecutive singleton births which took place in our hospital in 1975-1978, 260 were found to result in neurologically abnormal infants (Table 1). Fourteen of these appeared to be handicapped when examined at 4-7 years of age. Among a control group of 160 neurologically normal newborns, matched for date of birth, none were neurologically abnormal at follow-up. Children with minor neurological dysfunction occurred in both groups, but the number was three times as large in the neonatally abnormal group (Table 2).

TABLE 1. Results of neurological examination in the newborn period of 3162 consecutively born singleton infants.

	N	%
Abnormal	160	5.0
Suspect	679	21.5
Normal	2323	73.5

This does not imply that late handicaps are only to be found in children who exhibited a neurological syndrome in their newborn period. Apart from neurologically abnormal and normal infants, a third category was distinguished: those who, without showing a syndrome, performed abnormally in one or more neurological items: the neurologically suspect infants. This category comprised 21.5% of the infants (Table 1). Not all of these could so far be followed-up, but from available preliminary results it can be concluded that between 2 and 3 percent of them will be neurologically abnormal at about 9 years of age, or between 14 and 22 children.

Calculation of the 95% reliability interval of the follow-up result of about 800 neurologically normal infants shows that among the 2323 neurologically normal newborns at most 25 may be abnormal at follow-up. In conclusion: in total 28 to 61 children may turn out to be handicapped among those born in a birth-cohort of 3162 (1-2%). This is a high percentage, when compared with the usually accepted incidence of 1-3‰. It should be noted, however, that 1) the cohort is a negative selection, because in the Netherlands almost half of the births in the seventies took place at home and pathological pregnancies were concentrated in the hospitals; 2) the diagnosis 'abnormal' at follow-up included children with relatively minor handicap.

TABLE 2. Follow-up of 320 infants, 160 neurologically abnormal and 160 normal.

Neurological examination at 4-7 years	Neonatal neurological examination Abnormal	Normal
Abnormal	14	0
MND	31	10
Normal	105	145
Died	6	2
Lost to follow-up	4	3
Total	160	160

This is not the place for an extensive discussion of the merits of neurological examination in the newborn period as a screening procedure for late handicaps. The available results of the follow-up study can, however, serve as a basis for discussion of perinatal factors as aetiological moments in damage to the nervous system. Therefore we chose to select five factors known to play a role: severe congenital anomalies, peripheral nerve lesions (e.g. abducens nerve, brachial plexus), umbilical acidaemia (pH< 7.20), preterm birth (< 37 completed weeks), and intrauterine growth retardation (< 10th centile). In addition, the quality of the pregnancy and perinatal period was expressed in an obstetrical optimality score, which has been extensively described elsewhere (Touwen et al., 1980). A maximum score indicates a virtually flawless pregnancy and perinatal period (including social background). The tenth centile in the cohort studied was at a score of 54.

Table 3 shows the distribution of the 160 neurologically abnormal newborns over the categories just mentioned, and the follow-up results per category. It is clear that this classification, although attributing follow-up results to certain perinatal events, does not prove a causal relationship. In certain instances the quality of the neonatal condition makes such a relationship very probable (peripheral lesions and congenital anomalies) in others it is less certain, but the nature of the perinatal factors is such that it would be even less probable that other, unknown, factors would be causal.

From Table 3 it can be seen firstly that all of the congenital anomalies resulted in a very serious outcome. This is not surprising, as only serious congenital anomalies did lead to neurological abnormality in the neonatal period. The congenital defects were: Patau's syndrome, Prader-Willi's syndrome, Werdnig-Hoffman's disease, Möbius syndrome, Larsen's syndrome and spina bifida (3x). All children either died or remained neurologically severely abnormal.

In contrast, peripheral lesions have a favourable prognosis. None of the children were abnormal at follow-up, and only 5 out of 23 showed benign neurological dysfunction. Diagnosis varied from VIth or VIIth nerve palsy, diffuse hypotonia, or choreiform dyskinesia with mild motor retardation.

The next three variables: preterm birth, intrauterine growth retardation,

and acidaemia are well-known, or at least much discussed, as causes of permanent damage of the nervous system. We have distinguished them as solitary factors, and will discuss combinations apart. Umbilical acidaemia, in most cases indicative of more or less severe intrapartum hypoxia, appears to be relatively benign as a factor in the causation of late sequalae: only one out of fourteen children remained abnormal (mild spastic tetraplegia and psychomotor retardation) and two had minor neurological dysfunction. This is consistent with other studies both from our own department (Dijxhoorn, 1985, 1986) and from elsewhere (Low et al., 1983).

TABLE 3. Follow-up results in 160 children who were neurologically abnormal in the neonatal period, related to some perinatal factors.

		Follow-up				
Perinatal factors	n	A	MND	N	Died	Lost to follow-up
Congenital anomalies	8	3	-	-	5	-
Peripheral lesions	23	-	5	18	-	-
Acidaemia*	14	1	2	11	-	-
Preterm birth*	11	-	4	7	-	-
IUGR*	26	2	5	17	1	1
Combinations of*						
including IUGR	15	3	4	8	-	-
without IUGR	5	1	1	3	-	-
None of above						
Obstet. Opt. 54	12	1	2	8	-	1
Obstet.Opt. 54	46	3	8	33	-	2
Total	160	14	31	105	6	4

IUGR = intrauterine growth retardation, A = abnormal, N = normal, Obstet.Opt. = Obstetrical Optimality, MND = minor neurological dysfunction.

Even severe acidaemia (arterial umbilical pH below 7.00), as long as it remains isolated, i.e. unaccompanied by growth-retardation or preterm birth, has an excellent prognosis: in another study done in our Department it was found that none of 56 full term appropriate for gestational age infants were abnormal at follow up, and only 4 had MND. In contrast, nine out of 32 severely acidaemic infants who were either preterm, or growth retarded, or both, had neurological sequelae, 6 of them severely so, 4 among these having been growth retarded (Aarnoudse et al.).

Preterm birth, as an isolated event, did not occur very often (11 out of 160 neurologically abnormal newborns) and it is therefore difficult to establish its prognosis. Four children had MND, resulting in choreiform dyskinesia, clumsy motility or coordination problems with mild motor retardation.

If severe congenital anomalies are excluded, in 5 out of 11 cases of late handicap, IUGR figured in the perinatal history. Two cases occurred after isolated IUGR and 3 after IUGR in combination with acidaemia. Apparently prevention or a more adequate management of IUGR might prevent late

handicap. This will be discussed later.

In 4 cases of neurological sequelae none of the above factors had been present. In only one of them the obstetrical optimality score was below the tenth centile suggesting a poor quality of pregnancy and birth. The baby was born as an assisted breech, but did well in the neonatal period, apart from neurological signs indicating a hemisyndrome. At 6 years the child showed marked choreiform dyskinesia and inadequate motility. In spite of their more adequate obstetrical optimality scores only one of the three remaining children had an uneventful perinatal period. At follow-up it was an imbecile with severe psychomotor retardation. The two others had a disturbed perinatal period: in one case labour was induced at 42 weeks because of an abnormal cardiotocogram and bradycardia resulted in a forcipal extraction; the child later had diplegia and psychomotor retardation. The last baby passed meconium in its amniotic fluid, was depressed after birth and suffered from neonatal convulsions; at follow-up it was blind, had a tetraplegia and severe psychomotor retardation.

As far as the 5% of children are concerned, in whom dysfunction of the nervous system was already detectable in the newborn period, IUGR figured in the perinatal history of about one-third of those who showed serious late sequelae. Preliminary results of 298 neonatally suspect (but not abnormal) infants indicate that among 7 children with late handicap, 3 had been growth-retarded.The neurological follow-up diagnoses in these children were hemiplegia, epilepsy and psychomotor retardation, and severe psychomotor retardation.The frequency of IUGR among children showing handicaps without any neonatal signs of neurological dysfunction cannot be estimated precisely, since up till now we have found only 3 such children out of 800; one of these had been growth-retarded.

Nevertheless of 18 handicapped children (severe congenital anomalies excluded), 8 had been born growth-retarded. Prevention of growth retardation appears to be one of the most effective single factors contributing to the prevention of late handicaps. Until very recently this was not possible. Some recent publications, however, have shown that an effect of aspirin is to be expected (Beaufils etal., 1985; Wallenburg et al., 1986). In spite of the very favourable results, it is too early to conclude that a second aspirin age has alighted in obstetrics, and that an end has been put to the problem of fetal growth retardation. If not, the findings related above may alert the obstetrician to diagnose IUGR at the earliest possible moment and to try to prevent hypoxia in these cases as much as possible. Careful management may result in favourable results, even in case of Caesarean section before 32 weeks (Huisjes etal., 1985).

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The Significance of Neonatal neurological Diagnosis.

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Obviously a neonatal neurological diagnosis is based on a neonatal neurological examination. This trivial remark turns out to be very interesting when we wonder what is meant with a "neonatal neurological examination", or, rather: the neurological examination during infancy. A neurological examination during infancy is not similar to that of an older child or an adult, they are even hardly comparable. For the nervous system of a baby is strikingly different from that of the older child or the adult. The first difference is that the infant's nervous system is in another phase of development, characterized by a relatively low degree of differentiation. Secondly, it develops rapidly, whereas the adult's brain is both more differentiated and more stabilized. As for its functioning, the infant's brain serves other purposes than that of older children or adults: An infant is not a miniature child or adult, but a qualitatively different person. This means that the assessment of the neonate's neurological condition must be age-specific: the age-specific properties of the newborn's nervous system have to be taken into account. (Prechtl, 1972, Touwen 1976). Consequently the neonatal neurological examination focusses on other phenomena than the neurological examination of older children. Due to its age-specific, younger phase of maturation the infant's brain is not yet specialized to the same extent as it will be at a later age. This means that in the neurological assessment there are fewer localizing and topically diagnostic possibilities than in the case of older children or adults. Consequently, the neonatal neurological examination should be comprehensive. It has to incorporate all the functional abilities of the newborn, and it cannot be limited to a few reflexes and responses. Furthermore a strict standardization is required, not only with regard to technique, circumstances such as time of the day, relation to feeding time, light and warmth etc., but also with regard to the behavioural state of the baby during the various parts of the examination. Without this standardization there is a great chance that the neural responses of the newborn will be found to be highly inconsistent. The behavioural state is defined as a relatively stable condition, characterized by a specific relationship of parameters such as respiration, motility, eye

movements and vocalization - in the case of instrumental registration also of heartaction and EEG. Behavioural states of the newborn are: quiet sleep, REM sleep, quiet wakefulness, active wakefulness and crying. The intensity and even the presence or absence of many responses can be determined by the behavioural state in which they are assessed. Consequently the sequence of the items of the examination - and the assessment-technique - is largely determined by the interference of the manipulations with the behavioural state. A design for a comprehensive neurological examination of the full term newborn is described by Prechtl (1977).

What kind of neonatal neurological diagnoses can be established? As stated above the infant's nervous system hardly permits any conclusions about specific localizations, with the exception of disorders of the peripheral nervous system and sometimes of the spinal mark. Therefore we describe the deviations from normal functioning in terms of syndromes, i.e. coherent patterns of symptoms; the search for syndromes has to be followed by a search for a specific aetiology and pathogenesis. Table 1 shows the classification of the neonatal neurological syndromes that can be distinguished.

TABLE 1. Classification of possible neonatal neurological syndromes.

1. Increased or decreased excitability	hyperexcitability syndrome convulsions apathy syndrome coma
2. Increased or decreased motility	hyperkinesia hypokinesia
3. Increased or decreased tonus	hypertonia hypotonia
4. Asymmetries	peripheral e.g. lesion of a plexus central - hemisyndrome
5. Defects of the CNS	e.g. spina bifida
6. Combinations	

Abnormal = presence of one or more of these syndromes
Suspect = some symptoms of one or more of the syndromes
Normal = none of the syndromes

In the first place the syndromes of decreased or increased excitability. Extremes are coma and convulsions respectively, but in between there are two syndromes which deserve special attention. The apathy syndrome consists of hypotonia, slow and low intensity of motility, if present, and a high threshold for reactions and responses, many of which may, moreover, be absent. It reflects a severe depression of brainfunctions, without the infant being (as yet) comatous. The hyperexcitability syndrome is to a certain extent the opposite: the infant is briskly active, sometimes overactive, his movements are often of high intensity. During spontaneous motility and during the Mororeaction a usually slow tremor with a large amplitude is observed, and the thresholds for musclereflexes and the Mororeactions are conspicuously low. The syndrome reflects an often mild dysfunction of the brain, due for instance to asphyxia.

The next syndromes describe the infant's motility: a high amount and intensity: hyperkinesia; and a low amount and intensity: hypokinesia. Isolated, the syndromes are a sign of a usually mild dysfunction. Hypokinesia can be found as a reaction to many disturbing influences, ranging from mild dehydration to (mild) infections, hyperkinesia may result from irritating conditions, such as drug withdrawal or rapidly rising bilirubin levels in the infant's blood. But more often there is an overlap with other syndromes: hyperkinesia may occur together with hyperexcitability, and apathetic infants are usually hypokinetic. Also a combination with the next two syndromes is often found.

The syndromes of the sensorimotor apparatus are hypertonia and hypotonia. The former consists of an increased resistance against passive movements with usually increased muscle reflex intensity and low thresholds; the syndrome is a sign of a serious disturbance of brainfunction. Usually it is replaced by hypotonia after a few days or weeks. Postural mechanisms are often involved, and motor development retarded. In Hypotonia the resistance against passive movements is decreased, whereas the muscle reflexes can still be normal or are mildly diminished in intensity. Hypotonia has a very heterogeneous aetiology: an infant can react to a wide variety of adverse influences with a hypotonic syndrome, varying from dehydration or hyperbilirubinaemia to intracerebral hemorrhage or meningitis. Muscle diseases can show hypotonia with, initially, normal muscle reflexes. Usually the infant is also hypokinetic. If the muscle reflexes are weak or absent, the differentiation with an apathy syndrome may be difficult to achieve; it stands to reason that in such an instance the appreciation of the behavioural state is of prime importance. Bloodchemistry and (later) EMG usually help to differentiate.

Syndromes of asymmetry may be peripheral or central of origin. To the former category belong eg. unilateral cranial nerve palsies, such as facial nerve palsy after forcipal

delivery, or the wellknown VIth cranial nerve palsy, which may also be due to a central aplasia or hypoplasia of the abducens nucleus. Also cervico-brachial or, more rarely, lumbar plexus lesions belong to this category. Two cervico-brachial plexus syndromes are distinguished dependent on the localisation of the lesion: The Erb plexus lesion, i.e. a lesion of that part of the plexus which is formed by the third till sixth cervical roots, and the Klumpke plexus lesion, which involves that part of the cervico-brachial plexus which arises from the sixth cervical till the first thoracic roots. In the former the abduction of the shoulder and flexion and exorotation of the arm are impaired, often wrist extension also. Fingermovements and the palmar grasp reflex are intact. As the third cervical root may be involved, in which the phrenic nerve runs, movements of the ipsilateral half of the diaphragm may be abolished. The plexus syndrome called after Klumpke is characterized by an impairment of arm extension, wrist flexion and finger motility. Also shoulder adduction may be diminished. Sometimes also sympathetic nerve fibers are involved, resulting in miosis and a decreased eye spalt. The condition is rare compared with the Erb type.
The lumbar plexus lesion is rare, and consists mainly of signs of impairment of the ischiadic nerve and the n. obturatorius. The leg is kept in abduction and exorotation, knee extension is impaired and foot motility (dorsiflexion) is diminished.
Central hemorrhagies or malacies may be the cause of central hemisyndromes, in which usually both the upper and the lower extremity on one side are involved. Central hemisyndromes can be preceded by an apathy syndrome. The extent of the symptomatology may parallel the extent of the lesion. In the case of hemispheral lesions this need not be so, however.

Obviously we can also be confronted with syndromes consisting of congenital malformations. Spina bifida and congenital hydrocephalus are wellknown examples.

It is not surprising that combinations of the syndromes are often found. In all instances a search has to be made into the pathogenesis and the aetiology of the syndrome which is found, for that purpose instrumental techniques are often needed, such as ultrasound scanning or computer tomography. The EEG is often of limited value.

With regard to the significance of the syndromes two aspects should be discerned: an individual aspect, which is important for the patient, and a preventive aspect, which is important for the improvement of medical care, especially of pre- and perinatal care.

To start with the latter: Evidently the results of a neonatal neurological assessment can be fed back into pre- and perinatal care. It has been shown repeatedly that the quality of obstetric and pediatric care has a direct relationship with neonatal neurological outcome. This is an

important aspect of neonatal neurological studies, as it may help to improve and direct the development of appropriate obstetric and pediatric strategies. Preterm birth, intra uterine growth retardation and acidaemia of the newborn are reported to be related to neonatal neurological deviancy (Jurgens et al, 1979, Huisjes et al 1980, Touwen et al 1980). However, it is important to recognize the fact that with the exception of extreme cases, single obstetric factors are but rarely related to neonatal neurological morbidity. This holds true for preecclampsia, for cordstrangulation, for anaemia and for many other variables: single adverse factors are usually of little significance. The total obstetric condition, in other words the sum total of the individual qualities of the obstetric variables determines the risk for neonatal neurological dysfunction. This holds true also for eg. acidaemia: a pH v. umb. lower than 7.20 without other obstetrical adverse conditions carries hardly any risk, whereas acidaemia in combination with other obstetric problems carries a high risk (Touwen, 1983, Touwen and Huisjes, 1984, 1985, Touwen, 1985). The obstetric condition has to be considered in its complexity: single variables become meaningful only in their concurrence with other variables.

The individual aspect of the neonatal neurological diagnosis has three important sub-aspects.
1. the significance of the neonatal diagnosis for the immediate condition of the patient,
2. the significance of the neonatal diagnosis for well-baby care (short term prediction).
3. the predictive value in terms of later functioning (long term).

