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Review

Epidemiological and Preventive Aspects of Cerebral Palsy and Severe Mental Retardation in Sweden

Bengt Hagberg

The Department of Pediatrics, University of Göteborg, Östra Sjukhuset, S-416 85 Göteborg, Sweden

Abstract. The epidemiology and changing panorama of cerebral palsy and severe mental retardation in Sweden are briefly surveyed. Based upon the Swedish experience, present and future preventive measures are discussed. The main differences in the preventive approach when tackling cerebral palsy in comparison with severe mental retardation are outlined and summarized in Table 3.

Key words: Cerebral palsy – Mental retardation – Prevention of brain damage.

Retrospective epidemiological studies on the changing panorama of brain damage syndromes cannot be expected to give detailed and exact information about etiological and pathogenetic mechanisms. However, such general information—even if often incomplete—can help to indicate the broad abnormal mechanisms and the organisational and technological measures needed to reduce the incidence of damaged babies.

Cerebral Palsy

Active measures to prevent cerebral palsy (CP) have been taken in Sweden since the early 1950's. It started with a centralized regional[1] organization for exchange transfusion services, caring for all babies at risk for kernicterus from blood group incompatibilities. The results were dramatic! Within a few years, severe icterus was virtually eradicated as the major damaging factor which it had been in the 40's. Over the same period the number of new cases with dyskinetic (choreoathetotic and dystonic) forms of CP also decreased. From the middle of the 1950's onwards each county (population 200,000—400,000) has successively centralized the delivery and supervision of neonates to one or two large central county

[1] One region covers a population of 1—2 million and comprises 3—5 counties

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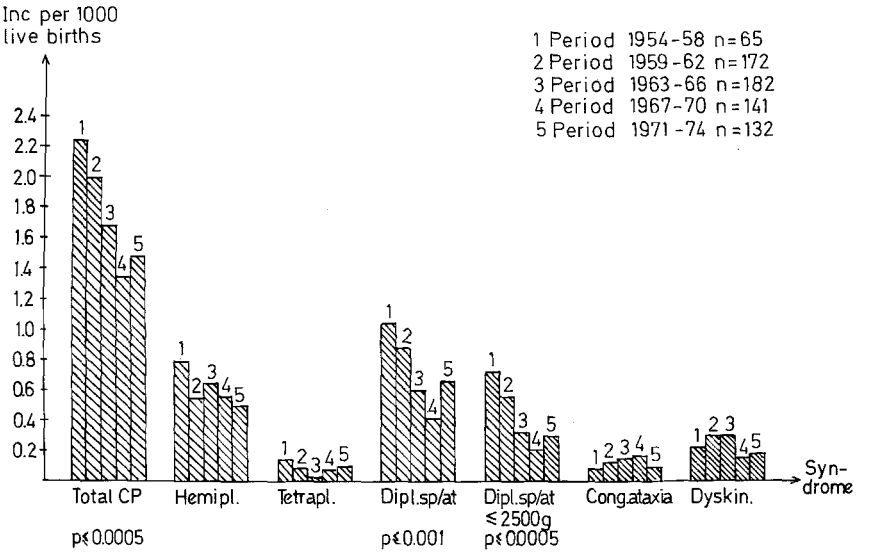

Fig. 1. Incidence of cerebral palsy according to neurological syndrome [11]

hospitals with well developed services for obstetrics and basic neonatology. Our studies [7, 8, 9, 10] reflect the changes during this epoch. While the percentage of low birth weight (LBW) infants has remained constant (4.3%) through the years, the number of LBW diplegic children decreased significantly through 1954 to 1970 (Fig. 1). This gain particularly applied to the LBW babies weighing 2000 g and less, for whom the chances of developing normally became remarkably good. The decline is unlikely to have been due to any single factor but more to a combination of systematic efforts to compensate for acidosis, hypoxia, hypothermia, hypocaloric states and hypoglycemia in the routines of the neonatal wards.

