

AGEING AND ITS CONSEQUENCES FOR PEOPLE WITH DOWN'S SYNDROME

Article written by Professor Tony Holland. University of Cambridge for the Down's Syndrome Association newsletter and reproduced here with the permission of the author and the DSA)

The importance of supporting children with special needs so that they have the opportunity to acquire the necessary educational, living and social skills to equip them for adult life has been recognised for some time. However, in contrast, the needs of adults, and the importance of supporting people with learning disabilities and their families at times of transition, has been relatively neglected. Whilst the potential difficulties associated with the transition from childhood to adult life is now receiving more attention the fact that needs may change yet again in later adult life is only now beginning to be considered.

In the transition from full-time education, a major concern is that there are a very limited selection of support services for adults, and individuals can move from a relatively structured environment of special education to very limited support and opportunities. The recent Community Care Act provides the framework for decision making at times of such change and has placed a statutory responsibility on social services to undertake a 'needs-led assessment' at this transition, the purpose of which is to help individuals and their families to plan for adult life. Whether this happens still appears arbitrary and the options available vary considerably across the country. In an ideal situation there should be a range of imaginative services that can cater for the considerable range of individual need and individual choice. This would include access to full-time employment, supported employment schemes, more sheltered work environments, adult education and so on.

Old age in particular is associated with social and biological changes. For example, family networks alter as parents age and for all of us there is an increasing risk of age-related health problems. Outlined below is the evidence which suggests that ageing and the problems of old age are particularly relevant to people with Down's syndrome as some of these age-related problems develop earlier in life than would normally be the case.

AGEING AND THE BRAIN

Throughout life there are changes occurring in brain structure and function. These are particularly marked at the two extremes of life, childhood and old age. In early childhood this is primarily

growth and the rationalisation of connections between the brain cells (neurones). It is a combination of these brain changes in childhood and the parallel educational and social opportunities, which result in the increasing acquisition of educational and other skills. The extent to which this developmental process can be modified in children with Down's syndrome has been hotly debated and is beyond the scope of this article. In any research designed to address this question it is clearly a complex task to disentangle the effects of the educational and social environment, nutrition and the fact that there is anyhow considerable variation in the extent and nature of developmental delay and learning disabilities in children with Down's syndrome. In any given child it is impossible to know how different he/she might have been if a specific intervention had not taken place. However, what has been striking is the marked improvement in life expectancy for people with Down's syndrome that has occurred in this century and the significantly better educational opportunities. As with any child good physical health, sound nutrition and excellent social and educational opportunities maximise the chance of optimum development.

At the other end of life neuronal cell loss in the brain occurs. Old age is associated with an increased risk of developing minor cognitive difficulties and the development of more serious mental health problems, such as depression and dementia, as well as physical illnesses. In the general population relatively minor cognitive difficulties in old age are common, however, the more serious brain changes associated with disorders such as dementia are relative rare, although the risk of such disorders increases as people live into their 70s and 80s. The most common form of dementia which occurs in later life is called Alzheimer's disease, named after Alois Alzheimer who, in 1906, first described the characteristic brain changes (called plaques and neurofibrillary tangles) associated with this disorder. In the past this was often referred to as senile or pre-senile dementia.

In Down's syndrome the situation is different. It has been recognised since the early 1900's that changes are observed in the brain from relatively early in life and by middle age the formation of Alzheimer-like 'plaques and tangles' has occurred. Strikingly these 'Alzheimer-like' brain changes, are almost always found in people with Down's syndrome who have died in middle age or later but are not found at such a relatively young age in people who have learning disabilities for reasons other than Down's syndrome.

The appearance of these brain changes in people with DS is only of great significance if they lead to loss of ability and the appearance of the clinical changes characteristic of dementia (i.e., the development of Alzheimer's disease). It is the extent to which these brain changes are associated with clinical changes characteristic of Alzheimer's disease that has been the subject of several studies in different countries, including our own in Cambridge, undertaken by Johnny Hon, Fran Stevens, Felicia Huppert and myself.

AGEING AND DEMENTIA

Dementia is the name given to a collection of illnesses, one of which is Alzheimer's disease, that have a characteristic pattern of symptoms and signs and generally occurs in later life. The main characteristics of several of the dementias is a deterioration in the person's memory (usually for recent events) and loss of other abilities such as the ability to find one's way around, to communicate through language and to undertake particular tasks, such as getting dressed.

Dementia due to Alzheimer's disease is a steadily progressive disorder with evidence of decline over time. It is important to stress that this is much more marked than the memory difficulties that many of us are aware of with increasing age! As described above the presence of Alzheimer's disease is associated with the development of marked plaque and tangle formation in particular areas of the brain.

