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Cholesterol and Alzheimer type dementia among adults with Down syndrome

It is clear that there is an increased incidence of early onset dementia of the Alzheimer type among people with Down syndrome. Estimates vary, perhaps due to different diagnostic criteria and population biases, but around 10% of people with Down syndrome may be diagnosed with Alzheimer type dementia between the ages of 40 and 49, rising to around 30% between the ages of 50 and 59.

Little is known about factors that influence the development of dementia of the Alzheimer type among people with Down syndrome. Increasing age, the presence of the $\epsilon 4$ allele of the apolipoprotein E (APOE) gene, and age at menopause have been shown to increase the risk. It has been suggested that greater mental activity and stimulation may delay the onset of dementia and that therefore improved community living and social inclusion may reduce the prevalence of dementia among people with Down syndrome, but this is yet to be clearly demonstrated.

The primary neuropathological features of Alzheimer's disease include protein deposits called β -amyloid plaques and neurofibrillary tangles. Cholesterol may be involved in the formation, deposition and removal of β -amyloid. It has been suggested that cholesterol levels may be a risk factor for Alzheimer's disease in the general population. If this is the case, then high cholesterol levels may be a risk factor for adults with Down syndrome. Conversely, the use of cholesterol-lowering drugs may delay the onset or reduce the incidence of dementia of the Alzheimer type among people with Down syndrome. Statins are widely prescribed to lower cholesterol.

Warren Zigman and colleagues followed 123 adults with Down syndrome between May 1998 and April 2006. The participants were aged between 41 and 78 years at the start of the study and did not have dementia. The participants were assessed regularly for behaviour changes indicative of dementia and medical records were reviewed. APOE genotypes were determined from blood samples. Choles-

terol levels were determined from medical records of tests prior to the start of the study.

The study found that participants with high cholesterol levels were more than twice as likely to develop dementia of the Alzheimer type during the course of the study. The study also found that participants with high cholesterol levels who used statins had a 40% lower chance of developing Alzheimer type dementia during the course of the study. The risk for participants with lower cholesterol levels was not influenced by statin use.

This paper suggests that cholesterol is an important risk factor for Alzheimer's disease among people with Down syndrome and that perhaps cholesterol-lowering drugs could delay or prevent the onset of Alzheimer type dementia. However, the authors note that clinical trials of statins among the general population have not been encouraging and emphasise the need for rigorous clinical trials to establish a protective effect (if any) among older people with Down syndrome.

Frank Buckley

Original research paper

Zigman WB, Schupf N, Jenkins EC, Urv TK, Tycko B, Silverman W. Cholesterol level, statin use and Alzheimer's disease in adults with Down syndrome. *Neuroscience Letters*. 2007;416:279-284.

Further research

Bush A, Beail N. Risk factors for dementia in people with Down syndrome: Issues in assessment and diagnosis. *American Journal on Mental Retardation*. 2004;109(2):83-97.

Puglielli L, Tanzi RE, Kovacs DM. Alzheimer's disease: the cholesterol connection. *Nature Neuroscience*. 2003;6(4):345-351.

Further reading

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Chicoine B, McGuire D. Adults with Down syndrome: Specialty clinic perspectives. In: Janicki MP, Dalton AJ, editors. *Dementia and aging adults with intellectual disabilities: A handbook*. Routledge; 1998. Available from: www.ds-health.com/adults.htm