After 1970 there has been no further decrease (Fig. 1) in the incidence of children with cerebral palsy [10]. However, further gains have been achieved as the simultaneous decrease in the perinatal and postnatal mortality rate has continued (Table 1). Very active perinatal measures, e.g. wider indications for respirator treatment, obviously save lives but at present cannot be expected to also reduce the handicap rate. However, the outcome for a series of children at our intensive care unit in Gothenburg has been remarkably good and surviving children are not severely damaged [14]. More worrying is a trend in the whole southwest area towards a slight increase in mild diplegic cases of normal intelligence, mainly among LBW infants between 1000—1500 g. This may be coincidental but is being continuously observed and analyzed.

More and more, prenatal negative factors appear to influence the series of events leading to the cerebral palsy syndrome. From our studies, fetal growth retardation, and other factors summarized in the term 'fetal deprivation of supply' (FDS) [9], stand out as being particularly important, probably both as predisposing and directly damaging factors (?). Figure 2 shows the progressively

Table 1. The rates of perinatal mortality, infant mortality, stillbirths and cerebral palsy in Sweden 1951—75

	1951—55	1956—60	1961—65	1966—70	1971—75
Perinatal mortality (stillbirths and deaths within 7 days) per 1000 births	30.1	26.7	22.2	17.7	13.8
Infant mortality (deaths within one year) per 1000 live births	19.3	16.9	14.8	12.3	10.0
Stillbirths (deaths before and during delivery) per 1000 births	17.7	15.1	11.5	8.9	6.9
Cerebral palsy per 1000 live births	2.3[a]	1.9	1.8	1.4	1.5[b]

[a] Herlitz and Redin, 1956
[b] 1971—1974

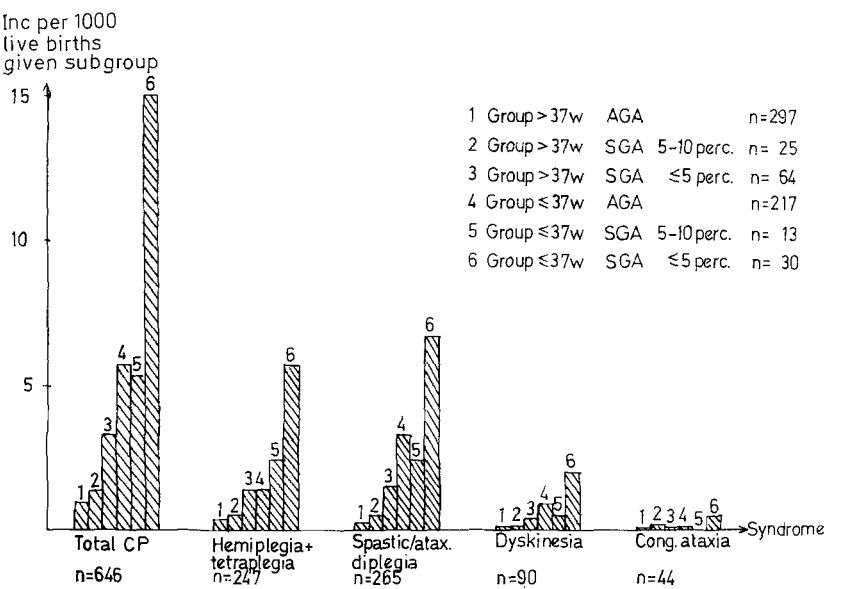

Fig. 2. Incidence of cerebral palsy for birth weight in relation to gestational age, according to the neurological syndrome (postnatal cerebral palsy excluded) ([12] p. 211)

Table 2. CP-panorama changes in Sweden

Birth year period	Decreasing syndromes	Decreasing factors
1945—53	Dyskinetic Other?	Hyperbilirubinemia "Kernicterus" Severe asphyxia
1954—70	Diplegic (Dyskinetic) (Hemiplegic)	Risk in LBW-AGA "Pure" perinatal
1971—74	None	None
"Visions"		
1975—85	All spastic?? Dyskinetic?? Ataxia??	FDS? + Asphyxia? Risk in LBW-SGA? Genetic? Hydrocephalic states?