The first sub-aspect is obvious: the diagnosis of dysfunction should lead to treatment. But this statement is only meaningful if treatment is considered in a very broad sense: The term comprises all the advice given to the parents. Treatment of the neurologically abnormal newborn embraces more than surgical or in another way instrumental attendance, or the prescription of drugs. Advice on the right way of nursing the hyperexcitable baby - too much stimulation should be avoided -, on the way in which the hyperactive or hypertonic baby is lying in his bed, or is held in the arm during feeding - avoiding hyperextension of neck and back -, on the amount of time spent on feeding hypotonic or slow babies - these types of advice are a very important part of the treatment of babies who show neurological abnormalities. Moreover, they may largely determine the relationship between mother and infant, and obviously for the sick baby this relationship is essential.

The second sub-aspect regards the meaning of the neonatal diagnosis for the organization of a proper well-baby care. The neonatal diagnosis offers a means to select those infants who carry a risk for developmental disturbances, and who should be followed closely for that reason. We know that the

majority of neurologically deviant newborns recover. This depends to a certain extent on the type of abnormality: peripheral syndromes, eg. plexus lesions or abducens paresis, generally have a good prognosis as long as the roots themselves are not damaged; also the syndrome of hypokinesia is usually benign, if, at least, it is not part of an apathy syndrome or a hypotonic syndrome. Central hemisyndromes, the apathy syndrome and hypertonia have a worse prognosis, as they are expressions of a severe brain dysfunction (Touwen, 1978). The hypotonia's significance depends of course on its aetiology.

Table 2 shows the follow-up results over one and a half year in a selected group of 69 neurologically abnormal infants who had been referred to the neonatal unit of the pediatric department of our hospital.

TABLE 2

Neonatal Diagnosis	FU Normal	FU Abnormal	Total
Hypertonia	3	4	7
Hypotonia	17	6	23°
Hemisyndrome	1	3	4
N VI Paresis	5	2*	7°
Hyperexcitability Syndrome			
<6 weeks	14	1	15
>6 weeks	5	10	15°°

Neurological findings at 1½ years in 69 neurologically abnormal newborns. FU = follow-up.

Legends: * 1 child VI paresis (both sides)
1 child hypotonia, VI paresis recovered.
o overlap of one child with VI paresis and hypotonia.
oo overlap of one child with hyperexcitability and hypotonia.

The fact of the referral in itself makes clear that it is a group with severe neurological disturbances. In all the infants a specific diagnosis could be made, in two cases there was a combination. The results show clearly that hypertonia and hemisyndromes of central origin have an unfavourable prognosis: more than half of the infants with one of these syndromes was severely abnormal at the age of one and a half year. The large majority of the hypotonic

newborns recovered, in only 6 cases a hypotonia was still present at the follow-up age. There were 7 patients with an abducens paresis - the sixth cranial nerve -, in all instances the ocular muscle activity recovered fully. In two cases at one and a half year another abnormality was present, a hypotonia and a spastic hypertonia. The latter child had also been hyperexcitable in his newborn period. But not only in his newborn period. Hyperexcitability which is present during a longer period than circa 6 weeks seems to have a worse prognosis than when it lasts for a shorter time. Short-lasting hyperexcitability may disappear without leaving any trace, although, as Prechtl and Stemmer showed, in the long run, i.e. after 3 - 4 years, mild dyskinesia of the choreiform type may occur in about half of the patients (Prechtl and Stemmer (1962)). But in 2/3 of the infants in whom a hyperexcitability was still found after 6-8 weeks, a cerebral palsy developed. It must be emphasized that the extent or intensity of the symptoms of the original hyperexitability syndrome were not different from those of the short-lasting type. This is an example of the fact that the very young brain has only a few clinical syndromes available with which it can express its dysfunction.

Still, in the majority of cases it was not possible in the first few months to predict which infant would recover, and which not. The infant with a hemisyndrome who recovered had been in a worse condition originally than the two infants who developed a hemiplegia. The same was the case with some of the hypertonic infants. As stated above, the symptomatology of the hyperexcitability as such did not make differentiation feasible. This means that every neurological deviation in the newborn period should be taken seriously, as it is an indication of a risk of abnormal neurological development. Neurologically normal newborns very rarely show an abnormal development, except as a result of serious interval complications. Thus the neonatal neurological diagnosis can form an indication for a careful follow-up during infancy, so that one is able to install and adapt specific treatment as soon as necessary.

The third sub-aspect concerns the long-term predictive value of the neonatal diagnosis. Our follow-up studies have shown that after 4-6 years about 10 % of unselected neonatally abnormal infants are neurologically severely abnormal, whereas in control groups of neonatally normal infants no severe abnormality was found (Touwen et al 1982, Hadders et al 1985). Although the majority of neurologically abnormal newborns recovered, the small minority who developed a cerebral palsy with or without mental retardation, originated in the abnormal group. Clearly the neonatal neurological diagnosis indicates the risk of deviant development - on short or longer term. At the same time it must be recognized that the good outcome of the majority of abnormal infants shows that it is possible for the brain to recover. The idea that a nervous system, once abnormal, remains abnormal - a notion which seems to predominate too often in a doctor's -

and a parent's - mind - must be rejected. A deviant nervous system can recover, although we often do not know why and how, neither which brain will recover, and which will not.

In summary: a neurological examination in infancy should be comprehensive, standardised and age specific. It must be recognized that at very young ages the symptomatology of the nervous system is still rather poor: a few syndromes are expressions of many aetiologies. Consequently the prognosis of identical syndromes may vary widely. The significance of neonatal neurological diagnosis is threefold: It is important because it enables the doctor to install treatment in the neonatal period; it selects the infants who must be followed up; and, last but not least, it gives the doctor a chance to feed back on obstetrics and neonatal paediatrics, with the aim of preventing abnormality. It is as important to state what is not the significance of the neonatal neurological diagnosis: Exceptions excluded, it can not predict the future neurological - or other - condition of the infant. Individual long term prediction, however desirable it may be, is impossible in most cases. It should not be the aim of the neonatal neurological examination.

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EARLY DETECTION OF VISUAL IMPAIRMENTS

J.van Hof-van Duin and G.Mohn

The immature visual system of human infants or animals is known to be capable of remarkable plasticity in response to functional or structural interferences with normal development. Experimental studies of the ontogeny of functional visual defects such as amblyopia or loss of binocular vision in the cat and monkey have led to the concept of the "sensitive period" early in development, during which the visual system is particularly susceptible to abnormal influences (1,2). Early visual deprivation in animals has been shown to result in behavioural, electrophysiological, and morphological neuronal changes which may lead to permanent impairments of visual functions. On the other hand, the very plasticity of the system often also allows reversal of the defects by appropriate treatment. In humans, the existence of a sensitive period for visual input restrictions, as well as for treatment of the resulting deficits is generally accepted, although its time course is still largely unknown. Early detection of visual impairments is therefore important not only for diagnostic purposes, but also in the interest of optimal therapeutic effect.

It is often suggested that the period of greatest susceptibility to visual deprivation is related to periods of postnatal neural growth and functional development. Since different cell types in different areas develop at different rates, this might be expected to lead to several sensitive periods in visual development, during which different neuronal systems in the visual pathways are sensitive to environmental manipulation. Recent investigations of human infant vision indeed point to the existence of different sensitive periods for the effects of various forms of visual deprivation, beginning at various times after birth. Thus the sensitive period for the effects of cataract, ptosis, or corneal insults has been reported to start in the first few months after birth (2-5) and that for strabismus at 4 months or 9 months of age (6,7), whereas the period during which high astigmatism may result in meridional amblyopia seems to start at 2 to 3 years of age (8-10). Little information, however, is available concerning the duration and time course of these various sensitive periods (5,11-13). The end of the sensitive period for human binocular vision is probably quite late; the binocular connections in the human visual system appear to retain some plasticity possibly even until the mid teen-age years.

The development of neuronal pathways in patients with neurological disorders, psychomotor retardation or delayed development is affected not only by possible peripheral obstructions to concordant binocular vision, but often by primary cerebral impairments due to structural damage. Nevertheless, functional sparing or recovery after early brain injury is often observed, and its extent has been described to vary with the age at which the damage occurred (14-16). This suggests that recovery from brain

damage, like recovery from functional impairments, may have its own sensitive period(s). Onset and duration of these periods would presumably depend on the location, etiology, and severity of the damage. At present, very little is known about the early development of visual functions in such patients. Early detection of visual impairments, followed by stimulation adapted to the specific deficit and remaining visual capacity of the individual child, may well be valuable.

Recently, clinical methods have been developed which allow quantitative assessment of behavioural visual functions in normal infants from birth onwards. These methods require only the fixation of a presented stimulus, but otherwise no active cooperation or verbal capacity and have been found useful for assessment of visual functions in children with developmental disabilities or neurological disorders (17-27). Electrophysiological methods such as pattern visual evoked potentials (pattern VEP's) have been found suitable for detecting abnormal visual development in infants with no other developmental disabilities (28-31). In our experience with mentally and multiply handicapped children, however, results of pattern VEP's alone would often have led to an underestimation of visual capacity (21), due to the interference of spontaneous eye movements or behavioural factors with the required prolonged stable fixation. For this reason, we have concentrated on behavioural methods.
For several years now, we have been engaged in studies of visual function in normal infants, as well as in infants at risk of neurological abnormalities due to perinatal complications and in children with definite neurological disorders. In the following section, we describe our findings in a population of prematurely born infants during the first year of life. Four visual functions were examined: the visual threat response, optokinetic nystagmus, visual acuity and visual fields. In the subsequent section, findings in a group of visually impaired neuropediatric patients and in a group of institutionalized mentally and multiply handicapped patients are presented.

PRETERM INFANTS

Visual development was studied in 288 infants born 4 to 14 weeks prematurely. Of these, 130 had experienced only minimal perinatal complications (low risk preterms),while 158 were considered at risk of later abnormalities acccording to one or more of the following criteria: an Apgar score of < 6 after 5 minutes, complications of postnatal development by more than 7 days of mechanical ventilation or phototherapy, surgery for open ductus arteriosus and/or necrotizing entero-colitis, convulsions, or persistent abnormal ultrasound scans. The group of high risk preterms was divided into neurologically normal (64%) or neurologically abnormal infants (36%) on the basis of neurological examinations at the time of testing. Evidence of abnormal neurological development ranged from rather mild deficits like hypertonia to symptoms like asymmetrical motorical development and beginning spastic quadriplegia and (surgical relieved) hydrocephalus. Age at testing ranged from 3 days to 91 weeks postnatally, or from -4 to 85 weeks from the expected term date (corrected age). The results were compared to those of 247 normal fullterm infants aged 1 day to 65 weeks.
In all infants, the presence or absence of strabismic deviations, and of spontaneous and/or latent nystagmus was noted. Direct and indirect pupillary reflexes were tested and the presence of eye-contact, fixation,

following and vergence movements, and ocular motility was examined. Maturation of the different structures underlying processing of visual information allows functioning of behavioural responses from as early as 25 weeks of gestation onwards. The blink reflex to light is present in preterm infants after 25 weeks of gestation (32,33). Pupillary light responses have been reported from 31 weeks of gestation (32), focussing and following eye movements to pattern stimulation appear after 33 weeks (34), and pattern preferences are seen after 34 weeks of gestation (35). Accommodative and convergence responses are possible in fullterm newborns but are still rather inaccurate; quantitative precision improves rapidly in the first three months of life (36-39).

Defensive blinking, i.e. an eye blink in response to a rapidly approaching object, consists of a tactile and a visual component. Presence of the tactile component indicates subcortical processing of tactile information and functioning motor pathways (40,41). Blink of the eyelid in response to

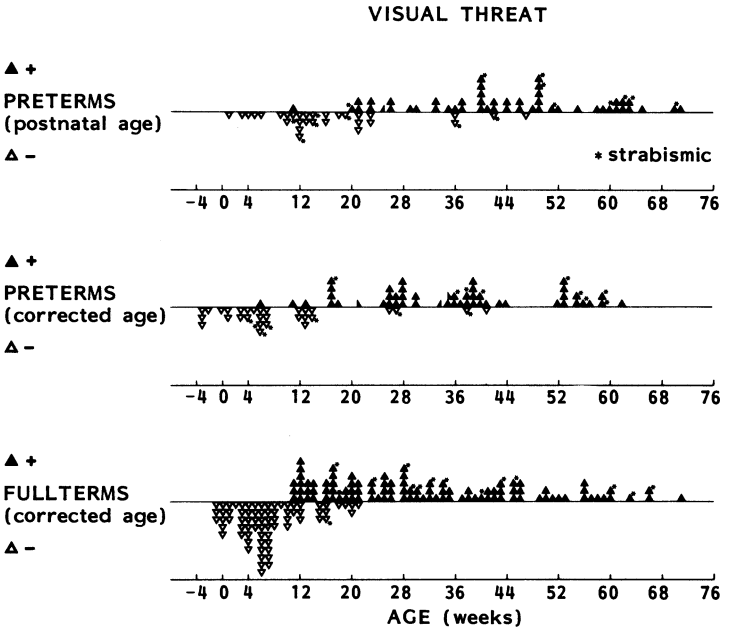


Fig.1: Development of the visual threat response in low risk preterm and fullterm infants. Absence or presence of the response is indicated by open or closed triangles, respectively. Age of the preterms is given either from birth (postnatal age: top row) or from the expected date of term (corrected age: middle row).
In this and other Figures, results of the preterm infants are grouped around corrected ages of 3,6,9,and 12 months. This is due to the fact that these infants were tested during outpatient visits arranged at these ages.

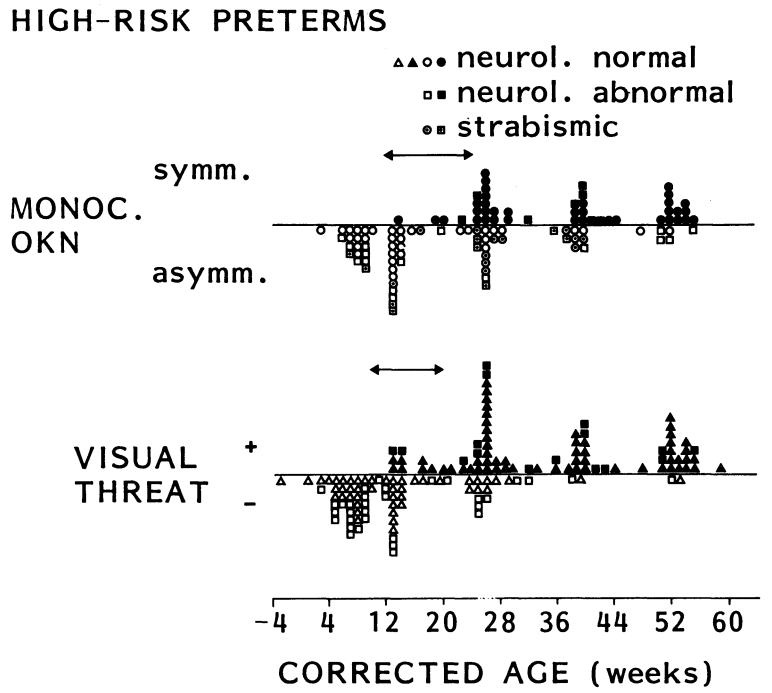


Fig.2: Development of monocular OKN (above) and the visual threat response (below) in high risk preterm infants. For further explanation, see Figs 1 and 3 and the text.

a tap by a finger on the glabella (glabellar tap response) appears in preterm infants between 32 and 34 weeks gestation (32). In our studies the tactile component was examined by a rapid approach of an object towards the infant's face, while the visual component (or visual threat response) was tested by holding a piece of clear plexiglass between the child's eyes and the approaching object, thus avoiding tactile stimulation. This response develops some time after birth (24,42,43), and has been shown to be processed cortically (44-47). Using our methodology, the visual component of the threat response was found to appear from 12 weeks onwards in normal fullterm infants, whereas the tactile and motor component was present from birth onwards (Fig.1).
Low risk preterm infants showed the same maturation of this response when their age was corrected for prematurity (Fig.1). When the results were plotted according to postnatal age, the transition from negative to positive visual threat response occurred later and more gradually (Fig.1), indicating that maturation is determined by age from term rather than age from birth. In preterm infants at risk of abnormal development, the appearance of the visual threat response was observed after 17 weeks corrected age or not at all in 12% of the cases (Fig.2). This suggests that the visual component of defensive blinking may be a useful indication of delayed or abnormal visual/neurological development.

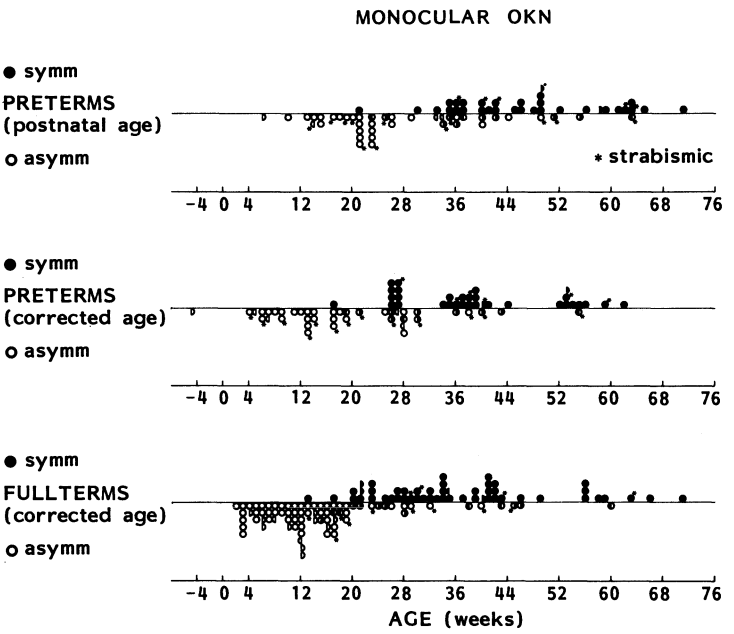


Fig.3: Development of monocular optokinetic nystagmus in low risk preterm and fullterm infants. An asymmetrical response, with a preference for stimulation from temporal to nasal, is indicated by open circles, a symmetrical response by closed circles. Age of the preterms is given either from birth (top row) or corrected for prematurity (middle row).