The key questions with respect to the effects of ageing in people with Down's syndrome is whether the plaque and tangle changes in the brain are or are not associated with the development of Alzheimer's disease. Our own work suggests that the characteristic features of dementia do begin to appear in some people with Down's syndrome with increasing age but not in as many as the brain studies of Down's syndrome originally suggested would be the case. We have seen 75, of a total of 77 people with Down's syndrome 30 years or old living in the Cambridge Health District. A small percentage of this group had evidence of dementia in their 30's, approximately 10% in the 40's and 40% in their 50's. This is about the same, as you would expect in the general population but 30 or 40 years earlier in life. For us an important research question is to determine why some people with Down's syndrome live into their 60's yet do not get Alzheimer's disease, whereas others do. What might protect some people and what might increase the risk in others?

APPARENT DECLINE IN LATER LIFE: CAUSES TO CONSIDER

This article has focused on some of the changes which have been described to occur in the brains of people with Down's syndrome as they reach middle and later life. As described above these changes only matter if they affect a person's ability and result in dementia due to Alzheimer's disease. Whilst rates of Alzheimer's disease do increase with age, its development is NOT inevitable. Outlined below and in the Table are some of the other factors that can result in apparent decline, particularly in later life, and which can be treated. This process of identifying the cause of apparent change is therefore critical.

Dementia, whatever its cause, effects a person's cognitive abilities and his/her ability to undertake tasks or to communicate. Whilst a decline in memory or the slow loss of specific abilities may be readily apparent in those without a pre-existing disability, it may be less easily noticed in people with Down's syndrome. There are two main reasons for this. First, unless someone has known

that person for some time and has observed the changes, the inability to do something is all too easily put down to his/her learning disability. The crucial question, in the case of an older person with Down's syndrome, is has he/she been able to do this in the past and now cannot? If so, why has this change occurred? Secondly, loss of ability may go unnoticed if the person is leading a life where he/she is, for example, not expected to take part in household activities or do tasks that require good memory. The fact that someone's memory may have deteriorated would under these circumstances go unnoticed.

Where there is good and reliable information available about how someone has changed and how he/she is now, the diagnosis of dementia can be made with a high degree of certainty. Those conditions listed in the Table can be excluded either on the basis of the history or through investigations. For example, depression can mimic dementia, but has other recognisable symptoms as well. They include a change in mood, loss of interest and ability to concentrate, together with changes in sleep and appetite. Thyroid disorders can be excluded both on the basis of clinical features and by a blood test. The decline may be for several reasons and those causes, which can be treated, should be treated. If there is doubt a computerised brain scan (CT or MRI scan) may help by showing evidence or not of brain changes which would normally be expected with Alzheimer's disease. Sometimes the reasons for change in later life cannot be established with certainty and it is necessary to follow-up over time. Detailed psychological tests of memory and other abilities can be particularly helpful in this situation. The most valuable information is invariably that given by those who have known the person over his/her lifetime or at least over many years. There is no substitute for this.

AGEING, ALZHEIMER'S DISEASE AND TREATMENT

Given that Down's syndrome is due to inheriting three, rather than two copies of chromosome 21 (trisomy 21), there has been much research interest in the genetic material (genes) on chromosome 21 which might account for these age-related brain changes. This genetic research has resulted in the discovery that the gene, which produces the 'amyloid precursor protein' (APP), is located on chromosome 21 and therefore occurs in triplicate in people with DS. In the general population, abnormalities (mutations) in that particular gene are associated with a rare form of early onset Alzheimer's disease. Much work is focused on the role of APP and the protein amyloid as it is this protein that is found in the brain plaques of Alzheimer's disease. The scientists engaged in brain research on Alzheimer's disease cannot agree whether abnormalities of how amyloid is dealt with in the brain, abnormalities of another protein called 'tau' (found in a changed form in the tangles) or a combination of mechanisms, are the fundamental abnormalities which leads to Alzheimer's disease in later life. There are also other age-related changes, which may increase the vulnerability to such problems as dementia. These include changes in the levels

of a particular steroid which may have a protective effect on the brain. As you can see, in this field there are competing hypotheses that need to be further investigated.

