Down syndrome
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There continues to be a steady growth in the published literature regarding issues for individuals with Down syndrome. This review highlights recent articles that contribute to the present scientific knowledge of the family, social, behavioural and health issues affecting both children and adults with Down syndrome. Curr Opin Psychiatry 14:431–436. © 2001 Lippincott Williams & Wilkins.

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Abbreviation

CVJ cranial vertebral junction

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Introduction

Over 200 articles about Down syndrome were traced for this review, testifying to the steady growth in published literature. Recent publications range from learning about happiness from individuals with Down syndrome [1], to ongoing studies [2\textsuperscript{*}], to embryonic research that might have the potential to revolutionize future care of individuals with Down syndrome [3,4]. Many publications use Down syndrome for a comparison with other conditions and tell us little about individuals with Down syndrome and those who care for them. These have been left out, as have the increasing number of studies on screening for the purpose of preventing Down syndrome births. Although screening is reducing the incidence, the survival of babies with Down syndrome has steadily improved. Recent figures for Australian babies born between 1980 and 1996 show a 91\% chance of surviving for one year and an 85\% chance of surviving up to 10 years [5]. The majority of publications tend to consolidate our knowledge about Down syndrome.

Nutrition and hormonal issues

Nutritional supplements as treatments for behavioural and physical aspects of Down syndrome have a long history. Pueschel [6] provided a detailed review of these, and concluded that in general individuals with Down syndrome do not need additional vitamins and minerals. He noted that congenital heart disease, thyroid deficiency and coeliac disease [7] may interfere with adequate nutrition. Certain trace elements and minerals such as selenium and zinc [8], as well as specific antioxidants, may be deficient and may also need supplementation. Ani \textit{et al.} [9] reviewed related studies and argued for evidence suggesting increased oxidative stress in the pathology of Down syndrome, including learning difficulties and the onset of Alzheimer’s disease. The authors argued for clinical trials on the role of antioxidants.

The full extent of hormonal abnormalities in adults with Down syndrome has not been fully researched. Previous studies along with a recent publication [10] highlighted the association between thyroid dysfunction and Down syndrome. Whether diabetes is associated with Down syndrome continues to be an area of debate. Ohyama \textit{et al.} [11], in their study of 40 adults with Down syndrome, found that none of the patients could be classified as having diabetes or impaired fasting glucose levels.
Family aspects

Several family studies confirmed previous findings: siblings of children with Down syndrome do not have increased behavioural problems [12] and have significantly fewer problems than those of children with pervasive developmental disorder [13]; generally good family adaptation to the child having Down syndrome [14,15]. However, parents of preschool children with Down syndrome have been reported to be experiencing more care-giving difficulties and parent-related stress than those of typical children, and this is expressed differently for fathers and mothers [16]. A descriptive study from interviews with families [17] highlighted the impact of the social context on parents’ personal constructions, life events and the need for inputs to trigger parental reconstructions and actions. A Portuguese study [18] compared the parental tutoring style and interaction of 36 dyads of children with Down syndrome with 36 typical children. The results suggested that parents of children with Down syndrome intervened less, and when they did, it was less directive. The authors argued that such a parental style may be more adapted to furthering autonomy. Although there are some concerns about the study, the results are of interest because they are the opposite of many previous mother-interaction studies, mainly from north America and the UK, and may suggest cultural effects. It may also relate to the issue of early intervention influences on parenting interactional style. Pino [19] found that mothers of pre-school children with Down syndrome ($n=16$) used more teacher and helper behaviour with fewer positive verbalizations than eight mothers of typical children at a similar developmental level, and concluded that this may reflect the types of parent training interventions. A study looking at the facilitation of pride [20] found that caregivers of children with Down syndrome did not provide more directive or responsive types of assistance than those of typical children, but did use a greater frequency of praise. Such studies reflect a shift in thinking from training parents to train their infant/child with Down syndrome on developmental tasks to asking what sort of interaction produces self-regulated children.

Parents are key figures in the issue of young people with Down syndrome discovering that they have Down syndrome, and many would not understand. Their offspring had little awareness of Down syndrome or disability and had mental ages of less than 6 years, thus validating the parental view. No relationship was found between parental telling, or not, and the reactions of the young people towards having Down syndrome. Generally, the awareness and understanding of disability appeared to be similar to that expected for typical development.