Table 3. Main different preventive approaches which are needed

Cerebral palsy

Organisational
- Centralization of obstetrics
- Centralization of neonatology

Technological
- 2nd—3rd trimester management
- Obstetric at delivery
- Neonatology

Severe mental retardation

Prepregnancy health service
- Vaccinations
- Genetic councelling

Early prenatal diagnosis
- Chromosomal
- Biochemical
- AFP-screening

increasing risk for CP with increasing fetal undernutrition and decreasing gestational age. Very small for gestational age prematures (group 6) have a fifteenfold greater risk for CP. However, they constitute a small number, only 5% of the total series. Babies born prematurely with a weight appropriate for gestational age (group 4) still represent the largest quantitative risk group. The common combination of 'fetal deprivation of supply' and asphyxia and/or cerebral haemorrhage suggests that the brain is more susceptible to perinatal complications—and perhaps also to 'normal' perinatal trauma—after negative intrauterine influences, and that the aetiology and pathogenesis of cerebral palsy

is mainly multifactorial. Disturbance of homeostasis by additive interactions of many pre- and perinatal factors may constitute the salient underlying feature of cerebral palsy today.

For the future (Table 2), more systematic and refined screening procedures to define fetuses at risk are urgently needed. When a threatening situation has been discovered, utmost care is needed to avoid further threatening factors and to bring the fetus to extrauterine life at the optimal time and in the best possible condition with a minimum of perinatal trauma.

Further preventive efforts should be made to improve the general health of pregnant women, e.g., by educating them about their general eating habits and pointing out the inherent dangers of smoking and alcohol to their unborn babies. The goal must be a health service which reaches all expectant mothers as soon as pregnancy has been confirmed—or preferably before! Such prevention is mainly a matter of organization and not of technology.

Even if all cases of cerebral palsy of perinatal origin or derived from brain damage in the 2nd or 3rd trimesters could be prevented, there still remains a group in which cerebral palsy is caused by prenatal factors of yet earlier origin. The magnitude of this group in an unselected series is incompletely known. Among others, the frequency of hereditary cases is difficult to determine, as the occurrence of cerebral palsy in siblings is sometimes related to prenatal factors of environmental origin. Genetically dependent syndromes have, however, repeatedly been described, particularly among the ataxias [1, 6], but they are also found among tetraplegias, diplegias, choreathetotics and even dystonics. The number of cases in which simple inheritance plays the major role probably does not exceed 2%. Chromosomal aberrations resulting in cerebral palsy are extremely rare and could not be expected to be prevented unless they were familial and associated with unbalanced translocations.

Severe Mental Retardation

Active preventive efforts against severe mental retardation (SMR) were not undertaken in Sweden before the early 1970's. Since 1970, in some parts of Sweden, e.g. Gothenburg, all pregnant women aged 35 years or more have been offered amniocentesis and prenatal screening for chromosomal abnormalities. Concurrently, there has been increased activity to get a centralized organization for prenatal screening for neurometabolic disorders in families with an earlier diagnosed 'key case'. Indirect preventive effects of a spontaneous nature have also been achieved with decreasing maternal age (fewer elderly pregnant women), resulting in a lowered incidence of Down's syndrome. This change probably occurred before 1959 in middle Sweden [3, 12], but could still be traced between the periods 1959—62 and 1963—66 in the northern county of Västerbotten [6]. In Sweden today the live births to mothers over 35 years of age are only one third of the number 20 years ago.

The main causative factors behind SMR [4] differ greatly from those in CP (Fig. 3). Chromosomal aberrations which do not play any practical role in the development of CP syndromes are the largest single factor behind SMR. Down's

