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Consequences of Down syndrome for patient and family

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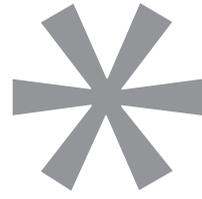
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Summary

This thesis describes the current state of children with Down syndrome (DS) in relation to the prevalence, morbidity, mortality and quality of life. DS is one of the most common chromosomal abnormalities and is characterized by several dysmorphic features and delayed psychomotor development. Children with DS also have an increased risk of concomitant congenital defects and organic disorders such as congenital heart defect (CHD) and gastrointestinal defects, celiac disease (CD) and hypothyroidism.

Because of medical improvements in overall DS related medical care, the survival of individuals with DS has increased considerably. The median age at death of individuals with DS has risen significantly, in the US for instance there was a rise from 25 years of age in 1983 to 49 in 1997. Estimates of life expectancy suggest, that about 44 % of persons with DS will reach the age of 60 and 14 % will reach the age of 68 in the near future. This life expectancy requires giving the necessary care to the individual with DS over their total longer lifespan, this should be taken into account.

Chapter 2 describes the morbidity and strategies on the base of “best evidence”, based on the most relevant literature currently available for optimal care of the child with DS. CHD and respiratory infections are the most frequently reported medical disorders on death certificates for individuals with DS.

Chapter 3 describes the prevalence, neonatal characteristics, and first-year mortality of children with DS. To a large extent, the prevalence of DS depends on socio-cultural variables. In countries where abortion is illegal such as Ireland and the United Arab Emirates, its prevalence is higher. Conversely, in France DS prevalence is low, and this is probably due to a high percentage of DS pregnancy terminations. In our study we estimated the DS prevalence in The Netherlands in 2003 at 16 per 10,000 live births, an almost 1½ time increase compared with Eurocat registrations in the northern Netherlands between 1981 and 1990, which show DS prevalences of respectively 10.6 per and 12.8 per 10,000 live births. Increasing maternal age and improved survival rates for infants with Down syndrome have outweighed the effects of prenatal diagnosis followed by the termination of pregnancy and a declining general birth rate. Recent decades have seen a substantial increase in the life expectancy of children with DS. In The Netherlands, the infant mortality rate in children with DS dropped from 7.07% in 1992 to 4% in 2003, this is in contrast with the 0.48% infant mortality of the reference population in The Netherlands in 2003. The fall in DS mortality was mainly related to the successful early surgical treatment of CHD and to the improved treatment of congenital anomalies of the gastrointestinal tract. The life expectancy of children with DS is primarily dependent on the risk of mortality in the first year of life. Furthermore our study showed remarkable observations, children with DS were less often breast-fed and 86% of the children with DS were hospitalized after birth.

Chapter 4 describes the prevalence of CD. We found a prevalence of CD in children with DS of 5.2% (10 times higher than the general Dutch population). In our study blood samples were taken from all 155 studied children with DS, and random we collected buccal swabs from 9 of them. Human leukocyte antigen (HLA)-DQ typing was performed, and immunoglobulin A anti-endomysium-(EMA) and anti-tissue transglutaminase antibodies (TGA) were measured. HLA-typing obtained on buccal swabs from the children with DS has the benefit of avoiding the unpleasant collection of blood. Sixty-three children (40.6%) had test results that were positive for HLA-DQ2 or HLA-DQ8. Results of HLA DQ-typing of DNA isolated from blood and buccal swabs were identical. Eight of the children in whom test results were positive for HLA-DQ2/8 also had positive test results for EMA and TGA. CD was confirmed in 7 of these children with an intestinal biopsy, and in 1 child, CD was suggested with improvement on a gluten-free diet. We recommend on the base of our results and literature HLA-DQ2/8 typing from buccal swabs in the first year of life and initiating serologic screening of children with DS in whom test results are positive for HLA-DQ2 or DQ8 at age 3 years. This would allow the further selection of a group needing to be screened and a group that can be excluded from further screening because the negative predictive value of the HLA-DQ typing is almost 100%. Early knowledge of negative HLA-DQ2/8 status can reassure those parents that their children do not have a CD risk. A positive HLA-DQ2/8 status may give the parents of the children with DS the opportunity to use preventive options (**Chapter 8**).

