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Gastrointestinal disorders in people with Down's syndrome: an overview

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There is an increased incidence of gastrointestinal problems among people with Down's syndrome. It is therefore important to be aware of the conditions involved, and of their presenting symptoms and management.

Gastrointestinal conditions associated with Down's syndrome can be roughly grouped into three problem areas (Panel 1).

Panel 1: Gastrointestinal conditions associated with Down's syndrome

- Embryological and structural
 - Anorectal (imperforate or stenosis)
 - Duodenal or jejunal (atresia or stenosis)
 - Hirschprung's disease
- Motility and co-ordination
 - Feeding difficulties
 - Constipation
 - Toddler diarrhoea
 - Gastro-oesophageal reflux (GOR)
 - Gall stones
- Autoimmune
 - Coeliac disease
 - Hepatitis

Embryological and structural problems

There is an incidence of about 10% of anorectal and duodenal atresia or stenosis and around 2% incidence of Hirschprung's disease in children with Down's syndrome. These figures are much higher than for other children. It is therefore very important to be active about diagnosis so that these conditions are recognised early and thereby better treatment can be achieved.

Duodenal and jejunal atresias and stenoses

The duodenal and jejunal atresias and stenoses tend to present with bile-stained vomiting indicating obstruction

until proved otherwise. Other presenting symptoms are regurgitation, diarrhoea and/or abdominal pain. These children usually do extremely well following surgery.

Hirschprung's disease

Hirschprung's disease is due to failure of migration of the ganglion cells to the submucosal and myenteric plexuses of the large bowel. The affected segment can vary in length from very short to much longer. It is important to remember that the affected area has a risk of stasis, infection, enterocolitis and perforation. This is one reason why early diagnosis is important.

Essential surveillance for all newborns with Down's syndrome should therefore include:

- An examination for imperforate anus in the delivery room in order to ensure that this has been excluded.
- Active observation of when meconium is first passed.
- Consideration of Hirschprung's disease following late passage (more than 24 hours) of meconium in a child with Down's syndrome.

Although Hirschprung's disease is usually considered to present very early, around 50% of those with Down's syndrome will present after one month of age. Presenting features include constipation in the first few months or constipation with failure to thrive in the first year.

Diagnosis involves suction rectal biopsy which can be carried out on the ward. However, this has to be done in conjunction with the laboratory as they will need to prearrange some tests. If the diagnosis is confirmed, management usually consists of a defunctioning colostomy to remove the cause of obstruction followed by resection of the abnormal aganglionic segment and pull through of the normal bowel to the anus. It is important to remember that even after surgery, children with Hirschprung's disease have a risk of enterocolitis which may be signalled by blood in the stools.



The outcome in Hirschprung's disease is problematic even in children who do not have Down's syndrome. Complications include the necessity for stomas where pull through has not worked, an ongoing risk of enterocolitis and difficulties with toilet training. The prognosis for continence in those with Down's syndrome is poor.

Hirschprung's disease

- Around 2% incidence in children with Down's syndrome
- 50% present after age 1 month
- Early diagnosis is important
- Careful early neonatal surveillance is required
- There is a risk of enterocolitis both before and after surgery
- Surgical outcome is variable
- Prognosis for continence is poor

Motility and co-ordination problems

Constipation

Constipation can be a major problem for people with Down's syndrome and appears to be very common in children. Mobility may be an issue here as mothers often say that when the baby started to move around the constipation problem eased. It is always worthwhile excluding hypothyroidism before moving on to treatment regimens.

Many children are prescribed lactulose for constipation, usually 5 ml twice a day. One problem is that parents are not given an endpoint – such as a soft daily stool – to work towards or advice about increasing medicines stepwise until that endpoint is achieved. An information chart about target stool consistency has been developed by Dr KW Heaton in Bristol, UK for people with irritable bowel syndrome and this is also very useful for those with constipation. The chart is illustrated and provided free by Movicol™ (iso-osmotic laxative, Norgine, Harefield, UK) representatives. Healthcare professionals should aim towards providing information of this sort, including leaflets, for parents. Two very useful publications are:

Constipation

- Worse before self-mobile
- Exclude hypothyroidism
- Clear endpoints (e.g. soft daily stool) necessary for treatment regimens
- Stepwise increase of laxative may be needed to achieve target endpoint
- Parent information leaflets are useful

- *Childhood Soiling: a guide for parents* – which includes a particularly useful section concerning the child who will only go to the toilet with their nappy on.
- *Helping children with constipation* – a very good publication with straightforward language and wording. One in a series of *Treatment Notes*, produced by the Consumers' Association for patients based on matching information from the *Drug and Therapeutics Bulletin*.

For further information on these publications, see *Further reading*.

Toddler diarrhoea

Toddler diarrhoea is a common problem which presents with a thriving child with undigested vegetable matter. It can be quite difficult to exclude constipation in this group hence a good history and an abdominal examination are necessary.