In the case of Down's syndrome the working hypothesis is that excessive amyloid production is likely to be a key factor, but this is far from being proven. Before the location of the APP gene was shown to be on chromosome 21, another gene on this chromosome and its product was the focus of attention. This was the gene coding for superoxide dismutase (SOD). Increased activity of SOD was found in post-mortem studies of people with Down's syndrome. It has been argued that this results in an increased potential for damage to cell membranes in the body due to the effects of SOD activity and increased oxidation. It is for this reason attention has focused on the use of 'anti-oxidants' (vitamins C and E), on the theoretical basis that they might prevent such damage occurring. There are of course many other genes on chromosome 21 and their products may be equally important but whether this is the case or not, is not known.

Treatments proposed in the hope that they might arrest or reverse the course of Alzheimer's disease are numerous but as yet no specific treatment has been found that stops brain cells dying. One key area of therapy has to focus on maintaining the levels of a key brain transmitter (acetylcholine). It is the brain cells that produce and use this transmitter which seem to be particularly affected in Alzheimer's disease. The earlier attempts to maintain levels of this transmitter resulted in medications that were unpleasant to take, caused serious side effects and of doubtful efficacy. More recent medications, which have a similar effect on brain chemistry but appear less unpleasant, have been developed. In trials that have been undertaken in the general population, temporary improvements have been reported.

There have been no trials of the treatment of Alzheimer's disease in people with Down's syndrome. There is however a number of potential treatment approaches. If amyloid were the main culprit, then when drugs that influence this are developed they would be potentially useful. Vitamin E has been considered because of its potential protective effect. There is no solid evidence to support this. The group of medications which affect acetylcholine may well temporarily improve function but have not been tried in people with DS. In Cambridge we are planning such a treatment trial but there are important scientific and ethical issues which have to be addressed. If medications appear safe, have minimum of side effects and if there is good reason to believe that it can temporarily at least arrest the decline, then in my opinion this needs to be tested out in a careful and thoughtful manner.

There has been much debate within the DSA and internationally about whether the consequences of having Down's syndrome or the potential for Alzheimer's disease can be modified through dietary supplements or by other means. This is a very complex issue and it has not been resolved. As readers will appreciate the issues are the same as with assessing the value of specific dietary or

other interventions in childhood. Trials, which are conducted in a carefully controlled manner, are essential if these questions are to be answered. If any treatment is to be used there is always a careful balance between the likelihood of improvement, on the one hand, and the risk of side effects, on the other. If trials have shown that the balance is towards the former then treatment can be justified.

SUPPORTING THE INDIVIDUAL

Identifying the cause of apparent decline in later life is crucial. Common causes of decline are listed below.

Cause	Characteristic features
Stress following life event	Deterioration follows stress e.g., after bereavement
Depression	Evidence of depressed mood, disturbed sleep and appetite, loss of interest, poor concentration
Underactive thyroid gland	Dry skin and brittle hair, intolerance of cold, weight increase, lethargy, abnormal blood test
Hearing or visual impairment	Evidence of sensory impairments on testing
Alzheimer's disease	Progressive cognitive and functional decline not due to the above

If decline is due, for example, to depression or an underactive thyroid gland, this can usually be reversed with the appropriate treatment. Similarly, people can be helped to get over the effects of life stresses or of life events such as bereavement. Carefully preparing and supporting people with Down's syndrome for adult life may help to minimise the psychological impact of family bereavements and other life events, which they will inevitably face. Knowing about the health risks associated with later life helps to ensure that they are detected and, where possible, treated.

The recognition that someone with Down's syndrome has Alzheimer's disease clearly is distressing but the positive aspect is that it helps to explain why that particular person has changed and has been behaving in the way that they have. The recognition that Alzheimer's disease is present should be the starting point for developing a package of support that will be able to meet the person's changing needs. The DSA has information which will be helpful in that regard. Once it is recognised that a person's memory is not as good or their ability to make sense and use language has deteriorated, then carers can compensate for this in the way they interact

with the person. Good and informed support can help to maintain the quality of life of the person affected.

THE FUTURE

The changing age structure of western society and the resulting increase in the proportion of older people has meant that there has been an explosion of research into those illnesses specifically associated with later life. This includes Alzheimer's disease. There is therefore a real hope that effective treatments will be developed. What is critical is that the needs of people with Down's syndrome are not forgotten. As research into Alzheimer's disease continues it is important to ask how this applies to people with Down's syndrome. Some of this research may or may not be directly applicable. We also need to tackle the question of treatment trials. A recent parliamentary question about research involving measles vaccine given to children with DS is in danger of missing the point. People with Down's syndrome have the right to expect that their health problems will be taken seriously and that treatments will be developed within the same high ethical and scientifically valid framework as should always be the case.

Tony Holland
Section of Developmental Psychiatry
University of Cambridge
July, 1997