

DOWN'S SYNDROME COELIAC DISEASE /GLUTEN SENSITIVITY

A DSMIG CLINICAL AWARENESS NOTE

(written on behalf of DSMIG by Dr Jennifer Dennis with advice from Dr Charlie Charlton (Consultant Paediatric Gastroenterologist, Nottingham) and Dr Geoffrey Holmes (Consultant Gastroenterologist, Derby)

Background

Coeliac disease is a permanent intolerance to dietary gluten in susceptible individuals. The prevalence of classical infantile coeliac disease with failure to thrive; bulky, loose offensive stools; pot belly; anaemia; and other problems associated with malabsorption is given as 1 in 2000 (0.05%) in the most recent edition of 'Essential Paediatrics' (Hull and Johnston 1999). The prevalence of symptomatic coeliac disease in Europe has been estimated to be between 1 in 330 and 1 in 1000 (Corrao et al. 1994). Recent estimates of the prevalence of a wider spectrum of gluten sensitivity with often less florid but more diverse symptomatology – gut dysfunction (both diarrhoea and constipation), abdominal bloating, dyspepsia, mouth ulceration, mood change, arthritis, general fatigue, mild anaemia – are in the 1 in 100 – 300 range (Catassi et al 1994 (Italy): McMillan et al 1996 (N.Ireland): Feighery 1999 (UK). Cook et al 2000 (N.Zealand). There are major national differences in prevalence. However screening of populations with Down's syndrome has revealed much higher prevalences (from 4 -17%) depending on age of sample and country of origin. In addition other conditions frequently associated with coeliac disease – type 1 diabetes, thyroid dysfunction, skin disorders - are overrepresented among those with the syndrome.

Prevalence of coeliac disease/gluten sensitivity in Down's syndrome

Authors	N	Age (yrs))	Prevalence
Zubillaga et al (1993) Spain	70	1 – 14	4.3%
Jansson and Johansson (1995) Sweden	65	< 18	16.9%
George et al (1996) Netherlands	115	5.8 +/- 3.8	7%
Csizmadia et al (2000) Netherlands	137	1 – 23y	8%
Carlsson et al (1996) Finland	45	ch and adolesc	17.7%
Pueschel et al (1999) USA	105	2 – 28y	4 – 5%

Many normal people with Down's syndrome have features commonly associated with gluten intolerance/sensitivity. In childhood, muscle hypotonia predisposes to potbelly. Disordered bowel function is common. General lethargy and fatiguability are not unusual, and arthritis occurs more often than in the general population. In addition other conditions associated with failure to thrive– eg congenital heart disease - are overrepresented in those with the syndrome. For these reasons clinical diagnosis of coeliac disease is likely to be difficult.

Some practitioners recommend that all people with Down's syndrome should be screened for coeliac disease.(George et al .1996, Pueschel et al 1999, Csizmadia et al 2000). Antigliadin antibodies (AGA) are present in over 50% of children with Down's syndrome (George et al 1995) so this is not a useful test for screening this population. Screening for antiendomysial antibodies (AEA) is reported to have 90% sensitivity and 98% specificity (Burgin-Wolff et al 1991). As with thyroid function tests fingerprick blood samples collected on filter paper can be used for screening. Russell and Gillett (2000) have suggested that this should take place alongside established thyroid screening programmes. The evidence base for this is not yet established.

AEA testing is relatively costly and is likely to be replaced for first line screening by the antitissue transglutaminase test (TGA) which is reported to have 90% sensitivity and 96% specificity (Fabiani and Catassi) and can be automated. Also, in the interests of cost effectiveness, various two stage screening programmes are being evaluated (Catassi et al.1994. Hill et al 2001. Sulkanen et al 1998). A cost sparing 2 step screening strategy based on HLA-DQ typing as a first stage screen has been suggested for those with Down's syndrome (Csizmadia et al 2000). Once in a lifetime screening is not enough (Csizmadia et al 2000. Holmes 2001). Definitive diagnosis remains the identification of villous atrophy on small intestinal biopsy.

Recommendations

Within the UK some blood screening programmes are running on an experimental basis. Currently DSMIG does not recommend universal screening but advises that whilst we await further information from these studies it is essential to have a low threshold of suspicion for the presence of coeliac disease or other manifestations of gluten sensitivity in those with Down's syndrome. **We recommend that all with the syndrome should be clinically screened by history and examination on a regular basis for features that would prompt a blood test to check for antiendomysial and/or antitissue transglutaminase antibody status.** These are:

- Disordered bowel function tending to diarrhoea or to new onset constipation
- Failure to thrive as indicated using Down's syndrome specific reference charts (Harlow Printing 2000);
- Abdominal distension
- General unhappiness and misery
- Arthritis
- Rash suggesting dermatitis herpetiformis
- In addition it is probably prudent to test all those with existing thyroid disease, diabetes (Holmes 2001) or anaemia. Once in a lifetime testing is not sufficient. All require regular surveillance as coeliac disease can develop at any time.

Those with antibodies should be referred to a paediatric or adult gastroenterologist for ongoing investigation and treatment as necessary. Apparent lack of gastrointestinal symptoms does not preclude the need for further investigation. Major improvements in well being for those previously considered 'well' may ensue in response to a gluten free diet. Those with positive serology but with normal villous structure should be kept under regular surveillance for life as villous atrophy may subsequently develop.

Some people, despite negative antibodies, nevertheless have coeliac disease. Hence a person who tests negative on screening but has significant symptoms should still be referred for a specialist opinion for consideration of small intestinal biopsy. If sub total villous atrophy is present and there is a response to a gluten free diet the diagnosis is confirmed. If the person is more than 2 years old when the diagnosis is established the condition will be lifelong. Those diagnosed before age 2 years may have other conditions which mimic coeliac disease and therefore should be rechecked with further gluten challenge before school entry.

It should never be assumed that because a person has Down's syndrome investigation for the presence of coeliac disease is unnecessary. Quality of life can be much improved on a gluten free diet. Nor should it be assumed that compliance with a gluten free diet would be impossible. On the contrary there is anecdotal evidence that because of the generally higher level of supervision compliance may be more readily achieved than in the general population. The increasing identification of milder forms of the condition has led to a vastly increased range of palatable gluten free products being available in general foodstores as well as from pharmacies and mail order outlets. Regular dietetic review is desirable. The Coeliac Society (coeliac.co.uk) also provides useful information. If carefully taught with regard to compliance issues most of those with Down's syndrome will tackle the necessary dietary restrictions in a responsible manner.

References:

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Zubillaga P, Vitoria, JC (1993) *Down's syndrome and coeliac disease*. J Ped Gastroenterology and Nutrition. **16** 168-171

See also:

Coeliac Disease. Fast Facts. By Geoffrey Holmes and Carlo Catassi. Health Press Limited (2000) ISBN 1-899541-23-3 <http://www.fastfactbooks.com/>

Information and research needs:

If you have information which might be useful to DSMIG about existing or planned screening programmes for the identification of coeliac disease in people with Down's syndrome within the UK or Republic of Ireland please let us know. If you are planning research in this area we may be able to help with advice re methodology, subject recruitment etc.

For either of the above contact jendennis@dsmig.org.uk

Other enquiries to:

Down's Syndrome Medical Information Services

Children's Centre, City Hospital Campus, Nottingham NG5 1PB. UK

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