The Danish Cerebral Palsy Registry

A registry on a specific impairment

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ABSTRACT


Cerebral palsy (CP) is the commonest disabling impairment in childhood, with a prevalence of 2-3 per 1000 live births. The Danish Cerebral Palsy Registry is a research registry that contains cases of CP from birth year 1925 and has estimated the birth prevalence since 1950. Data on children with CP are collected from paediatric departments and one special institution for disabled children. The children are included by a child neurologist and an obstetrician, and information on pregnancy, birth, neonatal period, impairments and demographic data on the child and mother are registered in a standard form. The uptake area is eastern Denmark, covering about 30% of the population, but the rest of Denmark is planned to be included from 2001. The Registry is large, well established and validated, and the definitions and collection procedures have not changed through several decades. It therefore has great research potential. Birth prevalence is estimated continuously, and changes over time are analysed and correlated with pre- and perinatal conditions. A correlation between increased survival of preterm babies and an increased prevalence was found previously, and a decreased prevalence in very preterm infants was later associated with Jess use of mechanical ventilation. A study correlating CP and maternal infection is ongoing. Collaboration between 14 European CP registries allows the true differences in prevalence between different countries to be studied. Linkage to other individually based registries in Denmark will allow the social consequences of CP to be described.

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Cerebral palsy (CP) is one of the most severe disabling impairments in childhood, with a birth prevalence of 2-3 per 1000 live births (1). CP is an umbrella term (2) for a group of motor disorders without any specific structural and functional manifestations, cause or prognosis. There have been many attempts to get an internationally agreed definition of CP since the first attempt in 1964 (3). Nevertheless, most European CP registries have agreed that CP should include five elements: 1) a group of disorders 2) that is permanent but not unchanging, 3) involves a disorder of movement and/or posture of motor function and 4) is caused by a non-progressive interference, lesion or abnormality of 5) the developing or immature brain (1, 2). The reason for this somewhat vague definition is that CP includes four different motor abnormalities: spasticity constitutes the majority (75%), and the others are dyskinesia consisting of dystonia and chorea-athetosis (20%) and ataxia (5%). The subclassification of CP has also recently been agreed upon using the Swedish classification including the following: hemiplegia, diplegia, tetraplegia, dystonia, chorea-athetosis and ataxia (1, 4). The Danish Cerebral Palsy Registry has been using these criteria for all cases born after 1978.

CP is an impairment that places severe demands on health, educational and social services as well as on the families and children themselves. Research into the origins of CP must therefore remain a high priority (5). Two areas have been focused on during the last two decades. First, babies born very preterm have a high risk of CP. The decline in neonatal mortality in the 1980s and 1990s has allowed more vulnerable babies to survive. There is evidence that the prevalence of CP has risen among preterm infants (4, 6) and that the degree of disability among survivors of CP is increasing (7-9). Continued monitoring of the comorbidity of children with CP is therefore highly important. The main question is whether the preterm child with CP was born with a brain injury caused prenatally or was born with a healthy but vulnerable brain that became injured during the perinatal period.

The second research area has focused on the relationship between the care given to mothers and full-term babies around the time of birth and the emergence of CP. Although it is widely agreed that few CP cases are associated with a major intrapartum event, there is still uncertainty and confusion in this area. Attention has recently been given to the antenatal period, with maternal infection as a possible factor in the causal pathway (10, 11).

Most research on CP has been based on CP registries. Such registries have existed in Australia, Denmark, Ireland, Japan, Sweden, the United Kingdom and the United States for many years. Even though CP is the commonest disabling impairment in childhood, occurring twice as frequently as Down's syndrome, only about 120 children are born with CP per year in Denmark. This means that large birth cohorts need to be studied, and the same method must be applied to the trends in the birth prevalence of CP over time to find true changes. The Danish CP registry is one of the largest and oldest registries still active, having CP rates going back to the birth year 1950.

OBJECTIVES

The objectives of the Danish Cerebral Palsy Registry are:

- to estimate the birth prevalence of CP in Denmark and analyse changes over time;
- to relate changes in the birth prevalence of CP to pre- and perinatal conditions;
- to describe changes in the proportions of subtypes and severity of CP;
- to identify cases for specific substudies (that is, risk factors, treatment and social consequences); and
- to describe the need for social and health services for people with CP.