Wherever possible, dieticians should be involved in management of these children. Excessive intake of fruit juice is often causative and may be a particular problem in Down's syndrome as fruit juice may have been given in an attempt to overcome constipation. If decreasing the intake of fruit juice fails, lowering the amount of roughage in the diet may be helpful. Alternatively, Calogen® (long chain triglyceride dietary supplement, SHS International Ltd, Liverpool, UK) has been demonstrated to reduce the amount of stooling in a significant number of children. Calogen® is available from hospital supplies and is quite palatable.

A key factor as far as parents are concerned is to be reassured that there is no underlying medical problem. That may be sufficient to avoid any intervention but as toilet training is often affected, a small amount of intervention may be enough to help relieve the problem.

Toddler diarrhoea

- Exclude constipation
- Reassure parents
- Involve dietician
- Reduce or exclude fruit juices
- Reduce roughage in diet
- Calogen® may help

Gastro-oesophageal reflux (GOR)

Children with GOR exhibit milk vomiting, even though they are often well and thriving. However they should be watched carefully for signs of complications and the development of gastro-oesophageal reflux disease (GORD) (blood in the vomit and failure to thrive).

Although it is not a major contributory cause, the mental state of the mother it is always worth consider-

ing as GOR often occurs when a mother is depressed. It is possible that the mother's mental state leads her to over-interpret the symptoms. It is also important to take a very careful history as some parents who complain about reflux and vomiting are not experiencing the amount of vomiting that others accept as being completely normal.

If the child is well and there is no evidence of GORD, the aim should be to avoid intervention as this is often the most reassuring course of action for parents. If the problem is socially unacceptable, thickeners such as Carobel Instant (Cow & Gate, Nutricia, Trowbridge, UK) and Enfamil AR® (Mead Johnson Nutritionals, Bristol Myers Squibb, Hounslow, UK) may be useful. As Enfamil AR® has a thin consistency in the bottle but a thicker consistency in the stomach, it is particularly useful in bottle-fed infants.

If there are signs and symptoms of acute GORD, further investigation is needed and the condition should not be treated pragmatically.

Gastro-oesophageal reflux (GOR)

- If there is no evidence of GORD, try to avoid intervention
- Consider mother's mental state
- Milk thickeners may help
- If GORD is suspected, further investigation is essential

Gall stones and abdominal pain

Gall stones are an uncommon, but increasing, finding in children with Down's syndrome and tend to be discovered by chance during radiological examination. Current advice is that if they are asymptomatic surgery is not indicated.

Autoimmune problems

Coeliac disease

Coeliac disease can present with diarrhoea, failure to thrive, general misery, abdominal distension and iron deficiency anaemia. Given this symptomatology, it is always advisable to exclude giardiasis.

Coeliac disease

- Universal screening not recommended
- Yearly clinical review of features that suggest coeliac disease (Panel 3)
- Exclude giardiasis
- Lifelong condition if diagnosed after age 2 years
- Treat with gluten-free diet as for all children

In the general population, the peak incidence of coeliac disease has been taken to be around eight years old, followed by a drop off at around age 10 and another increase in incidence in early adulthood. However, as there currently appear to be more people in the general population who present with the disorder later in life, the early adult peak is not so apparent. Also, increasing numbers are being diagnosed with lesser gastrointestinal and other symptoms but without florid signs of the disorder. Symptoms and general well-being are regularly improved by a gluten-free diet.

In the UK, there is probably around a 1–2% risk of coeliac disease in Down's syndrome and the figures are higher in some other countries. In individuals with Down's syndrome, as in the general population, the condition is lifelong if diagnosed after 2 years of age. Under 2 years of age, a transient enteropathy can mimic the disorder.

Screening for coeliac disease

Panel 2 lists serum markers currently used when screening for coeliac disease. It is important to remember that these are only screening tests and to make a diagnosis there should be increasing changes in the small intestine and a response to a gluten-free diet. Furthermore, if tests are negative but symptoms are present, a biopsy should always be considered.

Panel 2: Markers for coeliac disease

Gliadin antibodies – IgG and IgA. Many children have a late switch on of IgA; therefore in children below age ten, the IgG gliadin antibody must be checked.

Endomysial antibodies (EMA) – the most sensitive and specific test, with 95% of those with coeliac disease testing positive. Screening of symptomatic populations picks up only about 5% who do not have coeliac disease.

Tissue transglutaminase antibody – a relatively new test which is ELISA-based and less expensive than EMA. This will almost certainly replace EMA in the next few years.

Although antibody screening tests have undoubtedly identified children whose general well-being can be improved once the condition is recognised, whole population screening of individuals with Down's syndrome for coeliac disease is probably not warranted. A more useful approach is to make careful enquiry on a regular basis regarding symptoms and signs and to screen only those with possible symptoms. It is important to remember that symptoms may be relatively mild and not neces-

sarily brought to the attention of the doctor, and therefore specific enquiry is always needed. Panel 3 lists symptoms and signs which may merit coeliac screening.

