Hydrogen breath testing in children: What is it and why is it performed?

Abstract

Hydrogen breath testing (HBT) is a non-invasive, sensitive and specific means of diagnosing small bowel sugar malabsorption. They make use of gut bacteria’s ability to digest sugars and convert these to hydrogen, which is then absorbed in the blood and can be measure in exhaled breath. This article explores the use of the HBT in children. It looks at how the test works, and why and how it is used in children. The significance of correct preparation, performing the procedure, as well the importance of expert interpretation of the results are discussed. Finally, the varying conditions detected by the test are addressed together with their treatment.

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The hydrogen breath test (HBT) is a simple, non-invasive and reproducible test used to assess the activity of hydrogen-fermenting bacteria in the gut. The test is commonly used in children to diagnose malabsorption of the sugars lactose, fructose and sucrose. It is also used to investigate small intestinal bacterial overgrowth (SBBO) (Eisenmann et al, 2008). While the test is regarded as the gold standard for diagnosing certain conditions, i.e. fructose malabsorption and intolerance (Eisenmann et al, 2008), there is much debate around how it is carried out. Recent literature emphasises the need for care during the testing procedure and when interpreting the test results (Simrén and Stotzer, 2006).

It is, therefore, important that paediatric nurses carrying out HBTs are aware of the physiological principles of the investigation, as well as the importance of the correct preparation and protocol for the procedure (Romagnuolo et al, 2002). Appropriate training is required for the interpretation of results.

Key words
- Hydrogen breath test
- Lactose intolerance
- Paediatric gastroenterology
- Small bowel bacterial overgrowth

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Background

A HBT is based on the principle that in humans, anaerobic bacteria in the colon are able to digest sugars and carbohydrates and convert some of them into gases, most commonly hydrogen. Although a minimal amount of hydrogen is produced from the small amounts of unabsorbed food that normally reaches the colon, if a child does not digest and absorb sugar or carbohydrate completely, it travels through the small intestine and enters the colon where bacteria digest it, producing significant amounts of hydrogen. Some of this hydrogen gas is absorbed by the colon into the blood and is released and exhaled in the breath where it can be measured.

As hydrogen is only generated during anaerobic metabolism, if a child has fasted and is at rest, the hydrogen excreted with the exhaled air must originate from anaerobic bacteria (Levitt, 1969). If there is no malabsorption, sugars or carbohydrates should all be digested in the small intestine, leading to no rise in breath hydrogen. Other undigested food is exposed to intestinal bacteria and subsequent bacterial fermentation but produces no hydrogen (Hamilton, 1998).

The time at which the hydrogen concentration rises during a breath test gives an idea of the part of the intestines where fermentation took place (Lee et al, 2000). Hydrogen produced in the colon, and exhaled, does so in proportion to the amount of carbohydrate metabolized by bacteria in the colon (Burge et al, 2000).
Evidence suggests that portable devices, such as the Gastrolyzer™ (Bedfont, Rochester), can measure exhaled hydrogen accurately (Peukuni et al, 1998; Lee et al, 2000).

**False-negative breath tests**

Some children are colonized with more methane than hydrogen-producing bacteria in their intestine and these children exhalate mainly methane instead of hydrogen (Urata et al, 2006). This can result in a false-negative test, as these children will usually have readings of 0 ppm throughout the test. If low readings (<5 ppm) are accompanied by symptoms throughout the test, a false-negative reading should be considered, and a lactulose test may be carried out to confirm the lack of hydrogen production (Eisenmann et al, 2008).


**Preparing the child or adolescent**

Thorough preparation for HBTs is necessary to ensure accurate results (Romagnuolo et al, 2002), and to minimize anxiety in the child and family. Referral for a HBT should preferably be made by a paediatric gastroenterologist or someone with specialist training, as gastroenterologists are more selective in requesting HBTs (Ding-You et al, 2004). The nurse carrying out the procedure will need information regarding the reason for the breath test, the patient’s history (including other diseases, allergies and medication) and the urgency of the test. The nurse will then contact the child and family to explain the test and arrange a convenient morning for it. Mornings are preferable for children to avoid long fasting times before a test. A patient information sheet with specific instructions is helpful if given to familes in advance of the procedure. They can then contact the team with any questions they may have.

- The advice sheet should contain information on fasting times: children who are over 1 years old should fast for 12 hours and infants below 1 year of age should fast for 6 hours; only plain water can be drunk during this time. The last meal on the day prior to the test should not be too large, ideally be low in fibre and should not contain the substance being tested for (Eisenmann et al, 2008).