HISTORY OF THE DANISH CEREBRAL PALSY REGISTRY

The Danish Cerebral Palsy Registry was founded in 1967 by the Danish Society for Cerebral Palsy. At that time, Professor Erik Hansen had personally collected cases of CP from the birth years 1925 to 1953 (12). Although CP rates have been recorded since the birth year 1940, only the birth prevalence after 1950 is presumed to represent a reasonable ascertainment of eastern Denmark, which includes Bornholm, Copenhagen, Frederiksborg, Fyn, Roskilde, Stor- strom and Vestsjælland Counties and the Cities of Copenhagen and Frederiksborg, covering about 50% of the Danish population. From 1965, Paul Glenting, a paediatric neurologist, started collecting CP cases prospectively from the same area. The first article in an English-language journal was published in 1982 on the CP rates for the birth year period 1950-1974 (13). After the sudden death of Paul Glenting in 1988, Peter Uldall, also a paediatric neurologist, continued the Registry. In 1991, the Registry was placed at the National Institute of Public Health (formerly Danish Institute for Clinical Epidemiology). Monica Topp, an obstetrician, began to work with the Registry in 1994, and Susan Michelsen, a physician, is now preparing a PhD study on the social consequences of CP. Since 1997 the Danish CP registry has been an active participant in the survey of cerebral palsy in Europe (SCPE). This is a collaboration between 14 European CP registries among which the Danish Cerebral Palsy Registry is the fourth largest (1).

In 2001, the Registry will begin to cover western Denmark in cooperation with the Danish Epidemiology Science Centre, University of Aarhus. Hence, the Danish Cerebral Palsy Registry will become the largest in the world, covering more than 70,000 births per year, and the first national CP registry in the world.

Grants from the Danish Society for Cerebral Palsy and Helsefonden (Danish Health Insurance Foundation) have financed the basic operating costs of the Registry so far.

The Registry has published 20 articles in peer-reviewed journals as well as seven reports describing the birth year prevalence, the correlations with perinatal risk factors, comorbidity, social prognosis and mortality.
METHOD OF DATA COLLECTION

Data are collected based on voluntary reports from a specific contact person in all paediatric departments and one special institution for handicapped children (Vangedehuse) in eastern Denmark. Every child with known or suspected CP is reported, and then the paediatric neurologist at the Registry evaluates the diagnosis by reading a copy of the child's full case record. If the child fulfills the inclusion criteria for the Registry, further information is requested. This includes obstetric and neonatal discharge letters as well as the results of cerebral computed tomographic scans or magnetic resonance imaging. Based on this information, a data abstraction form is completed (See Fig. 1).

The criteria for inclusion in the Registry are as follows:
- born in eastern Denmark and living there at the age of 4-5 years (if the child dies between age 1 and 4-5 years, the case is included anyway if the CP diagnosis is certain);
- pre- or perinatal aetiology (events occurring before 28 days of age); and
- fulfilment of the diagnostic criteria.

CP children who dies before 1 year of age are not included because the diagnosis in these children is very unreliable. Also, children emigrating before age 4-5 years are excluded because information is too poor. However, the number of children in these two groups is very small. CP children born outside the region often come from totally different countries (adopted children, refugees from the Middle East and Africa) in the sense of complications and care in pregnancy and the perinatal period. Thus, the rate of CP is expressed by the birth prevalence, defined by the number of CP children at age 4-5 years per 1000 live births, in accordance with other international publications. The diagnostic criteria are similar to those adopted by the Surveillance of Cerebral Palsy in Europe (1) (Fig. 2).

To complete the registration, children born from 1979 have been linked with the National Patient Registry. This identifies children hospitalized with the diagnosis of CP but not reported to the Danish Cerebral Palsy Registry. Reports on these children are obtained to consider inclusion, and more information is then collected on the children included.