Panel 3: Symptoms and signs which merit screening for coeliac disease

- Failure to thrive
- Chronic anaemia
- Existing thyroid disease or diabetes
- Diarrhoea or other GI disturbance
- Abdominal distension
- General misery/lethargy

Diagnosis

Diagnosis involves identifying positive markers such as increasing changes in the small intestine (Figure 1) and a response to a gluten-free diet. Under two years of age, transient enteropathy is a possibility and therefore these children need to be rechallenged and a biopsy taken around age five to confirm the diagnosis of coeliac disease.

Autoimmune hepatitis

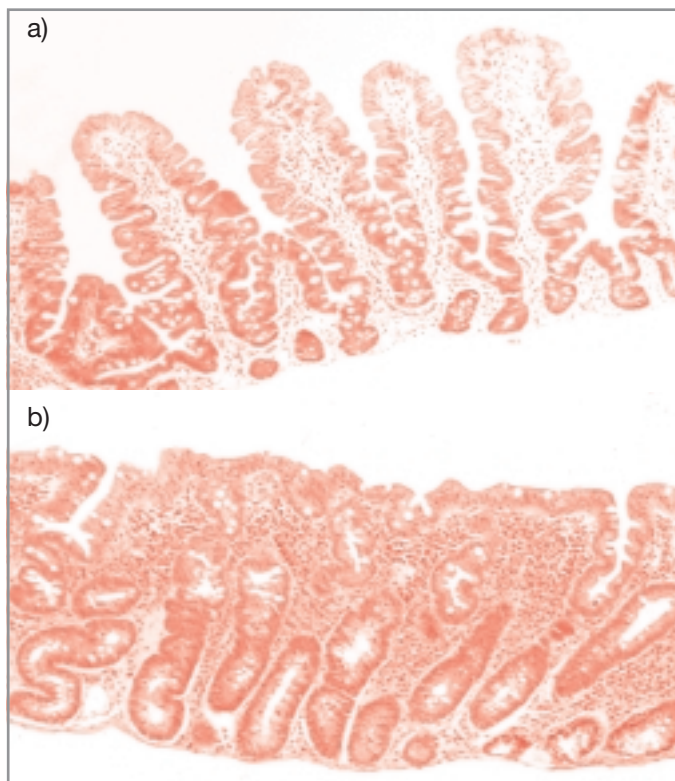


Figure 1: Biopsies from a) healthy patient demonstrating large villous height-to-crypt depth and a normal number of intraepithelial lymphocytes, and b) a patient with coeliac disease, showing total villous atrophy with a completely flat surface, very fine crypts and a very heavy infiltrate. Comparing the two biopsies, b) is dense with inflammatory cells. Figure reproduced from *Fast Facts – Coeliac Disease (2000)*, by G Holmes and C Catassi, with the permission of Health Press Ltd, Oxford.

Autoimmune hepatitis is a rare but recognised disorder which probably occurs more frequently among those with Down's syndrome. It may present with jaundice, but as this can also indicate hypothyroidism and gall stones these conditions must be excluded from diagnosis. Autoimmune hepatitis may present with general malaise and aches or a more definite arthropathy. Liver enzymes may not be dramatically elevated even in the presence of quite active hepatitis. Chronic ongoing hepatitis can also be due to hepatitis B infection, which is also over-represented in those with Down's syndrome.

Summary

The following gastrointestinal disorders occur more frequently in those with Down's syndrome:

- Structural/embryological conditions, such as atresias and Hirschprung's disease
- Motility and co-ordination disorders such as constipation, gastro-oesophageal reflux and feeding problems
- Autoimmune conditions, including coeliac disease and autoimmune hepatitis.

It is important to be active about diagnosing these conditions in order that they are recognised early and thereby better management can be achieved.

Further reading

Consumers' Association. *Helping children with constipation*

<http://omni.ac.uk/whatsnew/detail/1101236.html>

Dobson P. *Childhood Soiling: A Guide for Parents*. 1998 The Enuresis Resource & Information Centre (ERIC). <http://www.enuresis.org.uk/shop.html>

Heaton K. *The Bristol stool form scale*. In: *Understanding your Bowels*. 1999 Family Doctor Publications in association with the British Medical Association. ISBN 1-898205-08-6.

Marder, EM. Gastrointestinal problems in children with Down's syndrome. Down's Syndrome Association newsletter 1996. <http://www.dsmig.org.uk/library/articles/gastro-article-marder.pdf>

Pueschel SM. Gastrointestinal concerns and nutritional issues in persons with Down's syndrome. *Down Syndrome Quarterly* 1999;4 (no 4):1–11.

Quinn FM, Surana R, Puri P. The influence of trisomy 21 on outcome in children with Hirschsprung's disease. *J Pediatr Surg* 1994; 29(6):781–3.

A complete transcript of this presentation, together with references, is available at www.dsmig.org.uk.