Older children should be made aware that they should not smoke for 12 hours prior to the test, as this raises hydrogen concentrations (Thompson et al, 1985). Vitamins, laxatives and antibiotics should not be taken on the day of the test. All laxatives, in particular lactulose, should be avoided for 3 days prior to the test as these can alter transit times (Romagnuolo et al, 2002). The child should not have had antibiotics in the last 4 weeks as these can alter gut microbiota for up to 4 weeks and hence affect the test result (Solomons et al, 1979; Romagnuolo et al, 2002). Anti-reflux and proton pump inhibitors should not be given for 7 days prior to the procedure. If the child has had a colonoscopy in the last 4 weeks, the intestinal flora needs time to recover following bowel preparation (Eisenmann et al, 2008). All other medications can be taken with pure water on the day of the examination.

**The procedure on the day of the test**

Prior to undertaking the test, the child and their family should be introduced to the staff on the ward: the paediatric gastroenterology nurse (or equivalent) and the play therapist (if available). The nurse will explain why the test is being performed, what the procedure involves and answer any questions before obtaining consent for the procedure. The child is able to give consent if they are ‘Gillick competent’ or over 16 years of age. It is important to confirm that the child is well and has followed the patient information sheet correctly. It is also important to check that they have brushed their teeth well, to minimize contamination by oral hydrogen-producing bacteria.

The staff then explain to the child how they would like them to blow into the tube of the device, using age-appropriate language and pictures, teddies and reward stickers as appropriate. If the child is too young to blow into the tube, a facemask and sampling system can be used instead. There are child-friendly, portable handheld devices available, such as the Gastrolyzer™, which enable end-expired breath to be sampled simply and hygienically, using a single disposable mouthpiece. Children are given the opportunity...
If the nurse has any concerns about a more serious reaction during the test, they should stop the test and contact medical staff.

Safety

Although the HBT is considered a safe test, it is contraindicated in children with known or suspected hereditary fructose intolerance (HFI). The clinical symptoms of HFI and fructose malabsorption can be very similar, but particular care needs to be taken as a single dose of fructose can cause the serious symptoms of hypoglycaemic shock, i.e. pallor, poor skin perfusion, sweating, nausea and vomiting, tachycardia, tremors and confusion, reduced conscious levels and convulsions (Müller et al, 2003). It is also important to be aware of other existing conditions which can cause hypoglycaemia (for example, diabetes mellitus).

Although other complications are rare, appropriate emergency medications should be stocked (for example, antihistamines and cortisone) (Eisenmann et al, 2008). If the nurse has any concerns about a more serious reaction during the test, they should stop the test and contact medical staff.

The test begins

To ensure that the child has fasted correctly and has no contaminating oral bacteria, the child’s teeth must be cleaned and a baseline H₂ measurement is performed. Before the measuring can take place, the patient should sit down for at least 1 minute as hyperventilation may distort the readings. Exercise lowers hydrogen concentrations and is therefore not allowed during the test (Thompson et al, 1985). If the child has no more than 10 ppm (preferably <5 ppm) of H₂ in their expiratory breath, the test can begin. The procedure of exhaling should be carried out in accordance with the manufacturer’s instructions.

The child should hold their breath for 15 seconds and then exhale slowly and fully for as long as possible while sealing their lips around the mouthpiece. Alternately, in the younger child, the facemask is placed gently but firmly over the mouth and nose, avoiding any leaks, and kept in position until the connector steams up with expired breath. As hydrogen is distributed differently depending on the body position, the child should ideally adopt the same position throughout the test (Kagaya et al, 1998).

Dosages in children

The child should then drink the predetermined dose of carbohydrate. According to Eisenmann et al (2008), the following are recommended dosages:

- Glucose load test: 50 g glucose dissolved in 250 ml water. This test is generally not carried out on children. However, 2 g/kg body weight (BW) up to a maximum of 50 g dissolved in 10 ml/kg BW up to a maximum of 250 ml would be possible.

- Fructose tolerance test: 25 g fructose in 250 ml water. In children: 1 g/kg BW up to a maximum of 25 g fructose dissolved in 10 ml water/kg BW up to a maximum of 250 ml liquid. Importantly, the best dosage of fructose to use to diagnose clinically meaningful malabsorption in children is unclear (Simren and Stotzer, 2006; Anania et al, 2008).

