Fructose and lactose testing

Jacqueline S Barrett
Peter R Gibson

This article forms part of our 'Tests and results' series for 2012, which aims to provide information about common tests that general practitioners order regularly. It considers areas such as indications, what to tell the patient, what the test can and cannot tell you, and interpretation of results.

Keywords
breath tests; malabsorption syndromes/diagnosis; fructose; lactose

Functional gut symptoms are a common problem in the community and many patients present to their general practitioner for assessment and guidance. While part of the GP's role is excluding other pathology, helping patients to manage their symptoms is also important.

Breath hydrogen testing can be used to detect malabsorption of fructose and lactose. These short-chain carbohydrates can cause symptoms of bloating, pain and altered bowel habit in patients with irritable bowel syndrome (IBS) and related functional gut disorders. Consideration of these and other poorly absorbed, short-chain carbohydrates (collectively termed 'FODMAPs') provides a management strategy for these common symptoms. Unfortunately fructose and lactose tests, and their use, are poorly understood – this article aims to explain how these tests work and clarifies the role of breath testing.

What is the theory behind fructose and lactose tests?

Restriction of poorly absorbed, fermentable short-chain carbohydrates can provide relief from the symptoms of IBS.[1] This dietary approach has been shown to improve symptoms in up to 75% of sufferers.[2] There is emerging evidence that these carbohydrates can trigger functional symptoms in patients with inflammatory bowel disease (IBD).[3] Fructose, lactose, sugar polyols (sorbitol and mannitol) and the oligosaccharides, fructans and galacto-oligosaccharides are potential triggers. Poor intestinal absorption of these carbohydrates cause gastrointestinal upset in IBS through their osmotic effect[4] and fermentation by intestinal microbiota.[5] This leads to luminal distension, resulting in abdominal bloating, pain and altered bowel habit in those with visceral hypersensitivity.

Oligosaccharides in wheat, rye, onion, garlic and legumes[6,7] are poorly absorbed in the human gastrointestinal tract.[8,9] These short-chains of fructose or galactose units remain linked – as there is no human enzyme to cleave the bonds – and are fermented with gas formation, causing wind in healthy people and symptoms in hypersensitive IBS sufferers.[10]

The other short-chain carbohydrates – fructose, lactose, sorbitol and mannitol – vary in their degree of absorption across individuals. These carbohydrates only need to be restricted if they are poorly absorbed.[11–13] Breath hydrogen testing is used to assess carbohydrate absorption, most commonly fructose and lactose, to identify which carbohydrates should be restricted to improve symptoms. Unfortunately, variations in breath testing protocols, dosage of test sugars and interpretation has led to confusion about the accuracy and relevance of these tests.

When should hydrogen breath tests be ordered?

Fructose or lactose breath hydrogen tests do not diagnose an illness or abnormality; malabsorption of lactose and fructose is a normal phenomenon. The difference between a healthy bowel and IBS is the response of the bowel to the extra luminal water and gas. Visceral hypersensitivity and/or motility abnormalities lead to functional gut symptoms. Breath hydrogen tests for fructose and lactose malabsorption are useful in patients with functional gut symptoms (abdominal pain and discomfort, bloating, altered bowel habit) to

identify if fructose and/or lactose could be dietary triggers, ie. they are malabsorbed. The tests should only be ordered if there are symptoms, and the results used to guide dietary management.

Testing for both lactose and fructose malabsorption is recommended to inform dietary management rather than a sequential approach.

Some companies offer home breath test kits, which may be useful for people living in remote areas. If testing is not possible (eg. in young children) dietary modification may be trialled with guidance by a dietician. However, this may take longer.

How are the tests performed?

Breath testing is designed around the fact that all hydrogen in the breath results from fermentation of poorly absorbed carbohydrate in the intestinal tract (*Figure 1*). Interpretation is easier if breath hydrogen starts at zero – hence a diet low in fermentable carbohydrates is recommended the day before the test. Only one sugar can be tested each day, with an interval of at least 2 days between tests.

The amount of hydrogen appearing in the breath following fermentation of carbohydrates varies according to the individual's microbiota, as hydrogen is also used by bacteria for other metabolic processes, including conversion to methane. Some people produce lots of hydrogen in response to malabsorbed sugars, some produce lower amounts, and about 15% produce none (designated 'nonhydrogen producers'. Methane is also derived exclusively from intestinal fermentation and can be used as an alternative measure, although it is less reliable and only used if insufficient hydrogen is produced. Patients who produce neither methane nor hydrogen (about 5%) are not suitable for breath testing. A hand-held unit – called a 'gastrolyser' – tests expired air for hydrogen, or a 'microlyser' analyses the hydrogen or methane from samples collected in reusable breath collection bags.

What should I tell my patient?

Patients should be reminded of the importance of adhering to the recommended diet for 24 hours before the test to ensure low baseline hydrogen production. The laboratory can provide a list of foods to avoid. They also need to avoid exercise and smoking on the morning of the test and take no antibiotics or probiotics for 4–6 weeks prior.