Behavioural aspects

In recent years there has been an increase in studies looking at habits, ritualistic and repetitive behaviours in very young children, and noting the similarities with obsessive–compulsive behaviours in later pathology. Evans and Gray [22**] reviewed this in detail, and reported an investigation with 50 individuals with Down syndrome (chronological age range 3–21 years) matched for mental age (mean 59.72 months) with 50 typical children (chronological age range 2–7 years). Parents completed the Childhood Routines Inventory (standardized in earlier studies), which has two factors – ‘repetitive behaviours’ and the ‘just right’ phenomena, such as demanding particular orders of action or arrangements of objects. Younger children/lower mental-aged children (typical and Down syndrome) exhibited more compulsive-like behaviour than older children, suggesting a developmental phenomenon, and supporting the similar sequence model of mental retardation. The groups did not differ in terms of the number of compulsive-like behaviours, but the participants with Down syndrome engaged in the repetitive behaviours with greater frequency and intensity, which may reflect the mental rigidity behavioural phenotype for children with Down syndrome. Correlational differences suggested that ‘just right’ behaviours were related to adaptive behaviour in typical children but maladaptive behaviour in the Down syndrome group, and suggested that this may resemble the sensory/perceptual phenomena found in autism and obsessive–compulsive disorder. They related their findings to recent work in neuroanatomy. The study was exploratory and had several limitations; however, it did begin to highlight the importance of trying to integrate our knowledge from developmental psychology, the neurosciences and clinical psychopathology. Along similar lines, Glenn and Cunningham [23] investigated talking to self in 77 young adults with Down syndrome, using interviews with their parents. They noted clinical and anecdotal evidence of self-talk being mainly perceived as pathological. They found that self-talk was correlated with mental age, and appeared to follow the same sequences as found for typical children. They found no associations with social isolation, poor communication or difficult behaviour, as reported by parents.
They raised the issue that self-talk may be an adaptive and developmentally appropriate behaviour for these young people, and care should be taken in deciding if it is pathological or should be treated.

Ghaziuddin [24∗] investigated the family history of adults and children with Down syndrome who also had a diagnosis of autism. Findings for 11 Down syndrome subjects with autism were compared with seven controls (Down syndrome subjects without autism). For the former group there was an excess of first-degree relatives who met the description for the wider phenotype of autism. Seven (64%) of the autism group compared with one (14%) of the control group had an affected parent. A greater number of siblings of the autistic subjects also appeared to have an autism spectrum disorder. The study highlighted the importance of eliciting a detailed family history from adults with learning disability, and discussed the role of autism-specific genetic factors.

Chapman and Hesketh [25] discussed in detail the concept of a behavioural phenotype of individuals with Down syndrome. Cognitive, speech, language and adaptive behaviour issues were discussed. The paper highlighted the importance of a detailed and full assessment in deciding if a given behaviour is part of the ‘makeup’ of individuals with Down syndrome, is part of a developmental disorder (autism), or is a symptom of an underlying mental illness (e.g., depression or dementia).

**Social/emotional issues**

Positive results were reported for improving social skills through didactic training [26], and the understanding of self, using drama therapy [27]. Recent years have seen an increasing interest in self-concept and self-esteem in individuals with Down syndrome. Glenn and Cunningham [28] investigated self-evaluation using normative scales and interviews with 72 young adults with Down syndrome. Eight could not complete the scales and had mental ages of less than 3.5 years. The rest completed the scales, and the results appeared to be valid. This group all had very high self-esteem, and the results reflected the typical developmental pattern. Only those young people with mental ages above 7 years or so were making relative social comparisons. These young people also began to recognize some of their limitations, but this did not impinge on their positive feelings of self worth. Like most teenagers, self worth was more related to physical appearance and social acceptance than to academic ability.

A potentially interesting area is the recognition of emotion and emotional expressions. Kasari et al. [29] used a mental age match design with typical children (mental ages approximately 3–5 years) in three studies. They found similar patterns of recognition up to mental ages of 3 years or so, but poorer performance by children with Down syndrome from a mental age of approximately 4 years. They argued that this suggests both aetiological and developmental differences in emotion recognition. Wishart and Pitsira [30], using a similar design, also found that older children with Down syndrome had deficits in recognizing facial expressions, particularly surprise and fear. This suggests a specific deficit in recognizing emotional expressions, and possibly therefore learning about emotions. Clearly, such a problem could affect social skills and affective behaviour.

**Skeletal issues**

An association between atlanto-axial and atlanto-occipital instability and Down syndrome has now been well established. Previous research has often focused on the prevalence of the conditions, demonstrated the unreliability of routine radiological screening in detecting instability, or showing a poor correlation between the presence of instability and subsequent neurological involvement.

Merrick [31∗] continued to highlight concerns relating to individuals with Down syndrome, who have a high prevalence of musculo-skeletal problems, participating in sport. Taggard et al. [32∗∗], in a highly clinically significant paper, reported their experience regarding operative intervention for cranial vertebral junction (CVJ) instability in patients with Down syndrome. The medical and radiographical records of 36 consecutive patients with Down syndrome and CVJ abnormalities were reviewed. The most common clinical complaint included neck pain and torticollis. Cervicomedullary compression was associated with ataxia and progressive weakness. A number of patients suffered from varying degrees of quadriaparesis. Twenty-seven patients underwent surgical procedures without subsequent neurological deterioration, and a 96% fusion was observed. Overall, 24 patients enjoyed good or excellent outcomes. The authors concluded that good outcomes for surgical intervention for CVJ abnormalities can be obtained with low surgical morbidity rates.