- Lactose tolerance test: 50 g lactose in 250 ml water. In children, paediatric studies have included doses ranging 0.5–2.0 g/kg at 10% or 20% concentrations (Forget et al, 1985; Tadesse et al, 1992). Eisenmann et al (2008) recommends 2 g/kg BW in 10 ml/kg BW up to a maximum of 50 g in 250 ml. However, a dose of 1 g lactose/kg (maximum 25 g) at 10% concentration is recommended (Tadesse et al, 1992).

After taking the test substance, the child’s teeth must be cleaned once more. The child then produces breath samples by blowing into the hand-held monitor at predetermined time intervals. Generally, after measuring the basal fasting value (0 minutes), the amount of H₂ in the exhaled air is initially measured at 15 minutes and then at 30-minute intervals over the course of at least 2–3 hours. This means that H₂ readings are taken at 0, 15, 30, 60, 90 and 120 minutes. The test is usually considered positive if concentrations of greater than 20 ppm of hydrogen above the basal reading are displayed (Eisenmann et al, 2008).

The significance of H₂ levels – in particular the exact timing, dosage and concentration of the test substance – are controversial, as evidence-based standards are lacking and still
debated in the literature (Romagnuolo et al, 2002, Simren and Stotzer, 2006; Eisenmann et al, 2008). If a slow transit time and delayed rise are suspected, additional readings should be taken after 150 and 180 minutes respectively.

Once all the samples have been collected, the child will be allowed to eat and drink. If they are well, they will be able to go home and resume normal activities. The child and family are given instructions and contact information should they have any concerns, and details of the follow up and management plan.

Documentation

Exact documentation of the procedure and accompanying symptoms are important, as apart from recording measured H2 levels, it is important to note any symptoms at each time point (Eisenmann et al, 2008). Symptoms can include bloating, hyperperistalsis, diarrhoea, abdominal pain and dizziness. Any unusual symptoms should also be recorded (Eisenmann et al, 2008).

Results

The results should be discussed with the referring paediatrician if appropriate. It may be possible to act on the results of the test immediately and arrange for dietetic advice if there is a clear management plan in place already. The interpretation of HBT results is based on the hydrogen exhalation level, the appearance of symptoms and the timing of these two factors during the test (Eisenmann et al, 2008). If there is no malabsorption of the test substance, i.e. readings vary by less than 5 ppm above or below the basal value, and there are no symptoms, the test is negative. If the child has clinical symptoms but no increase in H2 levels, a lack of H2 production or slow transit time should be considered.

In general, an increase in hydrogen concentrations of more than 20 ppm above the basal value is considered to be a positive test result. A significant H2 increase and the appearance of symptoms, both occurring at about 60 minutes after starting the test, are diagnosed as an intestinal intolerance of the test substance.

Eisenmann et al (2008) have recently produced guidance on interpreting findings based on a total of 3374 patients in Austria who had breath tests to investigate functional intestinal symptoms.

Conditions diagnosed by a HBT

Fructose malabsorption and intolerance

The fructose HBT is a simple and sensitive method for diagnosing fructose malabsorption and intestinal fructose intolerance with sensitivity and specificity (98% and 86% respectively) (Gotze and Mahdi, 1993). Fructose is found in fruits, milk products containing saccharin, sweets and honey (Rumessen, 1992).

Fructose intolerance can result in abdominal pain, bloating, cramps, vomiting, malabsorption and hypoglycaemia (Walker et al, 1996). Infants and children in the developed world often consume large volumes of apple and pear juice, which contain a high fructose-to-glucose ratio. Consumption of these juices can result in fructose malabsorption and diarrhoea. A recent study concluded that fructose malabsorption may be a significant problem in children and that the management of dietary intake can be effective in reducing gastrointestinal symptoms (Gomara et al, 2008). Another study, using the HBT to measure fructose absorption in healthy children, found that the dose of fructose given caused significant differences in peak breath hydrogen excretions, and showed that the percentage of children incompletely absorbing fructose were significantly higher in children aged 1–3 years (Hoekstra et al, 1993).

If the HBT result is positive, the child is usually referred to a dietitian who will take a clinical history. The dietitian will often request that the family fill in a food-and-symptom diary before and after a fructose-free diet. This is done to determine what level of fructose is tolerated. In many cases, removing fruit juice from the diet is enough to alleviate symptoms; however, in more severe cases, dietary exclusion of fructose, sucrose (contains fructose and glucose) and sorbitol is necessary (Mahan and Escott-Stump, 2000). Asymptomatic fructose malabsorption (positive test result but no appearance of symptoms) does not require dietary intervention. The absorptive capacity for fructose varies between individuals, with a high number of healthy individuals demonstrating incomplete absorption of a 10% solution of 50g fructose (Truswell et al, 1988).
"In primary lactose intolerance, symptoms will usually resolve with avoidance of milk and other dairy products."