Optokinetic nystagmus (OKN) is the oculomotor response to movement of a large patterned stimulus and normally consists of slow eye movements in the direction of the stimulus movement, interrupted by fast saccadic movements in the opposite direction. The eye movements serve to stabilize the moving image of the world on the retina.
Binocular OKN can be elicited in preterm infants of 36 weeks gestation (48) and in fullterm infants from birth (49,50). The response is normally symmetrical, i.e. similar reactions are elicited by stimulation to the right and to the left. Monocular OKN, on the other hand, is asymmetrical, with a preference for temporal to nasal stimulation in either eye, until 14 to 24 weeks of age in normal fullterm infants (24,51,52). The presence of symmetrical monocular OKN appears to depend on (binocular) cortical processing of visual information (51,53).
OKN was tested by observing binocular and monocular eyemovements in response to movement of a large piece of paper covered with randomly spaced dots (dot size:1 square cm), which was moved to the right and to the left about 25 cm in front of the infant's head. For monocular testing, one eye was covered by an orthoptic eye patch.

Symmetrical binocular OKN was found in all low risk preterms from 35 weeks gestation onwards, and in normal fullterms from birth. By contrast, it was often asymmetrical in high risk preterm infants (32%). In many cases,these asymmetries were related to the location of brain dysfunction as demonstrated with ultrasound or CT-scans, with a poorer response to stimulation towards the damaged hemisphere. Examination of binocular OKN may thus provide an indication of the functional consequences of perinatal insults to the brain.
The development of monocular OKN in 97 healthy fullterm and 47 low risk preterm infants is shown in Fig.3. During the first 3 months after birth, all infants showed asymmetrical monocular OKN with a preference for temporal to nasal stimulation (open symbols). Symmetrical monocular OKN was first observed from 12 weeks onwards and was present in nearly all normal fullterms at 20 weeks of age (closed symbols). When the results of the preterm infants were plotted in terms of postnatal age, the transition from asymmetrical to symmetrical OKN occurred between 22 and 48 weeks, i.e. much later and over a longer period than in fullterm infants. When preterm ages were corrected for prematurity, however, most infants showed symmetrical OKN at 26 weeks (Fig.3). The apparent discrepancy with the results of the fullterm infants, in whom monocular OKN was generally symmetrical at 20 weeks, is probably due to the fact that the preterm infants were tested at fixed corrected ages which included 26, but not 20 weeks. In infants with manifest convergent strabismus, indicated with an asterisk in Fig. 3, the straight eye developed symmetrical OKN between 12 and 20 weeks as usual, whereas the monocular OKN of the strabismic eye often remained asymmetrical (half-filled symbols).
In about 54% of the high risk preterm infants tested for OKN, the onset of symmetrical monocular OKN was delayed or did not occur at all (Fig.2); 35% of the high risk preterms showed a manifest convergent strabismus. The asymmetry of the monocular OKN in high risk preterms generally consisted of the usual pattern with a preference for temporal to nasal stimulation. In some cases, however, it corresponded to an asymmetry of the binocular response, in which case each eye showed better OKN to stimulation in the same absolute (right or left) rather than relative (temporal to nasal) direction.In the presence of symmetrical binocular OKN, an asymmetry of monocular OKN beyond 6 months corrected age is suggestive of delayed or interrupted development of the cortical pathways underlying the monocular OKN response.
Some high risk preterms showed spontaneous (n=4) and/or latent (n=2) nystagmus. Spontaneous nystagmus is a condition in which involuntary eyemovements of a sawtooth or pendular type occur when both eyes are open. Latent nystagmus becomes manifest on occlusion of one eye and consists of a sawtooth nystagmus with the slow component nasalwards, i.e. towards the side of the closed eye. When spontaneous and/or latent nystagmus was present, it was often difficult to distinguish optokinetic responses from the spontaneous eye movements, and especially to assess a directional symmetry of the responses.

Central and peripheral vision have been shown to develop rather gradually from birth (for reviews see 54-57). While the peripheral retina appears to be relatively mature at term, the fovea still shows signs of immaturity and continues to develop for at least 45 months postnatally (58).
Visual acuity assessment has become possible from the moment of birth by means of the preferential looking technique, which is based on the apparently inborn preference of infants for a pattern over a uniform

stimulus (59). Investigations of the development of preferential looking acuity for grating targets have yielded very consistent results in different laboratories, and indicate an approximately ten-fold increase of acuity during the first year of life. Clinical studies have shown the method to be applicable to infants with ophthalmological disorders such as congenital esotropia, cataract, retinal degeneration, optic nerve coloboma etc. (7,60-63) and also to infants with neurological dysfunction (19-21,25,26).

In our studies visual acuity for high contrast square wave gratings was assessed either by means of the traditional forced choice preferential looking technique (FPL) developed by Teller et al. (59) or with a more rapid procedure using so-called "acuity cards" (64). With both methods, the infant was presented with two circular targets (diam. 13 degrees) in a large grey screen in each trial. One of the targets was the test grating (a pattern of black and white stripes) while the other contained a grating of very fine stripes assumed to be unresolvable by the infant. Test target and the so-called "blank" target were matched in colour and mean luminance to the grey screen. An observer watched the infant through a peephole from behind the screen and assessed his/her reactions while test gratings of various stripe widths were presented. With the FPL-technique the observer was unaware of the left or right position of the test stimulus, and had to make a judgement on the position of the grating on the basis of the infant's reaction, using any cues available. Acuity was taken as the finest grating for which the observer made a significant proportion of correct judgements. The staircase procedure used for presenting gratings of up to 8 different stripewidths, as well as the method of acuity estimation and reliability criteria were those described by Mayer et al. (65). With this method, a reliable acuity estimate is usually obtained in 34 to 40 trials. Because of the rather large number of trials, and thus the time required for a statistically reliable acuity estimate, this standard FPL-method has not been widely adopted for clinical use. For this reason a more rapid procedure, using acuity cards, was developed recently, with which an acuity estimate can be obtained in 3 to 5 minutes (64). In this procedure, the observer, instead of merely judging the position of the test grating as before, makes an integrated judgment as to whether the test grating is easy or difficult to see for the infant or not seen at all. This takes advantage of the fact that infants usually show quite different reactions to gratings of different stripewidth. When a grating of wide stripes well below the infant's acuity threshold is presented, this will often evoke a clear and long lasting fixation, while near threshold infants tend to show a much slighter preference for the grating, and scan back and forth between test grating and blank. These behavioural cues are used by the observer to estimate acuity as the finest grating which he/she subjectively judges the infant to just be able to discriminate. Test grating and blank were presented on a grey card (28 x 60 cm) held up to the infant through an equally sized aperture in the screen. In between trials, the observer was visible through the aperture and attracted the infant's attention by playing a peek-a-boo game before presenting the next card. Gratings of decreasing stripwidth were presented in rapid succession, often starting with one or two octave steps (an "octave" means a doubling or halving of stripewidth). Near threshold, stripewidth was repeatedly decreased and increased in 0.5 octave steps until the observer felt confident of his/her judgement.

With both methods, the infant was held in an upright position at 40 cm distance from the screen, and kept alert and active throughout the

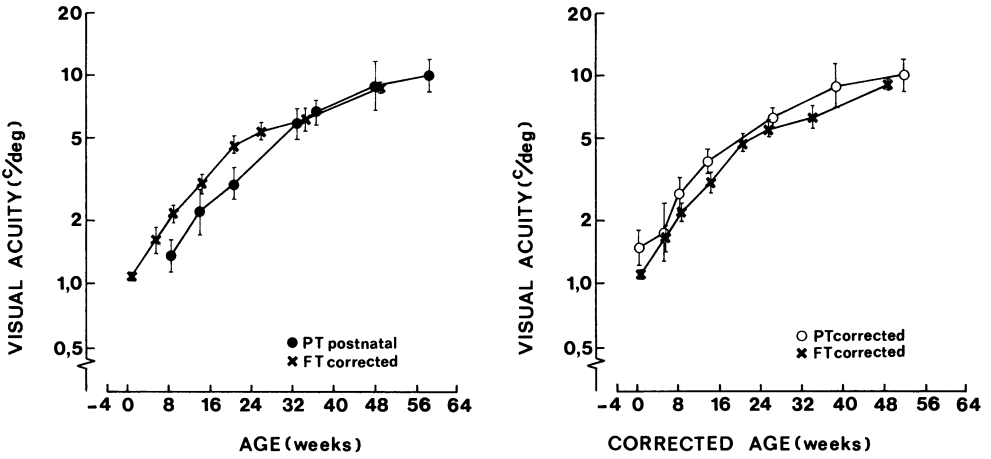


Fig.4: Development of FPL acuity in normal fullterm (FT) and preterm (PT) infants during the first year of life. Age of the fullterm infants (x) was calculated from expected date of term; for the preterm infants, development is shown according to both postnatal (•) and corrected age (o). Vertical bars indicate two Standard Errors of the Mean.

testing. The chin was supported to keep the head upright, and all infants were slowly turned to the left and to the right between the two stimuli to insure that both fell in their visual field. Older children were tested at a distance of 57 cm. With the FPL method, older children were tested with the operant preferential looking technique, in which the infant was rewarded for a correct response of the observer by the appearance of an animated toy via a one-way vision screen (66).

Fig.4 shows the development of FPL acuity in normal fullterm and low risk preterm infants. When the age of the preterm infants was plotted according to age from birth, the preterm infants lagged behind the fullterm infants up to an age of about 8 months. Using corrected age instead, preterm infants showed a slightly higher mean acuity than fullterm infants, suggesting a slight acceleration of acuity development in the preterm infants.

Acuity measurements obtained with either the FPL technique or acuity cards in normal infants and infants at risk of abnormal development are shown in Fig.5. Comparison of the results of normal infants showed very good agreement between the two methods. Results obtained with the FPL technique indicated that many high-risk infants with normal neurological development had low acuities during the first 4 to 5 months of corrected age, in comparison to the mean acuity of low risk preterm infants. By 6 months corrected age, however, acuity clustered more or less symmetrically around the mean low risk acuity, suggesting that acuity development was only temporarily slowed down by the perinatal complications. Acuity of neurologically abnormal infants was often low beyond the age of 6 months. Nevertheless, older infants usually had higher acuities than younger

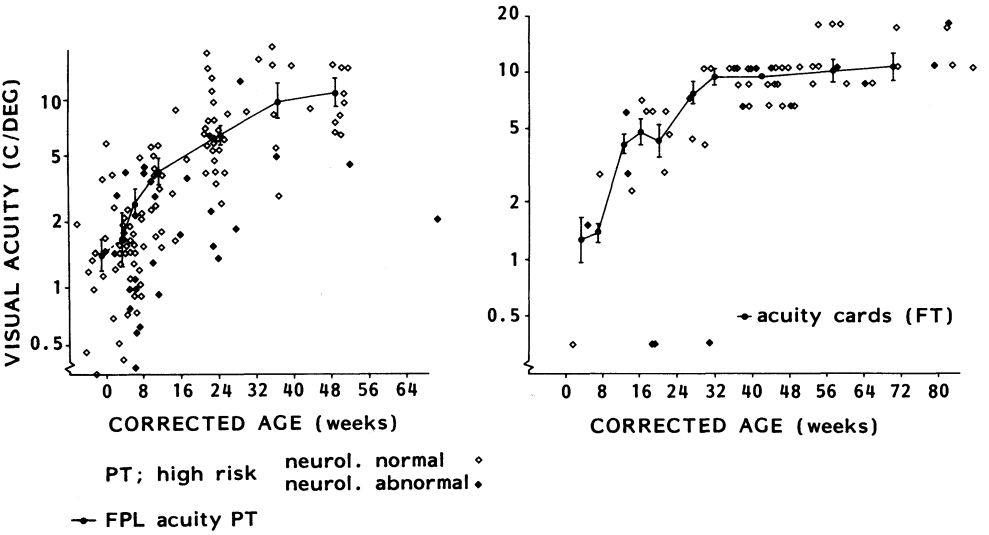
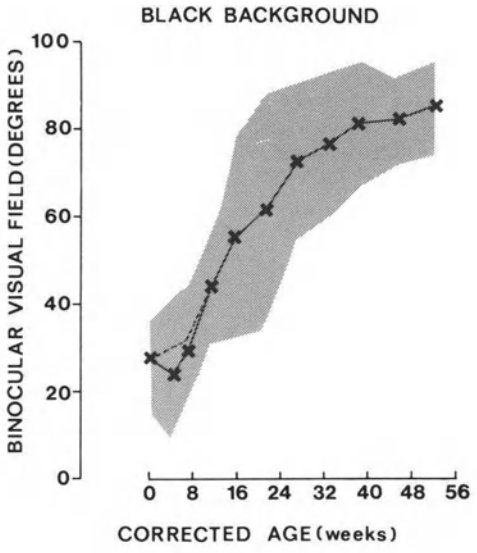
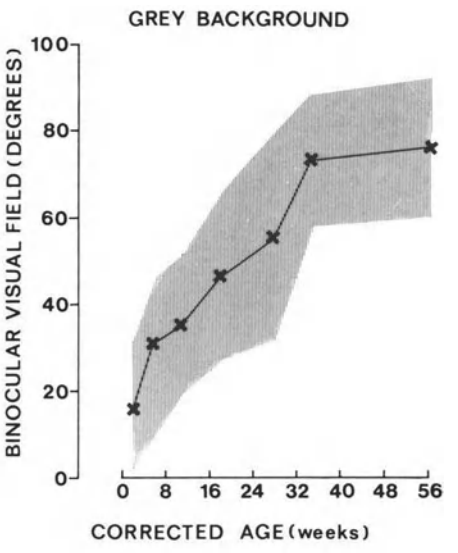


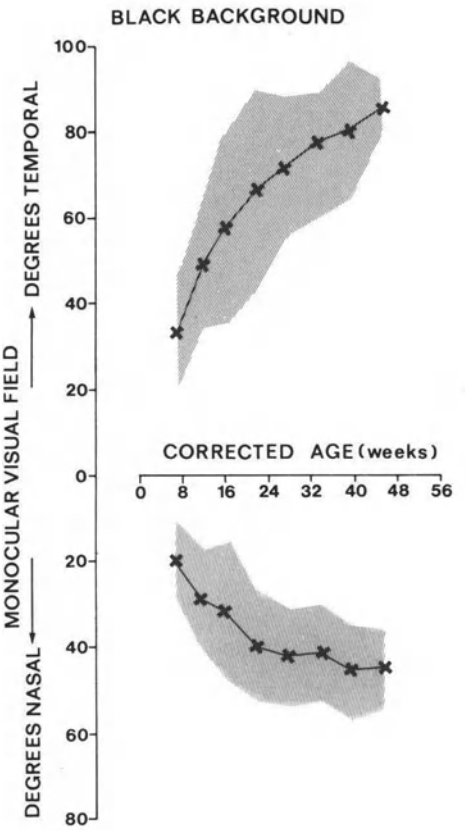
Fig.5: Acuity estimates obtained with FPL (left) and acuity cards (right) in infants at risk of abnormal development due to perinatal complications, with normal (◊) or abnormal (♦) neurological development at the time of testing. FPL measurements are compared to the mean FPL acuity of low risk preterms, acuity card results to the mean acuity of normal fullterm infants.

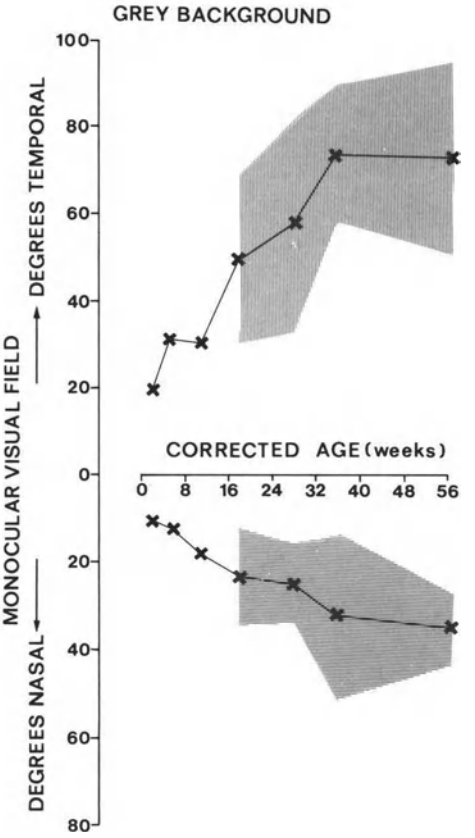
infants within the group of neurological abnormal infants, indicating that visual development was delayed but usually not arrested (Fig.5). Individual results obtained with acuity cards in infants at risk of abnormal development were again comparable to those obtained with the FPL technique (Fig.5). Due to the smaller number of infants tested with this method, the early delay of acuity development was not as evident in this group.
In general, acuity was found to vary with the severity of the neurological disorder, with normal or near normal acuities only in children with mild neurological symptoms.