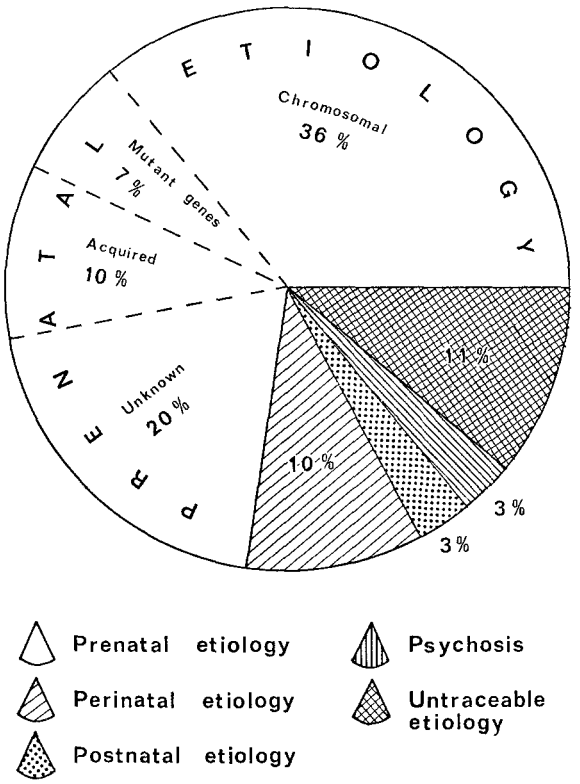

Fig. 3. Distribution of SMR cases in Uppsala county 1959—70 according to the main etiological groups (4)

syndrome amounts for about 30—35% in Swedish series today and a further 5—10% can be calculated to have rarer chromosomal abnormalities when banding techniques are systematically applied. Other hitherto unknown and very early prenatal factors, referable to the 1st trimester or before, are probably responsible for the 15% of cases with prenatal stigmata, malformations, and peculiar physiognomies, and in whom current chromosome techniques have given 'normal' results. Among these cryptogenetic MCA/MR syndromes—a designation according to the classification of Opitz [13]—embryopathies or fetopathies due to alcohol and antiepileptic drugs may occasionally be found. Defined neurometabolic conditions, usually with autosomal recessive inheritance, account for about 5%. Other mutant gene conditions differ greatly in number from county to county in Sweden (e.g. 2% in Uppsala county and 12% in Västerbotten county).

Thus, no less than about two-thirds of all SMR cases are caused by very early prenatal factors. To defeat these a quite different preventive approach to that used for CP must be adopted. A simple blood test to screen all pregnant women for a trisomy 21 fetus (e.g. increased levels of superoxide-dismutase bound to 21q) would be effective but at present is no more than a hypothetical possibility.

Today we have to restrict ourselves to the modest decrease in incidence which could be expected from selective screening by amniocentesis in the 16th week in women aged 35 years or older, and in women who have previously had a chromosomally abnormal baby.

Intrauterine infections during the 2nd and 3rd trimesters are sometimes manifested as the so-called ToRCH-syndrome with microcephaly, spastic diplegia, chorioretinitic changes and often intracerebral calcification. Rubella can be expected to be eradicated in the future by vaccination of all schoolgirls. CMV infections are a much larger problem. Elek and Stern's studies (1974) indicate that CMV alone might be responsible for near 10% of all SMR cases, many of them clinically untraceable without very thorough virological and serological testing of all mothers and babies at birth. Moreover, a vaccination programme for all schoolgirls seems to be a distant prospect. Existing vaccines are suspected of having oncogenic properties and therefore there is a risk of a potentially dangerous reactivation of the vaccine virus during pregnancy.

The 10% of SMR due to obvious perinatal brain damage—birth trauma and/or asphyxia, with or without intracranial haemorrhage—is nearly always combined with a CP-syndrome [12]. For this group, as well as for the cases affected during the 2nd and 3rd trimesters (together about 15 to 20%) the same preventive approach as for CP is applicable. Among these, 'fetal deprivation of supply' was also found to be of importance for SMR and was revealed as a suspected damaging factor in somewhat less than 10% of cases in two recent Swedish series [4, 6].

General Comments

The significant gains in surviving and non-damaged infants during the last 25 years in Sweden mainly refer to decreasing damaging factors in the perinatal period, defined as the day of delivery and the first neonatal week. Advances in obstetrics and particularly in neonatology may be credited for this. A factor considered to have been of utmost importance in the adequate use of improved technology is the gradual and consistent centralization of all deliveries in most counties to one or two large central county hospitals with basic facilities for advanced obstetrics and neonatology. This, in turn, has been facilitated by the organization of the Swedish health system and the decentralized responsibility and power for its effective realization at the county council level. It is a challenge for the future to also overcome the multifacetted difficulties associated with effective prenatal prevention.

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