A number of reports highlighted other important skeletal-related issues in adults with Down syndrome [33∗∗,34,35]. Tyler et al. [33∗∗] investigated 107 middle-aged adults with learning disability factors predictive of osteoporosis. A high rate of osteoporotic changes was found, and of the 10 variables investigated, Down syndrome, mobility status, and race were significant factors. The study further highlighted the importance of...
appropriate screening and the management of osteoporosis in adults with learning disability.

Ageing
Ageing in adults with Down syndrome is beginning to be recognized as a health ‘problem’ in its own right. Decline in neuropsychological performance with increasing chronological age in well Down syndrome adults was again recently demonstrated [36]. Holland [37] summarized the key biological, psychological, and social issues relevant to ageing in individuals with learning disability. The author highlighted the lack of a concerted response to ensure the provision of optimum health and social care to elderly individuals with learning disabilities. These concerns are supported by an article by Oliver et al. [38], which demonstrated that older adults with cognitive deterioration were less likely to receive day services, had more impoverished life experiences, and required more support compared with individuals without cognitive deterioration.

The effects of age on electroencephalograph frequency changes in adults with Down syndrome compared with controls was investigated by Katada et al. [39]. From cross-sectional and longitudinal studies the authors were able to show that there was a clearer slowing of electroencephalograph activity in the brains of adults with Down syndrome by the age of 40–44 years. Such changes could be seen by the age of 30–34 years in some subjects. The authors discussed these findings in relation to Alzheimer’s disease.

Alzheimer’s disease
Alzheimer’s disease remains the principal area of ongoing research in the Down syndrome population. Recent reports included ‘lab-based’ research looking at apoptosis in demented Down syndrome subjects [40], molecular dating of senile plaques [41], or investigating the reduction in specific proteins in Down syndrome brains [42]. Other ‘field-work’ studies investigated the occurrence of Alzheimer’s disease in parents of women with trisomic abortions [43], and the treatment of dementia in adults with Down syndrome with anti-cholinesterase inhibitors [44].

The neuropathological pathways for the development of Alzheimer’s disease remain to be fully established. Cataldo et al. [45] suggested that altered endocytosis (a process that is critical to the normal function of larger proteins such as amyloid beta peptide and apolipoprotein E) may occur many decades before the classic appearance of plaques and tangles are seen in Alzheimer’s disease. The role of the complement system (involved in the inflammatory response) and the development of plaques and tangles was investigated by Stoltznet et al. [46]. Their research suggested that for Down syndrome subjects with Alzheimer’s disease, the complement cascade system is activated after compaction of A-beta 42 deposits and is significantly involved in the subsequent development of Alzheimer’s disease pathology. Granholm et al. [47], experimenting on mice with segmental trisomy of chromosome 16, which are used as a model for Down syndrome, suggested that the loss of cholinergic function may directly correlate with cognitive impairment.

An association between apolipoprotein E4 and the increased risk of the development of Alzheimer’s disease in the general population has now been well established. The association was further investigated in the Down syndrome population [48,49]. Deb et al. [48,50] undertook a meta-analysis of previously published studies and found a significantly high frequency of E4 in adults with dementia compared with non-demented adults (odds ratio 2.02). No significant reduction in the frequency of E2 was found. The authors concluded that apolipoprotein E4 acts as a risk factor for the manifestation of Alzheimer’s disease in individuals with Down syndrome. Cavani et al. [50], however, found no correlation between plasma levels of A-beta 40 and 42 as correlated with apolipoprotein E genotype. The authors concluded that the accumulation clearance of plasma and cerebral A-beta are regulated by different and independent factors.

Research findings continue to be published regarding the cognitive changes of Alzheimer’s disease in adults with Down syndrome [51], along with research looking at the incidence and course of clinical dementia in adults with Down syndrome [52,53]. Holland et al. [52] hypothesized that personality changes and the disruption of frontal-lobe functions are the first observable features as Alzheimer’s disease neuropathology progresses. Cosgrave et al. [53,54], in a 5-year follow-up study of dementia in adults with Down syndrome, concluded, however, that the earliest recognizable clinical features of dementia were memory loss and increased dependency. Irrespective of what are actually the first identifiable symptoms of dementia of Alzheimer’s type, the accurate diagnosis of dementia also remains paramount. Burt and Aylward [54] proposed a test battery to aid the diagnosis of dementia in adults with learning disability. The battery includes the Dementia Scale for Down Syndrome, which was also supported to be a potential tool by Huxley et al. [55]. Burt and Aylward [54] suggested a working battery of tests for the diagnosis of dementia that could be used by researchers to improve international studies.

Conclusion
Although the above studies continue to highlight a number of issues regarding the health and social well-being of individuals with Down syndrome, further
research is still required. Developmental, familial, behavioural and ageing aspects of Down syndrome remain areas of active research, but there are still a number of important areas of future research. How best can we prevent secondary problems in children with Down syndrome? What is the best treatment for any given medical disorder? What is the outlook for individuals with Down syndrome? The recent publications are now beginning to answer many of these questions. Future research must, however, integrate developmental, social, neuro-biochemical and psychological findings into a more holistic model to enable research findings to have clinical significance.

References and recommended reading

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