The binocular visual field has been shown to be much smaller than that of adults during the first months of life, and to expand throughout the first year (for review see 57). The upper field reaches the adult extent by 12 months, whereas the horizontal and lower fields are still not adult at this age. The development of the monocular temporal visual field resembles that of the binocular field, but the nasal field is smaller than the temporal field from birth onwards (27,57,67,68).
In our studies, binocular and monocular visual fields were measured using white balls of 6 degrees diameter mounted on black sticks, and presented against a uniform grey or black background. While the infant fixated a centrally presented ball, a second target was slowly moved from the


BLACK BACKGROUND
BINOCULAR VISUAL FIELD (DEGREES)
100
80
60
40
20
0
0 8 16 24 32 40 48 56
CORRECTED AGE (weeks)


GREY BACKGROUND
BINOCULAR VISUAL FIELD (DEGREES)
100
80
60
40
20
0
0 8 16 24 32 40 48 56
CORRECTED AGE (weeks)


BLACK BACKGROUND
MONOCULAR VISUAL FIELD
DEGREES TEMPORAL
DEGREES NASAL
100
80
60
40
20
0
20
40
60
80
CORRECTED AGE (weeks)
0 8 16 24 32 40 48 56


GREY BACKGROUND
MONOCULAR VISUAL FIELD
DEGREES TEMPORAL
DEGREES NASAL
100
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CORRECTED AGE (weeks)
0 8 16 24 32 40 48 56

Fig.6 (opposite page): Normal development of the horizontal extent of the binocular (above) and monocular (below) visual field tested against a uniform black (left) or grey (right) background. The broken lines in the left upper figure show the results obtained when data from infants who were judged to be "staring" at the fixation target were excluded from the analysis (see text). The shaded areas indicate the 90% confidence interval.

periphery towards the fixation point. Eye- or head-movements towards the peripheral ball were used to estimate the border of the visual field. During our later studies, this method was quantified by using an arc perimeter consisting of 4 cm wide black metal strips, mounted perpendicularly to each other with a radius of 40 cm. The infant was held in an upright position in the centre of the arc perimeter, the background being uniformly black. Reactions were assessed by a concealed observer who was unaware of the location of the peripheral target. In most infants, the horizontal and vertical extent of the visual field was measured, while the diagonal meridia were occasionally also assessed in older infants. Orthoptic eyepatches were used to occlude one eye for monocular testing. Only the development of the horizontal extent of the visual field will be discussed below; most of the results were obtained against a grey background.

Under these conditions, the measured extent of the visual fields was found to be slightly smaller than when a black background was used, as can be seen in Fig.6. Little change in binocular field size was seen during the first two months of life in fullterm infants tested with a black background. This seems to be related to a characteristic rigid fixation behaviour, or "staring" behaviour, often shown by infants up to 7 -8 weeks (for review see 57). This apparent plateau in visual field development was not evident in the infants tested with a grey background, possibly due to the smaller numbers of infants tested. From two months onward, the horizontal extent of the visual field shows a gradual increase in normal fullterm infants up to the age of 8 months, with a slower expansion from then until 12 months.

Individual measurements of the binocular visual field of low risk and high risk preterm infants, assessed according to corrected age, are shown in Fig.7. As can be seen, the results of the low-risk preterm infants were very similar at all ages to that of the fullterm infants. High risk preterm infants often showed smaller visual fields and/or a bitemporal asymmetry. Nevertheless, a gradual expansion of the visual field was evident in older children, suggesting that visual field development was not arrested, but either delayed or slowed down. Neurologically abnormal high risk preterms showed the smallest visual field sizes and the highest incidence of asymmetrical bitemporal visual fields.

The development of the monocular visual field in the temporal direction was very similar to that of the binocular field in normal fullterms, while the nasal visual field was consistently smaller than the temporal field (Fig.6). With age corrected for prematurity, low risk preterm infants showed the same expansion of the monocular visual field as fullterm infants (Fig.7). High risk preterm infants, and particularly those with neurological abnormalities, frequently showed smaller monocular visual fields than low risk preterms of comparable age, and quite often interocular differences in the horizontal extent of the visual field (Fig.7).

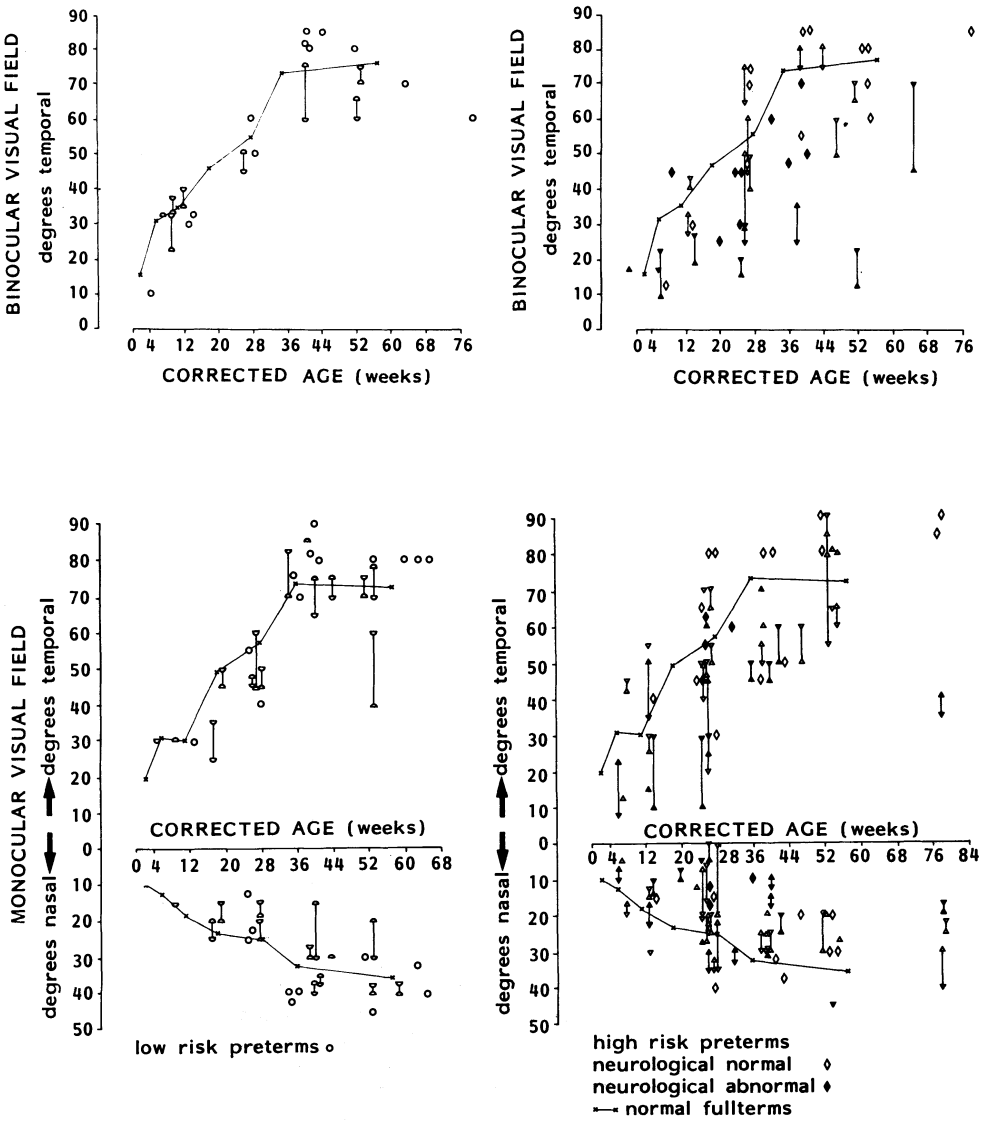

Fig.7: Binocular (above) and monocular (below) visual field measurements obtained in low risk (○, left) and in neurologically normal (◊) and abnormal (♦) high risk preterm infants (right), compared to the development of normal fullterm infants assessed against a grey background.

NEUROPEDIATRIC PATIENTS AND MULTIPLY HANDICAPPED CHILDREN

The four behavioural measures of visual functions discussed above, all of which require little cooperation and no verbal capacity, also allow assessment of visual impairments in older children with neurological disorders and in children who, due to severe psychomotor retardation, cannot be examined by standard ophthalmological tests. In the following section, we describe our findings in two groups of children either referred to us by neurologists and pediatricians, or permanently resident in a home for multiply handicapped children. The first group of patients, aged 2 weeks to 23 years, consisted of 69 children (or young adults) suspected of functional visual impairments, with a variety of neurological disorders (congenital disorders 59%, acquired disorders 41%). Ocular and neurological abnormalities included congenital cataract, coloboma, toxoplasmosis, albinism, congenital nystagmus, multiple physical deformities and none or slight to very severe motor defects and mental retardation. Etiology was similarly variable and included perinatal hypoxia, encephalopathy, tumors, trauma, etc., as well as congenital syndromes. All of these patients came to the laboratory for extensive examination. The second group of 67 patients, ranging in age from 1.5 months to 19 years, were permanently hospitalized and were all severely mentally and physically handicapped. Again, etiology included a variety of congenital and acquired disorders. These patients were examined in their residential clinic.

Methods of assessing visual functions were similar to those described above except for a more quantitaive OKN assessment in the neurological patients, and a more extensive use of the STYCAR Vision Test (69) in the hospitalized children. If the clinical conditions of the neurological patients allowed it, OKN was recorded electro-oculographically while the patient was held in the centre of a rotating drum (o.d.150 cm , height 120 cm) the walls of which consisted of paper covered with random dots. OKN was tested binocularly and monocularly with both clockwise and counterclockwise stimulus movement at velocities ranging from 7.5 to 75 degrees/sec. EOG signals, recorded on paper, were analysed for saccade frequency and the slope of the slow eye movements , which allowed a comparison of the relative response to different stimulus directions and velocities.

The STYCAR Vision Test was used to assess fixation and following movements, and also for acuity estimates. The test consists of a set of graded white balls ranging in size from 3 mm to 6.2 cm. These were presented to the patients at various distances before a gray or black background, while eye and head movements in response to movements of the ball were observed. When fixation and following movements could be elicited, it was nearly always possible to obtain an acuity estimate, defined as the smallest ball fixated at the chosen test distance.

The incidence of visual impairments in the two groups of patients was very high. Visual deficits ranged from minor impairments such as a slight acuity reduction or mild asymmetry of OKN to total blindness. Strabismic deviations and spontaneous and/or latent nystagmus were very common (both with an incidence of approx. 70%). No individual visual function appeared to be either specifically susceptible or resistant to impairment; instead, deficits were usually apparent across a range of functions. An overview of the findings in both groups of patients is presented in Table 1. Because of the variable severity of the impairments, the patients were divided into a number of different categories according to increasing levels of

TABLE I

ASSESSMENT OF VISUAL FUNTIONS IN VISUALLY IMPAIRED

NEUROPEDIATRIC PATIENTS

N=69, AGED 2 WEEKS-23 YEARS

FUNCTIONAL LEVEL	(n)	OBSERVED RESPONSES	NEGATIVE REFLEXES	POS.PUPILLARY REFLEXES	POS.OKN	POS.FOLLOWING	POS.VISUAL THREAT	RESTRICTED VISUAL FIELD	NORMAL VISUAL FIELD	VISUAL ACUITY ESTIMATE
NEGATIVE REFLEXES	(0)	–								
POS.PUPILLARY REFLEXES	(2)	–	2							
POS.OKN	(7)	–	7	7						
POS.FOLLOWING RESPONSES	(12)	–	12	6	12	4				
POS.FIXATION: RESTRICTED VISUAL FIELD	(39)	–	39	39	39	32	39	–		
POS.FIXATION: NORMAL VISUAL FIELD	(9)	–	9	9	9	9	–	9		
TOTAL	(69)		69	61	60	45	39	9	45	

MULTIPLY HANDICAPPED CHILDREN

N=67, AGED 1.5 MONTH-19 YEARS

FUNCTIONAL LEVEL	(n)	OBSERVED RESPONSES	NEGATIVE REFLEXES	POS.PUPILLARY REFLEXES	POS.OKN	POS.FOLLOWING	POS.VISUAL THREAT	RESTRICTED VISUAL FIELD	NORMAL VISUAL FIELD	SHERIDAN/ACUITY CARD VISUAL ACUITY
NEGATIVE REFLEXES	(3)	3								
POS.PUPILLARY REFLEXES	(5)	–	5							
POS.OKN	(7)	–	7	7						
POS.FOLLOWING RESPONSES	(12)	–	12	7	12					
POS.FIXATION: RESTRICTED VISUAL FIELD	(31)	–	31	31	31	20	31	–		
POS.FIXATION: NORMAL VISUAL FIELD	(9)	–	9	9	9	9	–	9		
TOTAL	(67)	3	64	54	52	29	31	9	33	

visual functioning, as indicated in the Table. In the group of multiply handicapped children, 3 showed no pupillary reflexes; this was taken as the lowest level of visual functions, i.e. total blindness. None of the 69 neuropediatric patients had negative pupillary reflexes, but two patients showed no visual response other than positive pupillary reflexes. This was also seen in 5 of the multiply handicapped children.In each group, 10% of the patients showed positive, but usually rather abnormal OKN (see below) in addition to positive pupillary reflexes, but no other sign of behavioural visual function. A higher level of visual functioning consisted of positive following responses to light in the absence of consistent fixation, which was found in 12 patients in each group. In only 4 of these 24 patients could the visual component of the threat response be demonstrated. Positive, steady fixation was considered the highest level, and was encountered in resp. 69% and 60% in the two groups. In these patients, the visual threat response was usually found to be positive, visual field size could be measured in resp. 70% and 60%, and acuity estimates were obtained in resp. 65% and 49%. The visual threat response was usually absent in patients in whom acuity could not be assessed, but was present in most patients with a restricted visual field and in all patients who showed a normal visual field extent (see Table 1). This assocciation of the visual component of the threat response with a relatively high level of visual function, together with the finding, described above, that the response is usually present at the age of 6 months even in high risk preterm infants suggests that persistent absence of the visual threat response after 6 months of age may imply a poor prognosis for later visual development.

Contrary to the visual threat response, positive optokinetic responses were frequently seen in patients in whom no other behavioural functions, like following or fixation, could be demonstrated. In 7 out of 21 "blind" patients with positive pupillary reflexes, OKN was evident on observation, while in 7 others, positive OKN could be recorded by EOG. Four patients of this group showed no ocular abnormalities and were diagnosed as being cortically blind. The presence of OKN in these patients confirms our earlier suggestion (22) that neural control of OKN in humans may be at

least partly independent of the cerebral cortex, which is also supported by a previous report in the literature (70). Spontaneous and/or latent nystagmus was seen in 72% of the patients and often interfered with OKN assessment. In 6 sighted patients, in whom positive following and fixation could be observed, no binocular OKN could be demonstrated: all 6 showed a strong spontaneous nystagmus. In 2 of these patients, who were tested at the age of 2 and 3 months respectively, the spontaneous nystagmus decreased some months later, and a positive OKN then became evident.
Symmetrical binocular OKN was encountered in only 20% of the neuropediatric patients. Several patients with a symmetrical binocular OKN showed a recovery or improvement of visual functions such as acuity and/or visual field deficits on repeated examination. Asymmetrical binocular OKN was seen in 80% to 90% of sighted patients, and usually could be related to ocular and/or neurological conditions. As mentioned above, asymmetrical binocular OKN may reflect an asymmetry in brain dysfunction, in which case poorer OKN responses are elicited with stimulation towards the (more) damaged hemisphere (23,71).
Monocular OKN was nearly always asymmetrical. In patients with symmetrical binocular OKN the asymmetry usually consisted of a superiority of the temporal to nasal component. This may reflect delayed visual development (see above), but is also seen in normal children and adults with strabismic deviations, amblyopia, and/or a loss of binocular depth perception (72-74). In patients with asymmetrical binocular OKN, the same asymmetry was often seen monocularly, providing further evidence for abnormal neurological development.

Measurements of acuity and visual fields were usually possible in patients exhibiting fixation and following movements. In the group of neuropediatric patients, the total success rate of acuity assessment was 93% in children with positive fixation. Reliable acuity estimates with either the FPL technique or the acuity card procedure, and in some cases with both methods, could be obtained in 45 of the 69 neuropediatric patients (65%). Six patients did not complete enough trials to allow a reliable acuity estimate. However, an estimate of "minimal acuity" could be made for all of them, based on the finest grating judged correctly in 80% or more of at least 6 trials, which may of may not have reflected the actual acuity threshold. Six patients did not react even to the widest stripewidth presented. One of these showed following responses to light, but not to objects, at the age of 3 months. Three months later, fixation was present and an acuity estimate could be obtained. In 12 patients, acuity assessment was impossible either due to inattention or insufficient cooperation, or because a strong spontaneous nystagmus prevented assessment of fixation.
Few patients reached normal acuity thresholds for their age. More commonly, acuity values were a factor of 2 to 4 lower than the age norm. Generally, acuity varied with the severity of the neurological disorder and developmental retardation, as well as with ophthalmological factors such as strabismus, cataract etc. These results are similar to those described in earlier studies of FPL acuity in neuropediatric patients (19-21).
In the group of multiply handicapped children, acuity assessment with the acuity card procedure was possible in 16 of the 19 patients in whom it was attempted. An acuity estimate using STYCAR vision balls was obtained in 20% of the 69 patients. Again, acuity varied with the severity of the neurological and/or ophthalmological disorder.

Visual field measurements indicated a very high incidence of deficits; only 13% of the patients showed a normal extent of the visual field. Deficits ranged from unilateral defects, bi-nasal and/or -temporal field restrictions, and homonymous or heteronymous hemianopia to tunnel vision. In many patients, the existence of field deficits had been unknown up to the time of the examination, although many of them showed suspect symptoms like torticollis, falling or stumbling over small objects, or anxiety in unfamiliar surroundings.
The observed field defects could often be directly related to the diagnosed neurological disorders. In other cases, our findings provided valuable additional diagnostic information, concerning e.g. changes in the neurological condition of patients with progressive disorders. In 2 patients with craniopharyngioma, for example, changes in intracranial pressure were reflected in changes in visual field size. In several cases, however, no neurological explanation of the field defects could be found.
Latent nystagmus often appeared to interfere with peripheral vision: many children showed bi-temporal restrictions with monocular field assessment, which disappeared with binocular testing.
In many patients, asymmetries of both OKN and visual fields were complementary and provided strong functional evidence for asymmetrical brain damage, which was often supported by CT-scan asymmetries. Similar complementary findings were obtained in some high risk preterm infants, in whom behavioural results were supported by asymmetrical abnormal ultrasound scans. In many cases, however, asymmetries were either evident only in visual fields or OKN, but not both, or even suggested involvement of opposite hemispheres. This is presumably related to the fact that the two functions are mediated only partially by the same neural pathways, so that impairment of one does not necessarily imply a deficit also of the other. Examination of both visual fields and OKN may therefore provide valuable additional or complementary diagnostic information.
Many of both the neuropediatric and the handicapped patients showed improvements in one or more visual functions on repeat examinations. Such improvements were not limited to the younger children, but were also seen in patients aged 10 years or more, even when the brain damage had occurred many years previously, or at birth.

