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CHAPTER 11

Prenatal and Perinatal Risk Factors in a Survey of 681 Swedish Cases

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I, that am curtail'd of this fair proportion,
Cheated of feature by dissembling nature,
Deform'd, unfinish'd, sent before my time
Into this breathing world, scarce half made up,
And that so lamely and unfashionable
That dogs bark at me, as I halt by them.
Shakespeare, *Richard III*

Introduction

The aim of this chapter is to try and shed light on more specific aspects of the main groups of prenatal causes and risk factors for cerebral palsy, their mutual importance, and particularly their relationship to superimposed detrimental perinatal events. This survey is based on an investigation of 681 cases born in Sweden from 1959 to 1976.

In our original retrospective analysis of causes of cerebral palsy (Hagberg *et al.* 1975*a*), it was found necessary to make certain generalisations about the aetiological groupings. Only the risk factor that was considered to be the predominating possible cause was used for classification. There is no doubt that this oversimplifies the issue as it neglects the complex network of different interacting detrimental risk factors that are present in the majority of cases, and in all probability underlie the development of brain lesions.

Definitions

For the purpose of the Swedish investigation, the following definition of cerebral palsy was used: a non-progressive 'disorder of movement and posture due to a defect or lesion of the immature brain' (Bax 1964).

Syndromes

The Swedish classification into syndromes was employed (Hagberg *et al.* 1975*a*). In mixed forms the predominating syndrome was chosen. Patients were assigned to the group of spastic tetraplegia when they had severe spastic pareses of all four limbs, the disability in the upper extremities being of the same degree or more pronounced than in the lower ones. Spastic diplegia meant spastic pareses of the lower extremities with variable, but lesser, involvement of the upper limbs. This group included very slight to severe forms; elsewhere the latter are probably often classified as tetraplegia. Children with ataxic diplegia had ataxic traits,

spastic diplegia, which most illustratively subdivides into clearly different preterm and term subgroups.

SPASTIC DIPLEGIA

This is the syndrome particularly associated with preterm birth, which was present in as many as 55 per cent of our 226 children with diplegia, the vast majority (95 per cent) of whom were of an appropriate weight for their gestational age. The neuropathological correlates in some preterm cases of diplegia are thought to be periventricular infarctions and/or haemorrhages (Pape and Wigglesworth 1979), although many low-birthweight infants with intraventricular haemorrhage do well. Other pathophysiological causes may be secondary to immaturity of circulation and the CNS. Why some of these sick infants develop spastic diplegia and others do not is still a puzzle to most workers.

Three-quarters of our children with preterm spastic diplegia were very preterm, and showed significantly lower proportions of prenatal risk factors than corresponding infants with other cerebral-palsy syndromes. Prenatal predisposing detrimental events, other than those accompanying preterm birth in general, seem to be of little importance for the development of diplegia among Swedish children of low birthweight, if this is appropriate for their gestational age. The major determining risk factor among such children is the degree of CNS immaturity.

For diplegic children born at term, the pattern of causes and/or predisposing risk factors is different, much more complex and heterogeneous. This topic has been surveyed recently in more detail in a separate study (Veelken *et al.* 1983). An attempt has been made to summarise relevant present-day knowledge in Table V. Ingram (1974) concluded from his studies that diplegia frequently seemed to be prenatally determined rather than the result of perinatal injuries. This was confirmed in our study, where 12 per cent of children with diplegia born at term had obvious prenatal conditions and another 16 per cent had purely prenatal risk factors. Perinatal detrimental events were just as frequent, however, as prenatal ones, and when compared with controls were of relatively greater importance (Table IVA).

There are obvious differences in background mechanisms between cases of term and preterm diplegia, with respect to the number of adverse factors present (reduced optimality) (Veelken *et al.* 1983). In contrast to preterm diplegic children, diplegic children born at term were more likely to have a history of the factors associated with fetal deprivation of supply (*e.g.* toxaemic signs, placental infarction, leanness at birth) and of intra-uterine asphyxia (*e.g.* abnormal fetal heart rate, discoloured amniotic fluid). Compared with a series of controls born at term (Kyllerman and Hagberg 1983), the excess adverse factors among our cases were both prenatal and perinatal (partum and postpartum). The common combination of various adverse prenatal conditions with complications at delivery, particularly asphyxia, suggests that the causes are multi-factorial, and the consequences of unfavourable interactions. It is reasonable to believe that birth asphyxia was the final decisive cause of the brain damage in a number of prenatally predisposed cases. However, it is of interest that in our intensively studied term

TABLE V

Summary of different causes/pathogenetic risk factors among diplegic babies born at term

Prenatal
- Simple genetic forms (Ingram 1964, Gustavson *et al.* 1969, Bundey and Griffiths 1977)
  - Familial spastic diplegias — different genetic types
  - Familial ataxic diplegias — different genetic types
- Cerebral malformation syndromes (Ingram 1964, Malamud *et al.* 1964, Christensen and Melchior 1967, Glenting 1970)
- Certain microcephaly syndromes
  - Cortical dysplasias
  - Corpus callosum agenesia
  - Teratogenic conditions (some?)
- Maternal deficiencies (Drillien *et al.* 1962, Glenting 1970, Veelken *et al.* 1983)
  - Subfertility, previous stillbirths/repeated abortions
  - Chronic maternal disorders
  - Chronic maternal abuses — alcohol, drugs
- Abnormalities of pregnancy (Ingram 1964, Lyon 1970, Hagberg *et al.* 1976)
  - Intra-uterine infections — TORCH complex
  - Intra-uterine circulatory failure
    - placental intermittent ischaemia
    - fetal brain perfusion failure
  - Fetal deprivation of supply syndromes

Perinatal
- Birth asphyxia (Norman 1963, Ingram 1964, Veelken *et al.* 1983)
  - Predisposed prenatal risk cases
- Neonatal hypoxia/ischaemia (De Reuck *et al* 1972, Veelken *et al.* 1983)
  - Predisposed prenatal risk cases?
- Hyperosmolarity leading to periventricular haemorrhages (Pape and Wigglesworth 1979)
  - Predisposed prenatal risk cases?

Postnatal
- Progressive infantile hydrocephalus (Hagberg and Sjögren 1966)
  - Predominantly non-shunted cases
- Cerebral-venous thrombosis (Ingram 1964)
  - Predominantly post-infectious
- Post-encephalitic states, encephalomyelitis (Glenting 1970, Lademann 1978)
  - Virus encephalopathies
- Purulent meningitides

diplegic series (Veelken *et al.* 1983), birth asphyxia was never found to have been the single risk factor.

In 28 per cent of cases no risk factor at all could be identified. On the assumption that this group was proportionally distributed among the prenatal, perinatal and postnatal periods (Table IA), 43 per cent of the term children with diplegia in our series were likely to have been prenatally determined, and a further 37 per cent prenatally predisposed.

SPASTIC HEMIPLEGIA

Until about 10 years ago, congenital spastic hemiplegia was considered mainly