If a child is included before the age of 4 years, a new report will be required at the age of 4-5 years to ensure that the diagnosis, subtype and mental development are correctly evaluated. For the same reason, and to make sure that all the mild cases are diagnosed, a birth year cohort is not closed before the children are 4-6 years old. The Registry also keeps all information on excluded children (such as postnatal, progressive and unclarified cases). These cases have not been analysed because of lack of resources and financial support.

DATA CONTENT

The Registry includes retrospectively collected cases born as early as 1925. Since 1965, the data collection has been prospective, and from birth year 1971 all data are computerized. A total of 2850 cases were born from 1940 to 1978. From the birth year 1979, the abstraction form was changed somewhat, introducing the Swedish definitions and classification of CP (4), and since then only mildly adjusted. Data on 908 CP cases have been published from birth year 1979 up to 1990 (6, 7, 14), and data abstraction on cases born from 1991 to 1994 is ongoing.

The abstraction form contains information on CP subtype, severity of motor handicap (ability to walk), orthopaedic operations and accompanying nervous system diseases, including mental retardation, epilepsy and problems with hearing, vision or speech. It also includes demographic data on the child and mother and information on chronic maternal disease and complications in pregnancy, at birth and in the neonatal period, including gestational age, birth weight, mode of delivery, Apgar score, congenital malformations and the results of neuroimaging scans. Finally, the timing of the brain damage is evaluated.

VALIDITY

A validation study was performed in 1997 to determine the completeness of the Registry and the validity of the data (15). Children born from 1979 to 1982 and hospitalized with the diagnosis of CP were identified by the National Patient Registry. These children were linked with cases in the Danish Cerebral Palsy Registry, and 35 children not previously included fulfilled the criteria for inclusion. This group did not differ from the hospitalized children already in the Danish Cerebral Palsy Registry regarding subtype, severity of impairment, rate of preterm birth, low birth weight or geographical
1. Spastic CP is characterized by at least two of the following:
   - abnormal patterns of posture and/or movement
   - increased tone
   - pathological reflexes
2. Ataxic CP is characterized by both of the following:
   - abnormal pattern of posture and/or movement
   - loss of orderly muscular coordination so that movements are performed with abnormal force, rhythm and accuracy
3. Dyskinetic CP is characterized by both of the following:
   - abnormal pattern of posture and/or movement
   - involuntary, uncontrolled, recurring, occasionally stereotyped movements

**fig. 2. Diagnostic criteria used for the Danish Cerebral Palsy Registry.**

The origins of CP are multifactorial and still under discussion. A study is being prepared on an association between CP and biochemical markers of inflammation and genetic coagulation disorders measured during pregnancy and at birth, linking the Registry to a Danish cohort study on 100,000 births (The Danish National Birth Cohort). This study will test the hypothesis that maternal infection is a causal pathway to CP and the impact of various genetic risk factors in a nested case control design (10, 11). When the uptake area is expanded to cover western Denmark, regional differences in CP rates could be correlated with differences in health care services and practices.

The collaboration between 14 European CP registries presents an unprecedented opp01unity to study true differences in prevalence rates between countries. Multicentre studies are planned to elucidate the different causal pathways to CP and the quality of life of children with CP.

Much debate on the fate of mentally impaired children has taken place in Denmark. Early intervention and a high standard of social services are hoped to lessen the burden on the family and increase the opportunities for children with CP. Precise knowledge on the quality of life in adulthood is sparse, however. The Registry can answer many of these questions in a cohort study by linking to other individually based registries in Denmark such as health and social services, education, job situation and civil status, using the personal identification number issued by the Civil Registration System. The outcome of such a study of CP cases birthyear 1965-1990 can be compared with a unique historical follow-up of children born with CP from 1940 to 1945. Of the 87% surviving children 30 years later (n = 569), 51% were fully socially competent, having an independent dwelling and an occupation; 32% were married and 28% had children. Intelligence decisively influenced social competence, almost fully compensating for the motor impairment (17).

Finally, social services authorities have noted a rise in the number of disabled children in Denmark requiring assistance in day care centres and schools. It is not known whether this increase reflects a real rise in the number of disabled children or increasing requests for assistance from the parents. The Danish Cerebral Palsy Registry is one of the very few reliable sources that can evaluate such questions.

**REFERENCES**