CONCLUSION

The various behavioural methods of assessing visual functions described above have proved very useful not only for the assessment of visual development during the first year of life in infants at risk of neurological abnormalities, but also in older pediatric patients who cannot be tested with standard ophthalmological methods. Using these methods, it has become possible to detect visual impairments practically from birth onwards, and thus to obtain an early indication of possible functional consequences of perinatal complications such as hypoxic events or intracranial haemorrhage, or congenital defects. The normal variability in the development of acuity and visual field size of healthy fullterm infants during the first two months of life often made a confident diagnosis of mild deficits difficult in infants of this age range, although severe impairments were usually detectable. From about 3 months onward, however, the normative data on normal development did allow the detection of even moderately delayed development. A number of visual functions, such as the visual threat response and symmetrical monocular

OKN, only appear at or after the age of three months, and thereby broaden the range of diagnostic tools. In our experience, no single visual function appeared to be specifically or particularly susceptible to impairment. Deficits were often apparent across a range of functions,but in many cases were also seen in only one or two of the measures used. Assessment of only one function would therefore often have led to incorrect conclusions, while the combination of a number of measures is clearly more likely to provide a representative indication of the level of visual development.

Another point emerging from our studies is that visual deficits are not necessarily stable over time, so that the diagnosis of a given visual defect in young infants should be substantiated by a repeat examination at a later age. We often found deficits to have lessened or even disappeared after an interval of a few months. This was especially true for the first 6 months after term, but was also seen at later ages. On the other hand, deficits sometimes only became evident at a later age, after an apparently normal initial development. In addition, repeated examinations will also indicate whether development is progressing, even if at a slower rate, or has been arrested.

The results of our studies in prematurely born infants showed that the normal development of visual functions is closely related to corrected age rather than age from birth, as has earlier been shown for neurological development (75). This is in agreement with previous studies of preferential looking acuity in preterm infants which used less quantitative methods (76,77) and confirmed our earlier results (24,78).

The findings suggest that early visual experience of preterm infants in the period up to the expected date of term may lead to a slight acceleration of the development of visual acuity. However, the superiority of the preterm over the fullterm infants was so slight that for clinical purposes, it still seems appropriate to expect preterm infants to show the same acuity as fullterm infants of comparable corrected age. No evidence of accelerated development was seen for visual field size, the development of monocular OKN, or the visual threat response. Perinatal complications, even in the absence of neurological symptoms, frequently delayed the appearance of the visual threat response and the transition of asymmetrical to symmetrical OKN, and often seemed to slow down acuity and visual field development during the first months after term. By 6 months, acuity was usually within the normal range, whereas the extent of the visual field was often still small at that age. Follow-up examinations of these infants are needed to determine whether the early visual defects are predictive of later neurological outcome as suggested by studies of Miranda et al. (79) and Harmant et al. (80). In neurologically abnormal infants, the incidence of visual deficits, seen on one or more occasions, was very high (50%). In many of these infants, however, acuity and visual field size continued to develop, although at a lower level than normal, at least up to a corrected age of one year. Examinations at later ages will be necessary to determine whether this developmental delay is only temporary and normal visual functions are eventually attained, or whether development ceases at some point, and the deficits become permanent. Also, future research will need to examine whether specific perinatal complications might represent a particular risk factor for later visual defects, and whether infants born after different gestational periods might be differentially at risk of later impairments.

Our experience with the neuropediatric and multiply handicapped patients indicates that improvements in visual functions are certainly not

restricted to the first months and year(s) of life, but may still occur in patients aged 10 years or more. The visual system of infants and children thus appears to retain at least some degree of plasticity for many years after the occurrence of structural damage. The findings so far do not point to the existence of a single, well-defined "sensitive period" for recovery after which improvement is rarely or never seen. A possibility which remains to be investigated is whether or to what extent the final level of visual development achieved after an initial developmental delay varies with age. Thus normalization might become less likely if deficits are still present at a certain age, and this age might vary with the visual function concerned,as well as with etiology of the deficit and the age at onset. Only longitudinal studies following visual development from the first year of life until the age at which the various functions appear to be stabilized will be able to resolve this question.
The possibiltiy of detecting visual impairments during the first months of life allows treatment or stimulation adapted to the specific deficit from a very early age onwards. On the other hand, the fact that improvements were still seen many years later suggests that therapeutic measures may also still be effective in these older patients.

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SOME PERSPECTIVES ON MANAGEMENT SPEECH AND LANGUAGE DISORDERS IN CEREBRAL PALSY

E. Davies

INTRODUCTION

The first indicators of an emergent communication disorder are the failure to acquire language or the inability to produce intelligible speech, within the 'normal' time scale. Whilst it is generally accepted that the cerebral palsied child is at high risk of speech and/or language problems referral for speech therapy is often delayed until the child has failed to attain the developmental 'norms' for speech production.

Early detection and intervention are acknowledged as important factors in preventive medicine. The same principles can be applied to the practice of speech therapy. Delaying referral until the child has demonstrated problems with the comprehension or production of language wastes valuable time.

EARLY DETECTION

Retrospective evidence suggests a high incidence of feeding problems in cerebral palsied infants. Although these early problems appear significant for the prognosis for speech there are no longitudinal studies to support this proposition. It would appear logical, however, that those infants who have significant problems in coordinating the musculature for chewing, sucking and swallowing are at greater risk of developmental dysarthria than those who have comparatively minimal feeding problems. The fine motor coordination of respiration, phonation, resonance and articulation for intelligible speech is more likely to be disrupted in those infants whose muscle tone is inadequate to support the vegetative functions of feeding. The existence of pathological reflex activity or persistence of primitive reflex activity also has a major disruptive effect upon the child's attempts at speech. The simple action of mouth opening may trigger the total response of jaw extension (with possible subluxation) tongue extension, head extension, arching of the back and extension of all four limbs reminiscent of embryonic behaviour (Gesell, 1945).

The importance of the early mother-child bonding, reinforced in the feeding situation, has been highlighted by a number of researchers (Snow, 1977); and supported by a number of excellent papers presented at this Conference. Feeding problems are likely to have a negative influence on the establishment of mother-child bonding. The difficulty in providing physical support for the flaccid or hypertonic child may not allow for eye-contact, or face to face presentation. Nor may there be an equitable balance in the social exchange between mother and child when the lack of response from the child may make the mother's contribution disproportionate. These factors may all have implications for the future development of communication as a two way dialogue making the cerebral palsied child a passive receiver, rather than an active communicator.

The speech therapist's role at this early stage of intervention may

be an advisory one as part of the multi-disciplinary team. The most effective therapy may be through counselling the parents in the management of chewing, sucking and swallowing problems; and training them to recognise and facilitate the pre-verbal responses of their cerebral palsied baby.

The rationale for long term management can be evolved through informal and formal assessment procedures as the child develops.

A model, based on an approach for acquired neurological disorders (McNeil, Rosenbek and Aronson, 1983) presents a comprehensive perspective for management of potential speech and language disorders in cerebral palsy.

The primary aims of early intervention are (i) to facilitate language acquisition and/or learning; and (ii) to provide as much volitional control for speech as is physiologically possible.

Language is normally acquired in context as the child explores the environment. The cerebral palsied child is at an obvious disadvantage - exploration being limited by poor motor coordination. Sensory feedback may also be impaired. Language delay may also be attributable to the inter or intra-systemic reorganisation which may be necessary to compensate for diffuse brain damage (Luria, 1961).

Language development may be informally observed or formally assessed, and, again, the parents used as partners in therapy to facilitate language learning in a natural context. Parents need to be counselled not to over-stimulate in their anxiety to succeed, but to allow time for the processing and learning to take effect. This stress on the function of language rather than its structure is a pragmatic approach supported by current research (e.g. Bruner (1975), Yoder and Calculator (1981)).

The second objective (i.e. the provision of as much volitional control for speech as is physiologically possible) goes beyond the boundaries of a purely speech oriented approach. It is a flexible view of management found to be effective in acquired neurological disorders. It takes into consideration the prognosis for intelligible speech and encompasses learning compensatory strategies; mechanical medical or surgical intervention; the introduction of supplementary means of communication; and the provision of maintenance and support.

Compensatory strategies to improve pulmonary air flow and the synchronous coordination of phonation and articulation can be turned into a game for the young child. Toys which provide visual or auditory feedback as a reward can be used as motivators for the child to sustain vocalisation. For the slightly older child a U-tube in water to monitor the effect of oral pressure may be sufficient incentive.

The traditional sucking and blowing games used in therapy are also effective in improving respiratory phonatory and articulatory valving. Although medical and surgical intervention are the specific responsibility of the medical team the speech therapist may be closely involved in monitoring the effect of drug therapy on muscle tone and the implications for feeding and speech. Follow up therapy may also be necessary for those children for whom pharyngo-plasty has been instigated to overcome palato-pharyngeal incompetence. Anastomosis of the salivary ducts has also been used conservatively with children with severe drooling problems.

Mechanical intervention is less traumatic than surgery and may be used as an intermediate measure. Palatal training devices - small acrylic plates (similar to those used for dentures) are secured to the hard palate by two retaining clips attached to the molars. A loop or bulb extends to the soft palate to provide support for the soft tissue. In some cerebral palsied

children (primarily the spastic category) these devices have been effective in helping to control dribbling (Ellis and Flack 1979).

A behaviour modification approach using a lip sensor has also been successful as an alerting device for the persistant dribbler.

Supplementary systems of communication have often been regarded as a last ditch approach in the management of children with speech and language disorders (Silverman 1981). Increasingly these augmentatives or alternatives to speech are being introduced to support poor functional speech or as a replacement for the child with no intelligible speech. Studies undertaken with deaf children introduced to sign systems (Wilbur 1976) suggest that those children provided with an expressive medium early in life are more successful cognitively, educationally and socially, than their non-signing peers.

The same parallel is drawn in studies with mentally handicapped children introduced to supplementary means of communication (Fristoe and Lloyd 1977). No longitudinal studies have been undertaken with cerebral palsied children using supplementary means of communication but one would assume that the same benefits would apply. The main objections that the introduction of an alternative or augmentative might inhibit language development or depress functional speech appear unfounded. Empirical data suggest the converse of this to be true.

Physical handicap may militate against the introduction of manual signing systems, but for those for whom upper limb function is adequate gestural or systematic sign systems may be appropriate. The more severely physically impaired have recourse to visual systems, e.g. picture boards, symbol displays or alphabet or word boards which can be indicated directly by hand, fist or finger pointing or indirectly accessed by switches operated by foot, hand or eye gaze. The tremendous advance in technology has ensured that there may be no child or adult too severely handicapped to communicate (Silverman 1981).

Supplementary, augmentative or alternative systems of communication in current use can be broadly sub-divided into those which are unaided (i.e. require no physical support) and those which are aided (i.e. require a visual display or technological support)(Vanderheiden and Grilley, 1975).

Of the unaided systems American Indian Hand Talk (Amerind)(Skelly, 1979) is probably the oldest, having been devised by the nomadic tribes of North America to overcome the communication problems created by the multiplicity of tribal languages spoken. Amerind conveys concepts through pantominic gesture, easily interpreted by the receiver. As the gestures are not modelled on spoken language Amerind is more accurately described as a gestural code. Many of the original gestures (e.g. raised hand, palm outward in greeting, and rubbing the thumb against the forefinger for money/commerce) have been absorbed into international signalling systems. Amerind has been used successfully as an alternative to speech for those who are at a pre-symbolic level of development or have lost the ability to communicate because of acquired organic or neurological disorders.

Sign languages devised by deaf people for their own use have been in existence for over a hundred years in their more systematic form, although idiosyncratic signing has obviously been used as a supplement to speech by deaf individuals throughout history. The adoption of these systems for non-speaking people other than those with hearing impairment has occurred comparatively recently. The debate still continues in the field of education of deaf children as to whether an 'oral' or 'signing' approach is more appropriate; for those working with non-speaking children and adults the advantages of sign as an alternative or supplement to speech often

outweigh other considerations. Signing is cheap, effective and immediate. It does, however, require adequate upper limb control, good kinaesthetic memory and face to face presentation. There are also difficulties, with the more structured sign systems, in their ease of interpretation by the 'receiver' or 'listener'. British Sign Language and its American counterpart Ameslan have been taught to non-speaking individuals since the early 1970's with considerable success (Wilbur, 1976). The major criticisms of these sign 'languages' is that they do not conform to the syntactic rules of spoken language. Systematic sign systems modelled on spoken output have been devised to overcome these reservations: Paget-Gorman Sign System (Gorman and Paget, 1976) and Signed English have been used with children with specific language disorders, in addition to those with hearing impairment.

A developmental vocabulary (Makaton) has provided a structured language programme for teaching mentally handicapped individuals. Makaton uses British Sign Language as its expressive medium (Walker, 1976a).

Aided systems use a visual referent and require some form of display. At the most simplistic level, photographs, pictures or line drawings mounted on a diplay board may enable the user to communicate basic needs. For children and adults at a pre-symbolic level of development, picture boards open the door to communication.

For those able to use a symbolic system of communication there is the possibility of expanding expressive output, reinforcing the two-way exchange of information and contributing towards the development of more abstract language. Symbols may be simple pictographic representations e.g. Rebus (Devereux and Oosterom, 1984) or conceptually based, e.g. Blissymbolics (McNaughton, S. 1985) and presented on a grid within the users visual scanning range and physical access.

Within the continuum of visual speech supplements, symbols, which have the written word accompaniment, provide reinforcement of traditional orthography, for the user, and an immediate translation for the receiver.

Visuo-graphic systems lend themselves to technological development permitting even the most severely physically handicapped individual the opportunity to communicate (Silverman, 1980).

Technological aids have revolutionised thinking in terms of the provision of an alternative or supplementary means of communication. They can be adapted to grow with the user, using pictographic, symbolic or traditional orthography to access printed or spoken output. Cost often restricts provision, maintenance is an important aspect, as for the user portability and reliability are major considerations. The whole area of matching the system to the user is fraught with problems.

The selection and prescription of these alternative or augmentative systems, either as temporary or long term supports for cerebral palsied children, is a multi-disciplinary responsibility; to ensure the child has the necessary cognitive skills to use the systems; has the physical ability to access the system; and has the social support to communicate with others.

Maintenance of functional communicative abilities is part of continuing care in speech therapy. Facilitatory techniques support volitional control by stimulating, strengthening or 'normalising' muscle tone. Many of these techniques are borrowed from physiotherapy approaches and applied in the practice of speech therapy. Proprioceptive neuromuscular facilitation (P.N.F.) uses the techniques of resistance, brushing and icing to improve targeting and performance (Darvill and Langley, 1979). Inhibition of primitive or pathological reflex activity to

normalise tone for respiration, phonation and articulation are techniques developed from the work of Bobath (1984). The principles of rhythm, repetition and intention used by Peto (Cottam and Sutton, 1986) may also be used in a group approach to the management of young cerebral palsied children (Miller, 1972).

The theme of maintenance can be extended to the upkeep of communication aids - the hardware provided to supplement speech. It is essential that aids, once prescribed, are regularly serviced to ensure reliability.

The communication process is a dynamic one and throughout its development, the cerebral palsied child will require support. Support within the home environment, support for parents and professionals and support for the child's changing communicative needs.

The role of the speech therapist in the detection and management of cerebral palsy is, to paraphrase Yoder and Calculator (1981), to ensure the child has something to say, provide a means of saying it, and a reason to communicate.

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THE IMPORTANCE OF EARLY TREATMENT

E. KOENG

1. DEFINITION OF EARLY TREATMENT

Early treatment starts before abnormal movement patterns are fully established, i.e. during the first year of life; the more severe the case, the earlier it is necessary to commence treatment. We than have a better chance to train normal movement patterns and to prevent the development and fixation of abnormal movement patterns. Without early treatment the baby experiences mostly abnormal movement patterns, uses these for his activities and learns to sit, walk and use his hands in an abnormal way.

Early treatment also includes advising and helping the parents with daily handling. This means having time for the parents, listening to them, answering their questions and trying to help with problems when needed.

2. HISTORY OF DEVELOPMENT OF EARLY TREATMENT

About 40 ears ago, E. Collis, an Irish physiotherapist, was the first to realize that cerebral palsy manifests itself only gradually and to recognize the chance of early therapy (4). But at the time effective treatment techniques for young babies had not yet been developed. Passive movements did not help. Voluntary training in the sequence of normal motor development proved too difficult, even when combined with play (a young baby does not move on command), and it reinforced abnormal postures and movements. Correcting splints and braces not only reduced mobility, but also increased spasticity in other parts of the baby.

The most important contribution came some years later from B. Bobath (1) in London, who found a way to control abnormal movement patterns of the child with the hands of the therapist. This control enabled the child to react with spontaneous normal movements. But it worked only in less severe cases. Subsequently, the combination with techniques to facilitate normal automatic reactions, also introduced by B. Bobath (2,3), was the decisive step towards a dynamic and more successful treatment of cerebral palsy. It provides the possibility of transmitting normal active sensorimotor experiences to the child, already to the young baby. This type of therapy is now called Neurodevelopmental Treatment (NDT). A child with a brain lesion, like a normal child, learns by active sensorimotor experiences. Repetition is needed. It is important that a potential cerebral palsied child experiences

the basic movements in many different ways, just as a normal baby does, only under control of the therapist's or parents's hands. Therefore, treatment must be integrated into everyday handling. Parents' cooperation is essential. This also encourages and supports the parent-child relationship.

The treatment of feeding problems, of sucking and swallowing difficulties is based on the same therapeutic principles. With head and jaw control, sucking, swallowing and chewing can be facilitated more easily, and in most cases, dribbling can be avoided. An early start is essential to obtain an understandable speech.

Neurodevelopmental treatment has gradually been more and more developed. Techniques have become finer, more adapted, nearer to life. We can provide pleasure, prepare the child for new activities which he enjoys (including sport for the older child) and include educational measures.