**Lactose intolerance**

The HBT is currently regarded as the most cost-effective and reliable way to diagnose malabsorption of lactose (Shaw and Davies, 1999; Di Camillo et al, 2006). Lactose intolerance is the inability to metabolize lactose (a sugar found in dairy products) because of a lack of lactase which is found exclusively in mammalian milk. Lactose is broken down into glucose and galactose. Symptoms of lactose intolerance include abdominal distension, mid abdominal pain, diarrhoea, flatulence and/or bloating following the ingestion of lactose or lactose-containing food (Heyman, 2006). There are three major types of lactose intolerance: primary, secondary and congenital lactase deficiency (Heyman, 2006).

Primary lactase deficiency is the most common cause of lactose malabsorption and intolerance; it develops at different times in life, and this varies among different racial groups and populations (Ennath et al, 2002). It is more common in Asian and African cultures, where industrialized and commercial dairy products are less common (Bulhès et al, 2007). In Caucasians, it usually starts to affect children aged over 5 years.

Secondary lactase deficiency can occur as a result of intestinal disease or, particularly in children, as a result of a temporary lactase deficiency resulting from viral or bacterial intestinal infections (Swagerty et al, 2002).

Congenital lactase deficiency is an extremely rare genetic disorder which prevents enzymatic production of lactase and is described in ethnic groups in Northern Finland. It is present at birth, and diagnosed in early infancy.

Developmental (neonatal) lactase deficiency is sometimes seen in premature babies as lactase is deficient until at least 34 weeks' gestation (Antonowicz and Lebenthal, 1977).

When lactose intolerance is suspected in children, there are several ways of making a diagnosis (Heyman, 2006). For example, following a 2-week trial of a strict lactose-free diet symptoms resolve and then recur when dairy foods are reintroduced, a diagnosis of lactose intolerance is probable.

The HBT is currently considered to be the most inexpensive, reliable and least invasive method of diagnosing subtle cases of lactose malabsorption. The test has been shown to be more reliable than a patient history because reporting of symptoms vary among patients (Suarez et al, 1995). If there are gastrointestinal symptoms during the test, they should be recorded to enable an evaluation of subjective lactose intolerance. Reported symptoms of lactose malabsorption vary greatly (Suarez et al, 1995; Vesa et al, 1998). Studies using lactose HBT showed lactose malabsorption in up to 40% of children and adolescents presenting with abdominal pain (Barr et al, 1979; Gremsie et al, 2003). Recent studies using the HBT in children found the prevalence of abdominal symptoms related to lactose intolerance ranged from 2% in Finnish children to 24% in southern US children (Webster et al, 1999; Kokkonen et al, 2004).

It is now possible to distinguish secondary lactose intolerance from primary lactose intolerance with the use of a complementary molecular genetic test (Kerber et al, 2007). Blood glucose level measurement has now been superseded by breath testing in children as it requires a cannula, frequent blood withdrawals and the results of the HBT are superior (Douwe et al, 1985). Other tests available to aid in the diagnosis of lactose intolerance include the lactose tolerance test (rarely used), intestinal biopsy to measure intestinal disaccharidase levels (invasive), faecal pH and reducing substance testing (Di Stefano et al, 2004).

**Treatment of lactose intolerance**

In primary lactose intolerance, symptoms will usually resolve with avoidance of milk and other dairy products (Heyman, 2006). However, because the amount of lactose each child can tolerate is variable, the extent to which each child responds to dietary restriction varies, and will depend on the amount of lactose consumed and the degree of lactase deficiency (Pribila et al, 2000; Jarvinen et al, 2003). Lactose-intolerant children and their families should be aware that the symptoms resulting from the ingestion of dairy products are generally transient and are unlikely to harm the gastrointestinal tract (Heyman, 2006).

If dairy products are completely removed from the child’s diet, alternative sources of calcium or calcium supplements need to be provided. Children who avoid milk have been found to ingest less-than-recommended amounts of calcium needed.

Enzyme replacement with oral lactase-replacement capsules, or dairy products containing lactase, allow a lactose-intolerant child to take at least some milk products freely (Boutroua et al, 2001).

The treatment of secondary lactase deficiency and malabsorption usually requires treatment of the underlying condition, thereafter lactose-containing products can often be reintroduced (Heyman, 2006).