Chapter 5 describes the assessment of the prevalence of CHD and persistent pulmonary hypertension of the neonate (PPHN) in children with DS and the impact of CHD on neonatal factors. It was a prospective study of a birth cohort of children with DS born between 2003 and 2006 registered by the Dutch Paediatric Surveillance Unit. A CHD occurred in 43% of 482 children with trisomy 21. Atrioventricular septal defect was found in 54%, ventricular septal defect in 33.3% and patent ductus arteriosus in 5.8%. The incidence of PPHN in DS was 5.2%, which is significantly higher than the general population. The reported mortality in newborns with DS was overall 3.3% and was still significant higher in children with a CHD versus no CHD (5.8% versus 1.5%). The presence of a CHD in children with DS had no influence on their birth weight, mean gestational age and Apgar score.

Chapter 6 describes the frequently occurring respiratory problems in children with DS. Recurrent wheezing has been reported in more than one-third of children with DS. The aim of this study was to compare the prevalence of current wheeze in children with DS, their siblings, and nonrelated population controls. This was a case-control study in which the International Study of Asthma and Allergy in Childhood questionnaire for respiratory symptoms was completed by parents of 130 children with DS, for 167 of their siblings, and

by the parents of 119 age- and sex-matched control children from the general population. Both wheeze ever and wheeze during the last 12 months were more commonly reported in DS than in their siblings or controls. The relative risk of current wheeze in DS was 2.8 compared with siblings, and 2.75 compared with controls. A doctor's diagnosis of asthma was found in 3.1% in children with DS, in 4.2% in siblings and in 6.7% in controls. During 4-years follow-up, the diagnosis of asthma could not be confirmed in the 24 DS children with current wheeze, and atopy was found in none of them. In children with DS and wheeze a number of DS specific pathophysiological factors should be considered, like anatomical and immunological problems. Wheeze is common in children with DS, we found it likely to be related to the factors specific for DS and probably unrelated to asthma and atopy.

Chapter 7 describes Health-Related Quality of Life (HRQoL) in preschool children with DS, compared to a reference group and identifies determinants for HRQoL. HRQoL was measured with the TNO-AZL preschool children Quality of Life Questionnaire (TAPQoL). Mental development was assessed by means of the Bayley Scales of Infant Development second version (BSIDII). Behavioural problems were measured with the Child Behavior Checklist (CBCL), functional status was assessed with the Dutch adaptation of the Pediatric Evaluation of Disability Inventory (PEDI). Health problems were studied using the medical file. Maternal education was defined as higher-, senior secondary- or junior vocational education. Fifty-five children with DS (mean age 40.6 months SD 12.8) and their parents participated in this study. In our study of preschool children with DS the HRQoL is influenced by developmental quotient, respiratory and gastro-intestinal health problems, problem behaviour, and maternal education, but not by CHD and adaptive function. Our goals for treatment should be altered and attention should be given to the underlying causes which influence HRQoL in children with DS.

Conclusion (Chapter 8)

Nowadays the outcome of medical aspects and mortality is improved and DS is more accepted in the Western World. Children with DS born recently meet family and community as well as health care attitudes, that are more positive and DS educated than years ago. The DS phenotype is well understood so we are better prepared to support the child with DS and their families. However, more work has to be done on the understanding of families and community processes that optimize function and independent living. In the parents' decision-making process, whether to continue or stop their DS pregnancy a pediatrician with sufficient knowledge of the current well-being of children with DS can play an important even central role for these parents. The prevalence of DS will always be the net effect of the balance of the technical possibilities on the one hand and the personal feelings of the future parents on the other hand and is not easy to predict on the base of evidence only.