Neurodevelopmental treatment looks very easy and natural, but it requires a good knowlegde of normal and abnormal movements and their development, some basic knowledge in language, mental and social development and in child psychology, skilful therapeutic hands, flexibility and adaptability to the ever changing situations, creative fantasy. It is never boring! In spite of this, parents can be instructed in a simple way in momentary important movements and in daily handling (therapeutic handling means that basic therapy principles are combined with the daily handling of the baby, i.e. with carrying, dressing, undressing, bathing, feeding, etc.).

3. WHEN TO START TREATMENT

With the newborn baby? During the first months of life? There are many babies who show apparently abnormal motor behaviour during the first months of life. Most of them overcome it spontaneously. Therefore, it seems rather a luxury to treat the newborn baby, except, for example, in the case of an extreme opisthotonus or feeding problems. Good handling by nurses and parents from the beginning, supporting normal development, is certainly an advantage for every baby. Still more important are check-ups by the pediatrician, not only during the first months, but during the whole first year of life, at least for suspect babies, and even better for every baby.

As indication of treatment, generally from the 4th month onwards, or, in more severe cases, even earlier, we consider increasing dominant stereotyped movement patterns, which appear with activities, with every stress situation. Very often, there exists competition between normal and abnormal movement patterns. With treatment, we try to intensify the active normal sensorimotor experiences.

4. POSSIBILITIES AND LIMITS OF EARLY TREATMENT

With early therapy, under favourable conditions, we have the chance to integrate active normal sensorimotor experiences, before abnormal movement patterns have become a habit, if the brain lesion is not too extended. The child will then be able to use spontaneously in every day life the movements

he has experienced in the therapy. We can use optimally existing potentials to obtain an optimal result for each individual case.

In children with additional severe perception problems and/or a severe mental handicap the treatment result is very limited. Children with severe proprioceptive and temporo-spatial perception problems perceive only to a small degree the normal reactions in therapy, and therefore their motor progress is slow. Severely mentally handicapped children don't use spontaneously in daily life what they have experienced in therapy.

We have also experienced that hemiplegic chlidren will always continue to favour their better side, even if the handicapped side becomes very mobile and automatic bilateral activities can be obtained. In potential diplegias, it is necessary to start treatment before the babies become very active in manipulating objects. Otherwise, due to associated reactions of the legs, daily therapy time, giving them more normal sensorimotor experiences, will be too short to win the competition.

Some external factors, such as quality and grading of training (therapy) and motivation, also have an influence on the result, in a similar way as for achievements in sports and skills in normal children:

4.1. Quality of therapy

It is essential to get active automatic reactions, to be able to wait for these reactions, to adapt the therapy continuously to the momentary situation of the child and to gradually withdraw control, so that the child can take over.

4.2. Grading of therapy

Challenge with therapy is necessary. If the child is not challenged enough, there is nothing for him to learn, it is uninteresting. On the other hand, overchallenge leads to fatigue and dislike of therapy. How much therapy is needed? One hour per week is too little, several hours per day are too much and provoke adversion to therapy. We recommend for babies and small children 10 minutes several times a day, possibly with mother or father; at preschool age and school age 1/4 to 1/2 hour a day, in some cases longer or shorter, depending on the individual situation, and with the aim that cooperation may continue for a long time. At the Centre, treatment with parent instruction is generally given once a week for most children, twice a week if there are special problems; for the older child less often, depending on the handicap.

4.3. Motivation

Engagement and the realistic belief of the therapist to obtain improvement (if the potential is there) are motivating for parent and child. Also the adaptation of the therapy to the personality and interests of the child contribute much to good motivation. It is important to give the child pleasure through the therapeutic movements, also by combining these

with new activities and games. And it is also essential that doctors and therapists explain their work clearly to the parents, in a way that they can understand. It has, for example, proved worthwile to let the parents themselves experience the movements one teaches them, the carry-over is easier. Also one should not overload the home program, but adapt it to the situation and capabilities of the family.

5. HOW LONG SHOULD THERAPY BE CONTINUED?

It is necessary to continue therapy until the obtained result is secured. Otherwise, if treatment is stopped immediately when a child makes its first steps, abnormal movement patterns may become dominant again.

With a residual handicap, even a slight one, it is well worthwile to continue treatment, in a reasonable way, until adulthood; mobility, stability and the quality of life will further improve. There are always things a child cannot yet do well, although he would like to (in daily life, in sports), and we can prepare these activities in treatment and in this way motivate him. The amount of treatment should be individually adapted according to problems and priorities. It can be reduced for the school child, even to 10 minutes a day at home (training just the individually most important movements, and thereby retaining the more normal sensorimotor experiences), alternating with more intensive treatment periods when necessary.

In the very severely multiple-handicapped child (with a mental level of a few months), help to the mother to facilitate nursing and prevent backstrain is most valuable, but neither therapeutic nor educational overstimulation are worthwhile. It is more important that such a child receives the love of his parents and siblings. Love is perceived even by the most severely handicapped child. The pediatrician's task is to be there, when needed, to listen, to give some help in daily life, to do his best to guide the family back towards a more normal life, which will also have a positive effect on the handicapped child.

6. IS EARLY TREATMENT STILL NECESSARY, IN SPITE OF PREVENTION?

During the last 20 to 30 years, the panorama of cerebral palsy has changed significantly. Hagberg (5) in Sweden has demonstrated this by his statistics. The same trend is observed in more and more countries. The classical clinical picture of athetoids and spastics is gradually disappearing. Mainly children with a slight or minimal motor handicap and a few very severely multiple-handicapped remain. Many factors have contributed to this improvement, mainly prevention (general health education, good parental care, optimal obstetrics and modern neonatology), but also the close teamwork between obstetrics, neonatology, developmental pediatrics and cerebral palsy centres which has helped towards early detection and therapy (8). There are still babies with a dominant abnormal motor behaviour.

In our experience, early therapy and early educational measures have in many cases a positive influence on the

degree of remaining handicaps (6,7). To illustrate this with an example: Even with modern neonatology, there is still a tendency to a few potential diplegias in premature babies. With early treatment, most of these remain with a minimal motor handicap and normal appearance, some with learning disorders. But occasionally, such a child still gets only referred for treatment in his second year of life when, unfortunately, he has already developed a pronounced spastic diplegia which could have been prevented.

It can thus be seen that early treatment gives us the chance to reach the optimal level of potentialities which helps towards a better quality of life.

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THERAPY FOR THE MOTOR DISORDERS

Sophie Levitt

For most medical conditions referred for physiotherapy, there are generally accepted physiologies and pathologies. The therapist devises or selects methods based on this knowledge. However, in the field of cerebral palsy, the therapist is faced with controversial theories upon which to base her work. It is not altogether surprising that there are different systems of therapy each with its own theory and set of methods.

Some therapists still follow one school of thought whilst others have preferred to draw on many different viewpoints. I have always found it difficult to confine myself to one viewpoint. This is not out of lack of respect for the particular authorities in the field, but for theoretical, clinical and research considerations.

Theoretically we still do not have all the answers on brain function, not only when it is normal, but more importantly when it is damaged as it is in cerebral palsy. Although it would be reassuring to know exactly why we do what we do, we have to live with the fact that there just is no proven all-encompassing theory for our treatments. Our methods must be based on careful observation of what cerebral palsied children do before and after our interventions. Clinical experience in any setting confronts one with children of different ages, different personalities, possibly the different sexes which have varied reactions to treatment methods. The medical pictures are also individual. Each child is in an individual cultural, social and emotional setting. Family backgrounds are well known to affect the response to physiotherapy. It is therefore important for each therapist to build up a repertoire of many methods and not limit herself to one set of methods.

It is extremely difficult to carry out research to prove which set of methods achieves the best results. There are many variables in clinical, psychological and social influences on the results of treatment. Thus far no reliable study has been possible, though a few have been carried out and heavily criticised.

How then does a therapist work who wishes to draw on apparently different therapy systems? In my comparative study of the work of Phelps, Collis, Fay, Bobath, Vojta, Kabat and Knott, Rood, Peto and other lesser known authorities, I find common ground for therapy. Differences do exist but they have received far too much emphasis. Terminologies also vary and make <u>apparent</u> differences in both methods and theories.

Common principles of treatment

Most therapy approaches agree on the following:

1. Early treatment
2. Use of Developmental motor stages
3. Use of sensory (afferent) stimuli to evoke activity or to reduce spasticity and other undesirable motor activity.
4. Some favour automatic movement reactions whilst others prefer conscious motor control.
5. Passive treatment is of little value, but has a place.
6. Deformities are prevented or corrected.
7. Repetition of motor actions in order to achieve them.
8. Motivation to move.

More of such common denominators are discussed in my book (Levitt 1982)

Common denominators concerning Posture and Movement development

All therapy approaches have methods to assess and treat the postural control and voluntary movements of the child. My studies reveal that some authorities use all the postural mechanisms - though they name them with different terminologies. Others have only observed a few of these mechanisms. I have found the following terms helpful in clarifying those mechanisms that we observe and treat. I shall discuss the terms used so that therapists are able to draw ideas and methods from any system in order to treat these aspects of postural control and voluntary motion. A practical framework for therapy has thus been devised and discussed in my book (Levitt 1982).

Postural mechanisms.

Postural fixation or Stabilisation.

This is also called "isometric muscle actions", "tonic activity", "static" or "holding muscle actions", or "heavy work of musculatures". The child develops the ability to hold his body up against gravity. The child from infancy develops abilities to hold parts of the body such as the head, shoulder girdle, pelvic girdle and trunk up against gravity. Stability of the body as a whole is also acquired.

Counterpoising or counterbalance, also involved in "weight shift", "balance during motion", "body sway, distal part moving on posturally fixed proximal part" or the term "movement superimposed on co-contraction". This mechanism involves the maintenance of balance while parts of the body move. The body, usually the trunk adjusts to allow the head or limbs to move so that balance is maintained.

Righting or rising reactions.

These make it possible for the child to rise from the floor to the uptight position. These reactions make position changes of various kinds possible. Terminologies vary from "assumption of posture", movement patterns" "moving in and out of positions" and other descriptive phrases. All the head, neck and body righting reactions are present in order to rise

and change positions.

Tilt reactions.

When a child is tilted well off the horizontal plane then the tilt reactions occur to prevent that child from falling. The tilt reactions are seen as adjustments in the head and trunk to avoid the fall.

Saving reactions.

When a child does fall despite the tilt reactions his/her limbs are used in a variety of saving reactions to prevent a complete fall. The saving and also propping actions of the limbs serve to widen the base to decrease the complete fall. There are many terminologies again. The "protective responses", "parachute reaction" and other specific saving reactions such as "head protection reaction" "arm balance responses" "precipitation reflex" "staggering reaction" and "hopping reaction". The "Equilibrium reactions "are terms used for combinations of Tilt and Saving reactions. It is more useful to isolate these observations as one reaction may be more active than the other. Both need to be developed in the child with inadequate balance control.

The Locomotive reactions

These are used to initiate stepping and to stop stepping. They are usually linked with a discussion of the postural mechanisms.

Voluntary motion.

Voluntary motion is purposeful, concious, willed movement. Voluntary movements use many different synergies of muscles or "chains of muscles" called "movement patterns". Abnormal combinations of muscles are seen in cerebral palsied children and called "spastic patterns" or "pathological movements" or "primitive patterns" and considered undesirable. They have been observed to result in inefficient motor control. These abnormal movements also result in deformities.

Perceptual motor function

Problems of sensory and perceptual development affect the development of movement and posture. Therapists together with teachers and psychologists contribute various methods for the development of the senses, linking of senses, sensory discriminations and sorting out of sensory information. Training is needed of the child's body scheme and spatial relationships as well as the speed and direction of the child's movements.

The role of the physiotherapist.

The physiotherapist contributes the following:

1. Assessment of the child's motor function and of his/her parents.
2. Selection of methods for specialised physiotherapy sessions.
3. Selection of methods for parents, teachers, nurses and others who care for the child.
4. Assessment and selection of appropriate equipment (aids),

playthings.
5. Demonstration and supervision of methods and equipment used by those who care for the child.
6. Reassessments to evaluate the progress.

Assessments.

The physiotherapists assesses the motor developmental levels in the child. Each motor developmental ability is analysed to detect postural mechanisms and voluntary motion. She detects which postural mechanisms and voluntary movements are absent, just beginning or are present. She detects any threatening deformities or established deformities which prevent motor developmental functions from being achieved. Other deformities may not prevent achievement of motor control but distort the way they are performed. For example, a child may walk, but its gait looks abnormal. Thus the physiotherapist assesses what the child can do, cannot do and how he does what he can do.

The physiotherapist assesses methods for each child. Which methods are relevant to the child's specific motor problems and which methods are also relevant to the whole child. In addition, the mother or parents and the other carers have to be assessed as to which methods suit them. Some parents are more skilled or can take on more home treatments than others. Some mothers can give more time to the cerebral palsied child at some periods than at others. Some parents may go through severe periods of stress and have to be relieved of responsibilities for therapy regimes during these periods. Older children may take on responsibilities for their own motor training. All these situations have to be assessed in relation to the selection of methods.

Selection of methods for specialised physiotherapy sessions.

These methods are selected from any system of therapy according to which show a response in the child in the first few assessment with that child. In time, the therapist gets to know the child by repeated observations of him or her during therapy. Other methods may then be tried which obtain an even better response from the child.

There are many "neuromuscular facilitation techniques" from different systems which are available today. These methods reveal any dormant motor activity in the child's nervous system. The physiotherapist can then advise other professionals and parents to train a motor function at the appropriate developmental time.

The physiotherapist's specialised neuromuscular techniques are used to reveal "flickers" of motor control, as well as to augment poor motor control. special skill is needed. Some mothers can be trained to use specialised neuromuscular methods. However, to my mind, it is much more important to spend parents' time augmenting poor motor control within the all-day care of the handicapped child. Parents also have to spend time consolidating the motor abilities that the child has acquired. The selection of methods for the child's all-day management can and should incorporate such treatments.

Selection of methods for parents, teachers, nurses and others.

The physiotherapist assesses which postural mechanisms and voluntary motion patterns are present in the daily functions of the child. Together with the occupational therapist she will assess these motor aspects in the activities of feeding, dressing, washing and bathing, toiletting and play activities. Other professionals also contribute to the learning of these daily activities or daily tasks. There are not only motor aspects to be trained by therapists but there are also emotional, mental, perceptual and social elements. All have to be integrated as total tasks for the child. Professional teamwork is thus essential.

The physiotherapist cannot consider the neurophysiological motor component of any daily living task in isolation. The motor components have to be integrated with the other aspects. The parents role is to do this as carers of the child. The parents should not be obsessed with the motor aspects only. Therefore, the physiotherapist should help parents train the motor controls within all the activities of daily life. The parents also come to appreciate this approach more as it is relevant to their daily life with the handicapped child. They train motor function as part of the child's growing independence in his or her daily life. This is particularly motivating for both child and family. They will then repeat therapeutic motor activities which directly creates independence in self help, locomotion and play.

These are the needs of child and family. Specialised treatment sessions do not always appear as directly relevant as the motor corrections and training within the context of these daily life activities.

Assessment and selection of equipment (aids) and playthings.

The physiotherapist together with the occupational therapist, assesses which equipment (aids) and playthings are required for each child. The child's particular level of motor development is important as equipment which gives too much help will deny these levels of ability. Equipment which is not carefully measured for each child will not be of value to the child. Equipment which is too small or too large for a child can lead to deformities of that child. The therapists have to check the environment of the child as equipment may be too bulky of too awkward to handle in particular nurseries or homes. Choice of any piece of equipment may require not only a motor assessment, but also the levels of mental, perceptual and motivation of the child.

Equipment selected by therapists include pushchairs, wheelchairs, standing and walking aids such as crutches, sticks, standing frames and walking apparatus. The child's furniture has to be checked so that he can function in them and so that no deformities are being generated during their use. Sometimes specially designed chairs and tables have to be selected for children.

At different levels of motor control the child will enjoy playthings which demand movement. The therapist will also select playthings which stimulate movements at a more advanced

level of motor development. Corrective movements and postures can be developed within play activities with and without toys. Physiotherapists and occupational therapists use various recreational activities as therapy for particular motor patterns. For example, play in adventure playgrounds, movements to music, horseriding and swimming are used as therapeutic activities.

Demonstration and supervision of methods and equipment.

Physiotherapists show parents and other carers of the child how to carry out the motor training methods selected. They show parents how to apply orthoses (calipers, braces) splints or plasters prescribed by the medical consulants. The use of any equipment and playthings as well as special aids for feeding, dressing, washing, toiletting and furniture are demonstrated.

The relationships with parents and carers are crucial in all these demonstrations. Much encouragement is given to those who care for the child during these practical demonstrations and by supervising their efforts. The therapist often finds varied skills and talents among carers. If she builds up their confidence in handling the child, training the child and playing therapeutically with the child there are many rewards. Parents and carers may contribute their own observations and ideas to help the child. The physiotherapist can learn much from this. She will obtain fresh ideas from the child's own environment which she can adapt for her aims of therapy.

Repetition of desirable motor activities are more likely if parents and carers are confident in their use and motivated to carry them out. They should also be encouraged to report their own opinions on when and where the child uses the motor activities recommended. Therefore, the physiotherapist has to allocate much time for parents and other carers.

Reassessments

The progress of the child is reassessed from time to time. Methods and equipment may be changed or modified according to these reassessments. Parents change in their attitudes to their child and this may need different therapy plans. The child may have moved from one educational setting to another which will also demand other more appropriate therapy plans.

The assessments and reassessments of the child are controversial. Some physiotherapists focus on either muscle strengths and relaxation or reflexes or tone assessments or joint ranges. These all have a place but it is a motor function assessment that matters most. In the end all systems of therapy aim to achieve independent motor function in the child. Analysis and degrees of motor functions seen in child development are the fundamental assessments and reassessments.

Conclusion

The therapy of the motor disorders does not only help to ameliorate the defects in cerebral palsy but develops potential motor abilities. The therapist develops the postural mechanisms and voluntary movements seen in normal child development. At different levels of child development different postures and movements are trained. Each child can only achieve those

postures and movements that his damaged central nervous system can learn.