Small bowel bacterial overgrowth (SBBO)

SBBO is considered in a child with chronic diarrhoea, weight loss, steatorrhoea, and macrocytic anaemia. Conditions leading to SBBO include impaired gastrointestinal motility (e.g. chronic pseudo-obstruction, post-surgical adhesions). Symptoms can also include abdominal pain, flatulence and malabsorption of nutrients and some vitamins (Elphick et al, 2005; Dukowicz et al, 2007).

The final section of the small intestine (terminal ileum) usually only has a small number of anaerobic bacteria in it (Zaire and Lin, 2003). If children have abnormally large numbers of hydrogen-producing anaerobic bacteria in the small intestine, this condition is known as SBBO. If food and nutrients move slowly through the small bowel and are not absorbed properly, it can result in an increase in the amount of bacteria in the terminal ileum (Dukowicz et al, 2007; Posserud et al, 2007).

The number of bacteria is greater in the terminal ileum than in the proximal small bowel, as the ileocaecal valve slows transit and bacteria can move into the small intestine from the colon. Any unabsorbed sugars and carbohydrates that reach the bacteria in the lower small bowel or colon produce large amounts of hydrogen. When the breath test is performed to diagnose SBBO, the hydrogen concentration usually peaks twice. Initially there is an early peak within 1 hour of ingestion as the sugar meets bacteria in the small intestine and then later when unabsorbed sugar enters the colon.

The lactulose test

HBTs using lactulose (a sugar not absorbed in the small intestine) is the most widely used non-invasive test for diagnosing SBBO and altered transit times (Kerlin and Wong, 1988).

Lactulose is a synthetic disaccharide consisting of fructose and galactose. It is not absorbed in humans and is, therefore, always fermented or excreted (Hamilton, 1998). If there are excess bacteria present in the small intestine, this results in a rise in exhaled breath hydrogen earlier than would be expected if bacteria are confined only to the colon (Posserud et al, 2007).

Another method of testing for SBBO is to culture jejunal aspirate to detect the presence of bacteria. The diagnosis is made if jejunal intestinal contents reveal more than 105 bacterial population (Dukowicz et al, 2007; Posserud et al, 2007). Breath tests, as an indirect test to identify bacterial overgrowth, are considered slightly less sensitive than jejunal aspiration (Elphick et al, 2005; Posserud et al, 2007); however, the latter is more invasive and hence rarely used alone in children. A recent study comparing the breath test vs SBBO with jejunal aspirate cultures in children provided experimental support for the use of lactulose in the HBT and validated it as a screening test in the diagnosis of small intestinal bacterial overgrowth in children (Mendoza et al, 2007). Care should be taken though when interpreting results of the lactulose HBT, as a delayed peak seen in distal SBBO is difficult to differentiate from the normal peak of the substrate reaching the colon. Patients with rapid transit, e.g. due to short gut syndrome, can also have a false positive result (Cole and Ziegler, 2007).

Treatment of SBBO

Bacterial overgrowth is treated by correction of the underlying small intestinal abnormalities (i.e. surgery to correct underlying disease or use of prokinetics) and the use of appropriate antibiotics (Lauritano et al, 2005). Antibiotics used include oral gentamicin, metronidazole or any other suitable broad-spectrum antibiotic with anaerobic coverage (Quigley and Quera, 2006). Most patients respond well to appropriate antibiotic therapy (Lauritano et al, 2005); however, if symptoms do not disappear following treatment with antibiotics, it may be useful to repeat the breath test. Prophylactic antibiotic therapy may need to be cyclical. It is occasionally necessary to correct nutritional deficiencies, and probiotics can be beneficial.
Transit time
If children have abnormally rapid passage of food through the small intestine due to hypermotility, there may not be enough time for the small intestine to digest and absorb sugars. This results in large amounts of sugar and carbohydrate entering the colon where bacterial fermentation converts them to gas. Hydrogen is therefore found in the breath very soon after ingestion of the sugar. If there is a complete absence of a rise in hydrogen concentration, this could be due to excessively slow intestinal transit time (greater than the 3 hours of testing), as normal small intestinal transit time is approximately 90–120 minutes (Lindberg, 2009).

Conclusion
Hydrogen breath tests are a simple and safe tool used to investigate the cause of often non-specific but troubling gastrointestinal symptoms in children. When used and interpreted properly, they provide a cost-effective way of diagnosing these conditions, which are relatively easy to treat, resulting in a better quality of life for the child and their family. Although alternative treatments are available, these are often impractical, invasive and time-consuming, particularly for children. When carried out by experienced nurses, the hydrogen breath test provides a safe and simple diagnostic tool, with a high sensitivity and specificity to diagnose sugar malabsorption.


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