The learning of postures and movements depends on many factors and not only on the medical picture. Thus therapists work closely with other therapists, teachers, parents and other child carers. The postures and movements that these people, in their own situations face in the child, are the ones where they need help from the physiotherapist. These are the motor functions of the daily life activities of the child.

Specialised neuromuscular techniques used by skilled physiotherapists are also needed to detect what level of motor activity is present in the child as well as to build up such activity. Treatment sessions with physiotherapists are required. However, they must not be given preference to the all day corrective motor training of the child in feeding, dressing, washing, toiletting and playing. Both aspects of the therapy programme are important. Some even argue that the all-day management is a priority for many families and the child.

The knowledge therapists have today of working with parents and developing motor function in everyday activities should be used as early as possible. Before a medical diagnosis is made, it is still helpful to have a physiotherapist show a mother how to handle a baby, stimulate movement and balance and motor activity within the child's daily care. Whilst parents wait for the accurate diagnosis they can be given confidence in living with the child and helping its motor development as one would help any child develop.

The role of the therapist is in Assessment, Therapy planning and Evaluation of the motor disorders. This she does in a team of many other professionals as well as together with parents.

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Intuitive Parenting Behaviors: An Early Support for the Infant's Mental Health and Development

Introduction

Advances in pediatrics and neurology in the past 20 years have resulted in a vastly improved survival rate for at-risk infants. During this same period psychologists, ethologists, and members of the medical profession have become increasingly interested in chronicling and understanding the course of normal early development and the genetic and environmental factors that influence it. The apparent but insufficiently understood links between physical health, psychological processes, and social interaction have reduced the isolation and sharp distinctions between the fields of psychology, psychiatry, neurology, and pediatrics and have led to the recognition of areas of mutual concern in dealing with developmental and behavioral problems in infancy and childhood. In turn, this has resulted in the awareness of the need for a more comprehensive, multidisciplined approach to the diagnosis and treatment of at-risk infants (Herskowitz & Rosman, 1982). Combining a neurological approach with a psychosocial one has been proposed as a means for increasing the predictive validity of an "at-risk" designation and enhancing the effectiveness of professional interventions with these infants and their families (Beckwith, 1976).

The designation of "high-risk" or "at-risk" is assigned to those infants whose medical history or home environment may put the infant at greater statistical risk of experiencing some sort of handicapping conditions during childhood. "At-risk" includes not only preterm infants

and those infants with a history of prenatal or perinatal complications but also infants from stressed, unstable, and poor families. Not all infants who are designated at-risk, who have medical histories that would indicate the possibility of central nervous system damage, and who display some behavioral symptoms of early central nervous system impairment or injury show clear neurological signs of damage. Additionally, there exists tremendous and unexplained individual variability in the behavioral and developmental responses of at-risk infants to specific pre- and perinatal hazards. Increasing evidence indicates that environmental factors, especially those factors that are related to the caregiving environment, strongly influence the developmental outcome for all infants (Beckwith, 1976; Sameroff & Chandler, 1975; Werner, 1980).

The earlier notion of the infant as a passive recipient of environmental stimulation and socialization has been replaced as research evidence has accumulated demonstrating that newborn infants actively organize, integrate, and adapt to experiences, and appear to be biologically programmed to initiate and respond to human interactions (Beckwith, 1976; Papoušek,1967, 1977). This change in perspective has led researchers to question the role and effect of the infant on the interaction patterns that develop between parents and their children. The developmental effects and reciprocal nature of parent-infant interaction in both normal and at-risk populations have since become the subject of an ever increasing number of research efforts and review articles (Belsky, 1984; Jones, 1978; Kearsley, 1979; Lewis & Rosenblum, 1974; Lipsitt, 1981; Papoušek & Papoušek, 1978, 1979, 1982, 1983; Richter & Boger, 1983; Sameroff, Seifer, & Barocas, 1983; Silverton,

Finello, & Mednick, 1983; Stott, Musick, Clark, Cohler, 1983; Vietze, Abernathy, Ashe, & Faulstich, 1978).

Research evidence indicates that characteristics of children hypothesized to make them more or less difficult to care for seem to shape the quality and quantity of parental care they receive (Belsky, 1984). Beckwith and her colleagues (1976) found differing patterns of maternal behavior in relation to the assessed developmental levels of preterm infants. The results indicated that differing patterns of social interaction between mothers and infants at one month of age were related to infant performance on developmental assessment tests at nine months of age. Vietze and his colleagues (1978) found that mothers of developmentally delayed and nondelayed children showed similar patterns of reciprocal vocal interaction. However it was speculated that differences found in infant-contingent responses to maternal vocalizations might eventually affect the interactive style of the mothers by decreasing the amount of maternal-contingent behavior in response to those infants who failed to respond contingently to their mothers.

Research efforts to learn what kinds of parenting behaviors appear to promote optimal development in children suggest that parents who display behaviors that are sensitively attuned to their children's capabilities and to the current developmental tasks of their children tend to promote a variety of highly valued developmental outcomes including behavioral independence, social competence, emotional security, and intellectual achievement (Belsky, 1984). Additionally, research has indicated that infants who were either classified as at-risk because of pre- or perinatal complication or who at later ages were found to be learning disabled were more frequently described as

temperamental, fretful, or not good natured by their mothers. The behavior of the mothers of those children who could be described as difficult to care for were more frequently described as erratic, worrisome, and tending to foster dependency. It appeared that negative patterns of interactions were being established between difficult or nonrewarding infants and their increasingly frustrated mothers (Werner, 1980).

Thus there is increasing evidence that early social interaction between infants and parents can effectively contribute to the infants' optimal development and therefore lessen the impact of various environmental or genetic risk factors. But it is also clear that interactional difficulties or failures can lead to a vicious cycle of mismatched or destructive interaction patterns with serious consequences for the socioemotional, cognitive, and behavioral development of the infant.

In previous writings (Papoušek & Papoušek, 1979; 1983) we have proposed a psychobiological model to describe the process of parent-infant interaction. This model assumes that the course of these interactions is determined by two major factors: integrative competency on the side of the infant and a repertoire of intuitive behaviors on the side of the parents. Within this model, the origins and consequences of interactional failure and success can be seen. Although both the infant's competence and the parent's repertoire of intuitive behaviors are dependent on genetic and sociocultural influences, they also have a significant biological basis and are under significant biological control which we believe can help to explain why under similar circumstances interactional failures may or may not occur.

We would like to discuss the important role that parent-infant interactions have in influencing the cognitive development of infants. Specifically, we want to discuss in greater detail those initial forms of what we call intuitive, didactic parenting behaviors that we believe have the potential to overcome negative influences on parent-infant interaction, and the implications of these didactic behaviors on the developmental outlook for at-risk infants.

Precocious Integrative Capacities of Infants

In order to understand the process of parent-infant interaction it is necessary to review briefly the infant's integrative capacities as they relate to early dyadic social interaction. From the early conditioning studies by H. Papoušek (Janoš, Papoušek, & Dittrichová, 1963; Papoušek, 1967; Papoušek & Bernstein, 1969) which detailed the adaptive processes in learning behavior in infants, we became aware that newborns were able to learn and integrate experiences within the first few days of life. It was shown that there was marked interindividual variability in the learning capacities of neonates and that preterm infants frequently appeared to learn more slowly than full term infants (Papoušek & Papoušek, 1979). The ability to learn was shown to increase rapidly during the first half year of life not only due to maturation but also under the influence of experimental interventions (Papoušek, 1977). Thus environmental changes were proved to be effective as didactic supports for the infant's learning capacity.

Additionally, these studies provided us with information concerning the necessary preconditions that must be fulfilled in order for learning to take place in very young infants. The need for

simplicity in the learning task, for repetition in the presentation of the task, for the contingency of these events on the infant's behavior, and, for the infant to be in an optimal emotional-behavioral state were all found to have tremendous influence on the course of infant learning. Contingency and the course of emotional response to the adaptive process of learning gave us new and exciting information concerning the role of intrinsic motivation connected with this fundamental process of integration.

With this startling laboratory evidence of the newborn's precocious capacities for the integration of experiences, as well as information concerning the necessary conditions for the didactic support of infant learning we began asking questions concerning the circumstances in which such conditions existed in the everyday life of the infant that would support the further development of these innate capacities. We began to film parent-infant interactions in order to determine what were the typical behaviors to be seen in parent-infant interaction and what role parents played in the didactic support of integrative development in their infants. Using microanalytic methods to study the extremely rich temporal structure that existed in the interactions filmed between parents, mothers in particular, and their infants, we were surprised to discover a repertoire of parental behaviors that were not consciously controlled by parents, that appeared consistently in response to certain infant behaviors, and that fulfilled the requirements of didactically supportive structures for infant learning. This is the focus of our present research and in the next section we will describe these behaviors and address their meaning in relation to the role of parent-infant interaction in the cognitive development of the infant. We will also discuss the role of these intuitive behaviors in overcoming

negative influences on the processes of interactions based on our previously mentioned psychobiological model of parent-infant interaction.

Intuitive, Didactic Parenting Behaviors

Intuitive parenting behaviors became evident to us only with the use of microanalytic techinques to analyze filmed and videotaped parent-infant interactions. Our interest was and continues to be the function of these behaviors within parent-infant interactions. To us they represent a potential means through which learning and cognitive processing, which we consider to be the most fundamental adaptive capacity of the infant, can be encouraged by the parent. These behaviors can best be understood when viewed as a biological model of early didactic care for the communicative and integrative growth of the infant, which ranges from the basic forms of learning and cognitive operations to the development of self-concept, intentionality, speech, and self-consciousness. The evolutionary advantage of their nonconscious or intuitive character can be seen in their weak dependence on sociocultural impact, their universality, and the ease and speed with which they can be carried out without taxing the caregiver. According to this model, the parent intuitively creates an abundance of learning situations that support the growth of the infant's integrative capacities and that the parents are further motivated to persist in these behaviors by the increased responsivity, predictability, and infant-provided contingency experiences from these interactions.

With the knowledge gained from H. Papoušek's early learning studies (Janoš, Papoušek, & Dittrichová, 1963; Papoušek, 1967; Papoušek &

Bernstein, 1969) concerning the conditions necessary for infant learning, parental behaviors were analyzed in relation to the fulfillment of these requirements. Several parental behaviors were found to fulfill the necessary conditions for infant learning. For example, parental speech directed at the infant, often referred to as babytalk, illustrates the adult's adjustment to the infants need for simplicity and repetition while providing a wide range of rich and contingently related stimulation. Such speech is slower in tempo and has a higher pitch than speech directed at adults; the prosodic features are strikingly overexaggerated; the structure is simplified and repetitive; and, it frequently includes imitation of the infant's own vocalizations. It is often accompanied by visual, tactile, kinesthetic, or vestibular stimulation as well. Vivid parental responses to some infant behaviors are as consistent as if they were unconditioned responses to specific eliciting stimuli. Such responses may function as early natural contingencies in which the newborn may through instrumental conditioning learn how to control parental behavior.

Parents show an interest in the state of the infant which has an important influence on the receptivity of the infant to stimulation and the course of learning in the infant. They frequently make comments concerning infant state and they regularly carry out behaviors similar to the laboratory testing of muscle tone in the infant's hand and fingers and around the mouth and cheeks. They also seem to adjust the amount of stimulation they offer in response to the emotional-behavioral state of the infant. This sensitive adjustment of stimulation by the parent to the state of the infant can be seen as well, but in a different time-frame, in the adjustment by parents to the developmental changes that occur so rapidly in the first years of life.

Visual contact has many important functions in early human communication and interaction. If it accompanies other behaviors it increases their effectiveness. It is crucial for the delivery of other than auditory stimulation and information to the infant. Through its visual behavior the infant is able to selectively increase or decrease the amount of visual input it receives from the very beginning of life. The infant's visual behavior also provides parents with important feedback information about the amount of attention they attract, what the infant is interested in, and what it prefers to avoid.

There are several parental behaviors that confirm the significance of visual behavior and contact between parents and infants. The initiation and maintenance of visual contact and the monitoring of visual behavior are behaviors seen frequently in parents. Parents try very hard to stay centered in the infant's visual field at a distance of 20 - 25 cm and in response to visual contact they reward the infant with a typical greeting response: a slight retroflexion of the head, raised eyebrows, and widely opened eyes, generally followed by a smile and/or verbal greeting.

Another example of contigent responsiveness in the parental repertoire of behavior is imitation. Parents tend to imitate the newborn from the very first contact with the infant. They show a distinct preference for imitating facial expressions and vocalizations, often exaggerating while imitating as if to demonstrate in full what the newborn cannot yet display distinctly enough. Parents also tend to imitate new behaviors just developing in the infant. We interpret such imitations as serving as a "biological mirror" or "biological echo" and consider them to act as a display of contingent events facilitating instrumental learning and to be crucial for the development of imitation

and self-awareness in the infant. Echoing is also a chance for the infant to match and to learn the relation between vocal sounds and oral behavior.

The examples given above have hopefully shown how important this repertoire of intuitive parenting is for social interaction and cognitive development in infancy and how subtle are the mechanisms involved in this process. Both parent behaviors and infant competencies function in a chain of interlocking events in which each event gains new dimensions and meaning resulting from its position in the chain, its role in past interactions, and its impact on the social environment. For the infant it is important that the parent's behavior is predictable and contingent in relation to the infant's own behavior. Parents' social behavior in turn indicates a great deal of interest in any signs of cognitive progress in the infant; they tend to select the type and amount of stimulation according to the infant's capacity to process ;t, and they are very sensitive to feedback cues from the infant.

Our own findings as well as other research evidence concerning parent-infant interaction indicate an urgent need for more precise information about the behaviors, the mechanisms, the processes, and the effects of early parent-infant interactions. More information is needed about the individual variability of these interaction patterns over time, the adaptive flexibility of the adult partner in response to deviations in infant behavior and developments, and the clinical significance of these behaviors.

The behavioral plasticity and sensitive, compensatory adjustment of intuitive, didactic parenting behaviors can function as a buffer to protect the interacting partners from a variety of adversive factors of genetic or environmental origin. If a mutually rewarding pattern of

interaction can be established in spite of the presence of adversive conditions, a positive course of development may occur. On the other hand, the presence of such adversive factors in either the parent or the infant, can disturb parenting behaviors to such an extent as to foster the development of secondary deviations in the infant's behavior. This can lock these reciprocal interactional difficulties into a vicious cycle of interaction failure that can eventually lead to serious clinical problems (Kearsley, 1979; Papoušek, 1979; Sameroff et al., 1983, Stott et al., 1983). The exact source of interactional failure is presently very difficult to determine but we believe that by revealing specific behaviors and their functions in healthy parent-infant interactions we can provide more effective interventions for those families in which interactional failure may occur. The evidence is very strong that parents can be the most effective influence on the course of developmental competence in the infant. We believe that in cases of interactional failure or in families who have at-risk infants, intervention to assist parents in the development of interaction patterns that are sensitive, predictable, and contingent to the behaviors of the infant is of crucial importance to an optimal developmental outcome for the infant.

Summary

Research evidence from the past 20 years has shown that infants have a much more active and influential role in interactions with both the social and nonsocial environment than was previously thought. It is still true, though, that caretakers must sensitively adjust their behaviors and the environmental conditions to constraints in the

infant's competencies and capacities in order to facilitate and maximize the infant's ability to learn. There exists evidence that the developmental and reciprocal effects of positive, successful parent-infant interaction can act to contribute to the optimal development of the infant. Interactional failures resulting from deficits or maladaptation on the part of the infant and/or the parent can lead to a vicious cycle of mismatched or destructive interactions resulting in serious consequences for the developmental outcome of the infant. We have presented here two major factors that we believe to be crucial in determining the course of parent-infant interaction: infant integrative competence and intuitive parenting behaviors. The biological basis and function of these behaviors in the course of parent-infant interaction and their potential significance and importance in devising preventive or therapeutic interventions for families with at-risk infants was discussed.

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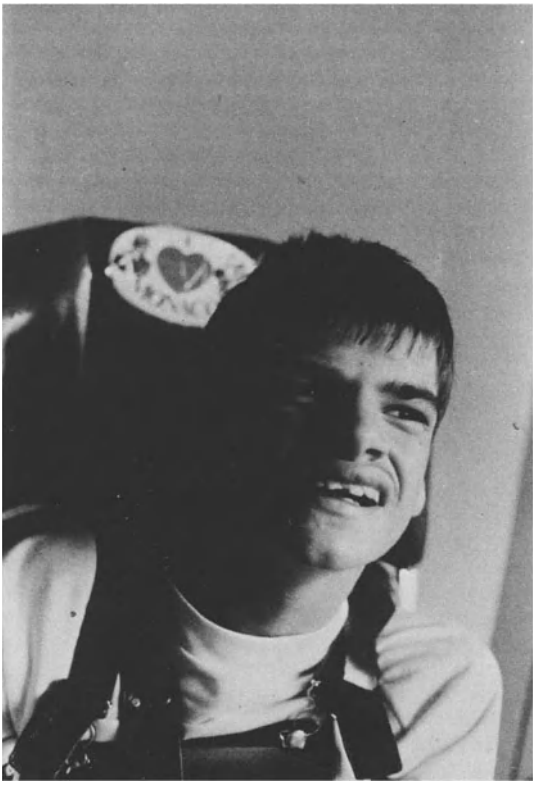
MOTHERS - A PRIVATE DEPRESSION

Andreas Frölich



1. THE DISABLED CHILDREN

Since 1976 profoundly, multiply handicapped children have been furthered in a scientific project. The children were before well cared for only. This project had several interesting results, the most important being that even extremely handicapped children are able to make some progress in their development.

- they could communicate non-verbally their basic wants and

needs.
- they could learn to improve and extend their perceptions. Seeing and hearing can become very important for the individual child.
- they could learn to receive different foods without probing.
- depending on the individual motoric disfunction they could learn to sit upright, to control the head and also occasionally to move (ref. 1).

2. CONFLICT SITUATIONS

All children in our project came to the institute every day on the bus. None of the children lived in a nursing-home. Thus they all had contact with their parents.

All changes in the child concern both the parents as well as the co-workers at the centre. Changes, connected e.g. with

- transport
- method of posturing
- wheel chairs
- plasterbeds

and also

- attacks of convulsions and their medication
- other acute or chronic illnesses
- nourishment and bowel movement.

In particular: conflict situations can also arise in planning

- aims of physiotherapy
- aims of pedagogical-psychological treatment.

"What can we do <u>with</u> this child, what can we do <u>for</u> this child?" is answered in a different way by parents than by the workers of the institute. Always when parents and the institute are responsible for a child, there is potential tension, because their aims and methods are not necessarily the same (ref. 2). One could observe latent or open competition between the mother and the staff. This could lead to mutual accusations:

"They torture and don't understand my child".
(mother)

"She neglects her child - if the mother would be more willing to work with us, then we would be able to do more for the child"
(staff member).

3. SPECIAL PEDAGOGICAL THEORY

In the literature (ref. 3) these conflicts appear on a theoretical level time after time:
Parents are nominated "cotherapists"; the experts "permit" them to take part in the education and advancement of their child. But parents divide into "cooperative" and "uncooperative" groups! If parents are "uncooperative" the professional

therapists are apt to engage themselves less in the work with the child.

We find often in the literature, that parents must learn to understand and accept the disabilities of their child. Therapists may only see and work on the disabilities of the child.

I only mention this point - a more detailed analysis would require too much space.

4. THERAPEUTIC CONVERSATION WITH THE MOTHER

It is also noticeable to us that a large number of these women are mostly very tense and depressed. Even young women radiate no attraction, they seem to be physically damaged. This can only partly be understood as due to the severely disabled child, because in most cases the major of the physical work with the child was taken over by the institute.

In intensive conversations with thirty mothers we have tried to obtain more information on the cause of the tension between mothers and co-workers.

These conversations followed the biography of the handicapped child. It was not important to recall certain dates. Rather, the mother tried to remember psycho-emotional experiences. That means:

not questions like,	"birth and condition of the child after birth"
but rather,	"how did you feel at the birth, and how did you react as you saw your child (or did not see it) after the birth?"

These questions (that are more than just a conversation stimulator) produced a dynamic wealth of personal memories, that are still relevant today.

These conversations which can lead to tears and great shock nearly always give a feeling of relief. The conversations were conducted after principles due to Rogers which have proved successful (ref. 4).

From these conversations and the years of long contact with the mother and her handicapped child emerged a better understanding of these problems. The "private depression" of these mothers had a frightening dimension. The society picture of the "victim-mother" had led for these mothers to many routs of depression and depriving factors

- depressive symptoms
- psychosomatic illnesses
- wearing down illnesses
- medicine and alcohol abuse

also occurring

- thoughts of suicide
- death wishes towards the handicapped child
- corresponding illnesses of the husband
- strong anxieties about the future.

One had received no information, at most from a student who knew nothing.

He had so screamed during the infusion. It was awful. One could not take him out. He was hanging on bottles. It was so awful. When I saw him it was better. I have cried a lot, so much fear, what they do with him. It will be very hard when I must give him away.

It was terrible, he looked like a skinned rabbit, totally blue and crushed, it was so awful. After five months as I first held him, when we came to fetch him, I had the feeling that he was not my child.

The doctors are not bothered; they preserve life, and thus destroy the life of the parents.

In the neighbourhood people ask about the child. When you explain then they begin to feel sorry. They don't understand. I prefer to leave it at that.

Mostly it gets on your nerves. It tingles in the fingers. One can be happy when somebody visits, I am missing it. Yes, you must be there for your child, that is the only support.... I can honestly say. Everything is so deep inside. The pressure, one can not get rid of.

For me there is nothing left there, during the whole day (school-holidays). I become quite mad. I always have a bad conscience, and that wears me out.

Not many do come. I cannot say whether that is connected with the girl. Two married couples have left us. We are not angry, perhaps it's connected? We cannot very often go out. Their children are no longer bound to them. We remain bound.

I felt badly, raged, and ripped out the infusion. I wanted to home. I was so afraid.

"You must think about your child." I cannot bear to hear that - why must I always think about the child. I will not any more, I will think about myself.

5. ANALYSIS OF THE CONVERSATIONS

It is noticeable that the mother complains very much about the burden of the housework. When one has a severely handicapped child, then much additional work is required. Nearly all the women have no help in the household.

We have, together with the mother, analysed the exact daily and weekly worktimes, and have established that our women spend less time with household work than the average housewife (ref. 5). One can suppose that these women are in a similar situation concerning housework as do families with a baby - but during ten or twenty years.

If one further analyses the living situation of these women, then it is seen that their perception of the social environment is strongly tinted. She supposes that the neighbourhood and acquaintances have rejected her, and has the feeling the her husband more or less neglects her. She feels bound to the house and that nobody shares her worries about the child. This corresponds to the subjective, depressive reality of the women.

6. RISK-COMMULATION

In our study we saw marriages collapse, other children have been disturbed from their normal development, two women have attempted suicide, another one with success. The handicapped child is irritated in his simple relation to its "disturbed mother". It seems to be absolutely necessary to find the context in which the situation can be caused to change. It shows, that the time of the birth and during the first year of life of the handicapped child are very important for the mother, the family and the child itself.

We have tried to list the risks. This list comes from about 1500 single details we obtained from mothers.

We observed the following areas of risk:

- The pregnancy and its psychosomatical and socialpsychological viewpoint.
- Length and form of the first separation from the hospitalized child (4 weeks).
- Relationship development between mother and child.
- Communication possibilities between mother and child.
- Reduction or conversation of the relationships of the family with its social environment.

(All births in this study were difficult or entailed risks, and offer no significant differentiation possibilities).

7. INTERPRETATION

We came to the following explanation:
Following a difficult pregnancy (55%) when the mother had all sorts of problems, there comes in a difficult birth, when the mother had the feeling of being badly looked after. She does not see her child, she is not allowed to hold it. Nobody tells her what is the matter with the child (which in her physical state she would not comprehend).

She experiences a shock, if she must go home without the

child.
For her were the nine months "in vain". She has no chance for the child in her to become the child with her. The important "individualization" of the relationship does not take place. At an unbiological, beforehand not determined time, she receives her child back. It is a stranger to her. The handicaps make it nearly impossible to ethologically love the child.

The child is rigid - it is difficult to cuddle.
The child sputters - it does not enjoy drinking.
The child screams - and does not smile at the mother.
The child is constantly ill - and does not make any daily progress.

The mother has a child; one she never expected or pictured.

We, experts demand from her just then an intensive activity and concern for her child. It depends on the mother, at least the therapists think so, whether the child will become "something". She must thus be "brave" and work and gets no chance to be sad, to cry and shout, to argue with somebody else that she does not want this child.
She must excessively accomodate to society's expectations - represented by doctors, therapists and also the family, and suppress her own feelings and needs. In this process, she suppresses the strong ambivalent feelings towards the child, because she has no chance to work them out.

"You" must love such a poor child. You cannot hate it, although it ruined all your hopes, and yourself too".

The woman experiences many burdens, permanent influences and meddling of strangers (ref. 6); fear and rage, and pain too remaining always present.
Often it happens that these feelings show themselves in a massive depressive form which for her situation seems logical: "the poor person has so much work to do". From here the offers of help develop, which only seldom improve the situation of the depressed woman, but for the child are usually useful.
The components of rage, fear, pain keep recurring, when challenges arise, or for situations that remind the mother in some form of the early times with her handicapped child. She usually withdraws, becomes perhaps aggressive, cries and has no inhibitions - she is not "co-operative" and is also "punished" by her child's therapists. Thus we have gone around a further circle.

8. CONSEQUENCES

For us there are two evident conclusions:

First,
- mothers with a high risk-quota definitely need early psychological relief, even during their time in the delivery clinic. (In Germany one has about an 8 - 10 days stay). Her

advice and suggestions from counsellors should not dominate, but rather her existential-psychological state.

All expressions of feelings are permissible and would not be depreciated. No appeals to bravery, no false comforts.

Second,
- all families, whose handicapped child will later be cared for by an institution need the offer of conversational Therapy help. It has been shown that this cannot be done independently of the work with the child. The parents and especially the mother need someone that knows their child and has experienced the difficulties in his development.

Thus we have reached a further stage in the rehabilitation. Up to now we have worked "child centered" with certainly much success. But one must also recognize that not only the child, but the entire family too is influenced through the disabilities. If the social integration of the disabled should remain an important goal, then this can only occur if integration in the family and integration of the family is assured.

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PARENTS AND HANDICAPPED CHILDREN

David Morris

It is always bad news when parents learn their child is handicapped. Whilst nobody can ever say it is good news, parents can and do acquire a different set of values from their work with their child in the process of helping him to realise the optimum of his potential.

How parents learn, who breaks the news and how it is done, the support and encouragement they are given by professionals and friends, what services there are and their access and availability and above all being helped to know and understand the nature of the handicap and the aims and objectives of professional help, all play a big part in helping them to cope with what quickly becomes a professional task. Professional in the sense that in contrast to ordinary instinctual child rearing, the parental role with a handicapped child entails the development of increasing skills and the conscious understanding of the use of these skills: parenting a handicapped child becomes a vocation which like all professions involves advanced learing, namely to pre-empt what may occur in different circumstances.

Social attitudes towards the handicapped have changed remarkably in the last two decades. Whereas previously no parent would have chosen to have a handicapped child, there are an ever increasing number of parents who choose to foster or adopt such a child. The rapid growth of 'self-advocacy' and 'People First' and those who volunteer to become 'advocates' is testimony to the more humane and more civilised attitude of society towards those who are less fortunate and have special needs.

In spite of the existence of religious cults and the attempts by Judeo-Christian-Moslem-Buddhist institutions to point the way for a richer spiritual life, "the lame, the halt and the blind" were never seriously recognised or respected let alone provided for their special needs. They were treated as lepers and isolated away in institutions far from the hub of everyday society. Compassion was a key component of spiritual dogma but it was meaningless without accompanying action. Historically the humanitarian changes which have occurred originated from the families with a handicapped member to try to put right the paucity and barrenness of services and the lack of provision for their children's needs. They banded together and formed self-help groups, primarily to try to improve the lot of those in need, never realising what a force the "voice of the people" could be. They have had the greatest single influence on state, government and society leading to a

dramatic change in the services for the care and well being of handicapped children. There are now in the U.K. very few children left in institutions because a rich alternative is being provided for them to live in the community in homes and to be provided with educational and social services like ordinary children. This is but one example of what has been achieved.

Every family that embarks on having a child is making an investment for the future. They do their utmost to realise their expectations and leave no stone unturned: ante-natal care, diet during pregnancy, avoidance of smoking and alcohol, preparation for childbirth classes. The "nesting" process is continued throughout pregnancy and while some of the hazards are recognised they are conveniently put aside and out of mind: premature birth, Caesarian section, congenital abnormality of stillbirth. Fortunately the majority of babies are born mature and healthy and the hazards are the exception and justify parents feeling confident that all will be well. Parents during pregnancy are susceptible and vulnerable and by and large try to spare themselves the agony and anxiety of something going wrong. When it does happen the situation is intense and calls for great skill and experience in its management. The impact is not only on the parents but on the professionals involved who find it difficult emotionally and tend to take avoiding action. Much of the retrospective research work that has been carried out shows how unsatisfactorily this was handled and the high degree of dissatisfaction parents experienced. A growing awareness and sensitivity to the feelings of parents and their own personal feelings has led to a much better mode of practice. Parents are now being told when the doctor knows the baby's condition, unlike in the past when parents queries were fobbed off or nothing was said sometimes for months and parents had to find out for themselves. More time is now being spent at the initial interview without interruption and in privacy and preferably with the nursing colleague caring for the newborn baby.

New methods have been evolved which may soften the blow. One such which I have been practicing for some time is to treat the parents and the baby in the same routine manner as all other parents and their babies. All newborn infants are routinely examined within the first 48 hours after birth preferably as soon after birth and as soon as the mother is fit enough.

Before the clinical examination of the baby I go through the family history, the pregnancy and the delivery, how they find their baby, how the mother proposes to feed, what name they have in mind and above all they are given the opportunity to ask any questions they may wish. Then in their presence I examine the baby after either having been undressed by the mother or by me when in so doing I can see and feel how the baby is reacting to being handled. In carrying out such a routine examiniation I can verbalise the baby's normal features and comment on my findings of an abnormality such as a spinabifida, the increased head circumference or the single palmar crease in Down's syndrome babies.

Whilst this procedure calls for experience and a mature approach it can be taught and can be learnt by any qualified doctor or for that matter by an experienced nurse. The basis for this form of management is that the baby becomes an identified person with a name and not a disability and his normal features are consciously appreciated. In the past and unfortunately still at present, the news that "you have an abnormal baby" is broken as a 'death knell' with total concentration on the abnormality without reference to the baby as a person and all the rest of him which is unaffected like his heart, his genitals, his limbs and his eyes and ears. In this way a partnership between the parents and the doctor is established which can be most effectually used for ongoing support and advice. The real snag is the absence of the father, for most such routine examinations since they are carried out whilst fathers are at work. To help the mother in such a situation the routine examination should be done at visiting time with both parents present. Fortunately it has become widespread practice for husbands to be present at the baby's birth and this opportunity could be used more often by the paediatrician.

Each individual patient's reaction when they learn something is wrong will have a great deal to do with their own persona, psychology and life events and for some it can be too painful for them to bear. No individual prediction is possible but a greater respect can be paid to past events in the life of the family which can render them more susceptible and vulnerable: a previous stillbirth or a neonatal death, another child with a chronic disability or a single parent family.

The experience of a late recognition of a child's handicap is quite a different situation but equally traumatic for the parents. Too often they have been suspicious that the baby was not quite as he ought to be either in appearance or behaviour. Professionals involved with children like Health Visitors and Family doctors are constantly being questioned and behind the questions lies the unspoken agenda of "is my baby alright?". Instead of allowing the parents to expand on their observations and inviting them to voice their thoughts and feelings all of which take more time, a brief dismissal statement is made of "each baby is different" and "no baby is ever exactly like another" and the final statement of "there is nothing wrong" said in a confidently dismissal voice to ensure reassurance. Parents are very interested in their babies and are very observant. They are at the same time sensitive to criticism and of being regarded as 'over-anxious' which makes them cover up their doubts or even turn a blind eye. Comparisons are indeed odious, babies do vary enormously in their timetables, a baby born prematurely may take longer to pass his milestones and expectations are confused with wishes. Some babies are placid and contented from birth whilst others are constantly demanding and are at sixes and sevens with the world. Be that as it may I always listen carefully to what a mother says and asks and try never to dismiss it out of hand before checking up for myself what it is that she is saying about her baby. Parents are the best witnesses of the hearing

defect as they are about the way their baby moves. It is comforting to be able to say with professional confidence that what they are asking or commenting about is part of the range of normality. If the professional is brave or bold enough to ask how they now feel about the baby after the doctor has said what he thinks and if they are still concerned more time will be needed to examine the nature of this anxiety rather than dismissing it with attempted reassurance.

Developmental screening and child health surveillance now so widely practiced by family doctors, local authority health clinics and paediatric departments, have given families a new lease of life and enabled earlier detection possible which has led to corrective intervention.

Every child is special and has special needs. This applies to a child with a handicap but more so. The basic requirements of ordinary children are no different from the basic requirements of a child with a handicap. He is a member of a family and the family as a whole should always be the interest and concern of the professional worker. The "special" child can too easily become the focus of all the family's attention at the expense of the whole family's well being. It is not in the best interests of the child or his family if he is occupying the majority of the mother's time for it can interfere with the parental relationship and threaten the integrity of the family. Children in their growth and development have to learn to wait and take their turn much as they may protest. They all need tender loving care and their response and feedback is what keeps the mother and father going. Children's security is all important and they need and respect authority as long as it is reasonable and can be understood. None of us react well when we are bullied by those in authority because it lowers our self esteem and stops us from being ourselves. Treated with respect and dignity we are all the more responsive and children even more so. We thrive on encouragement and approval and need all the support we can get to help us to learn and to develop our independence.

A child who has a disadvantage needs to have it seen in perspective and to avoid it becoming disproportionally dominant. A blind or a deaf child can be helped to function just as well as others within him limits imposed by his impairment. Because a child is blind or deaf does not make him a second or third class citizen, in fact he may develop compensatory skills which may quite outstrip those of his peers. Because you have cerebral palsy it does not mean that you cannot learn to ride a bicycle or to ski.

The new British Education Act of 1981 is a significant and remarkable step forward indicating a civilised respect for all children and gives them the opportunity and facility for optimum growth and development. Integration into ordinary education is going to change the life of children with special needs and their families. They will no longer be made to feel outsiders and inferior or so different from others and in the process of being with ordinary children it will enable these ordinary children to have a healthier attitude to those no so well off as themselves.

There are of course great difficulties for parents in "coming to terms" with their child's disability and his handicap and there are many setbacks, disappointment and times of grief. It takes a great deal to see the child in his own right and not a comparison if not contrast with other children. This loss of normality can become a bereavement and a grief situation with which parents become fixed an preoccupied, unable to see anything except what the child cannot do. This concentration on what is missing, on the child's inabilities leads to a state of hopelessness and forlorn despair, rejection and final placement in an institution. Such was the previous attitude of society and of the medical, educational and social professions which led to the barbaric institutions of the past where the inmates were faceless and anonymous with no identity, self esteem or personal possessions. The breakthrough in the '30s has avalanched and we are beginning to reap the rewards of the pioneers who cut a path through the impenetrable jungle of ignorance and prejudice.

The battle is only just begun. Parents and professionals need the support of each other to help the disadvantaged person to function more efficiently and effectively by having the opportunity and facility of access to loving encouragement and stimulation, through adventure and experimentation of trial and error. But above all the respect and dignity that will help them towards their optimum performance and achievement and the happiness and fulfillment that these bring. We are all impaired to some degree. None us can say we are without some disability. We have to learn to live with our handicaps be they of unavoidable environmental circumstances or by inherent endowment. Our reality is to do the best we can with what we have and above all to share with others especially those not as well endowed as we may be.

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