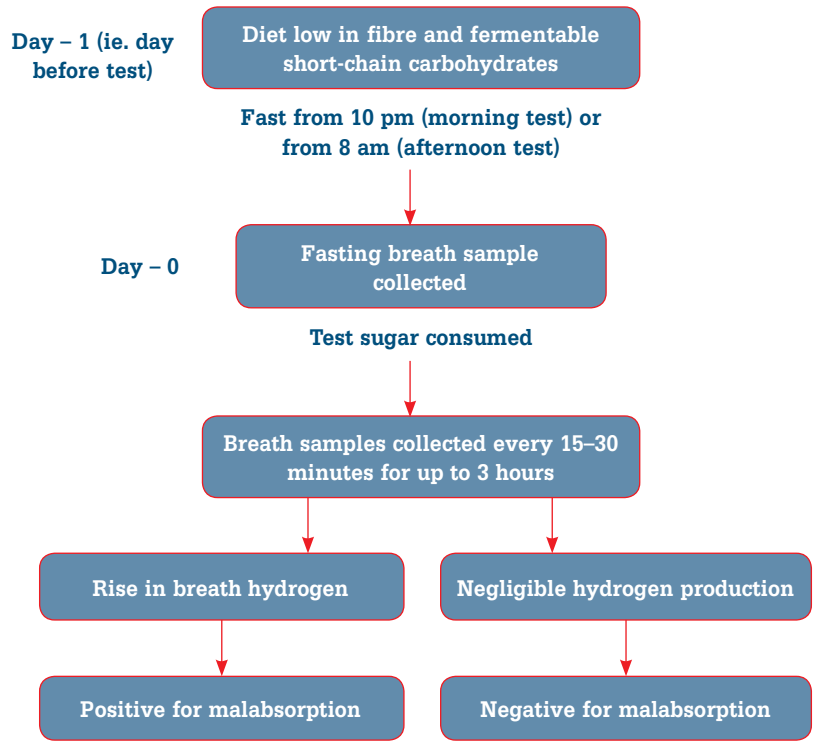

Figure 1. Flow chart for breath testing protocol
The pretest diet is important to ensure low baseline breath hydrogen. The test solution is consumed after a baseline breath sample, followed by repeated breath samples over 3 hours. A rise in breath hydrogen (or methane) indicates malabsorption through fermentation of the test sugar

Patients should be aware that testing may take up to 3 hours and that they will need to attend on different days for testing different sugars, but should be aware that testing is painless and safe. Testing is often available within a week or so and costs vary but around $100 per test (ie. $300 for lactulose, fructose and lactose) with no Medicare rebate.

Which carbohydrates are tested?

Lactulose

A 'control' sugar that is 100% malabsorbed is best tested first. Commonly, 15 g of lactulose, a nonabsorbed, manufactured disaccharide used to treat constipation, is used. There are three reasons to recommend a lactulose test before other breath tests:[14]

- it identifies low or nonhydrogen producers guiding interpretation of other results and indicating methane measurement may be required
- the time to the first rise in breath hydrogen indicates how long to continue breath samples in subsequent tests before declaring a negative result. For example, if it takes 3 hours before the first rise in breath hydrogen after lactulose, subsequent sugars must be tested for at least 3 hours, whereas a rise after 30 minutes after lactulose means that subsequent tests could be abandoned earlier (eg. 90 minutes)
- an early rise in breath hydrogen (before 90 minutes) after lactulose has been used as a marker for small intestinal bacterial overgrowth (SIBO). However, this is more likely to reflect rapid small intestinal transit than SIBO. Glucose is the preferred sugar for detection of SIBO.

Lactose

Lactose is a disaccharide that requires lactase to split it into glucose and galactose for absorption. This highly efficient enzyme is present in the brush border of the proximal small bowel. Its activity reduces with age and is low in certain ethnic

groups, such as Asian and Mediterranean.[14] Fifty grams of lactose is usually used in testing – if this large dose is completely absorbed, dietary lactose restriction is unnecessary. A rise in hydrogen and/or methane indicates malabsorption.

There are alternative methods to detect lactose malabsorption. A lactose tolerance test involves serial blood tests for 90 minutes after a lactose load with a rise in blood glucose presumed to indicate breakdown of lactose and release of glucose. Duodenal biopsy can be used to estimate lactase activity. This has been used in the paediatric setting as serial blood tests are impractical and breath tests require cooperation. However, extrapolating enzyme activity from the biopsy to the functional capability of the proximal small intestine is of questionable accuracy. Some practitioners trial a lactose free diet, but this is inaccurate half the time and is not recommended.

Fructose

Fructose is a monosaccharide, hence no enzyme is required. Fructose is absorbed by two pathways: the first is specific for fructose (via GLUT5 fructose transporter), occurs along the entire small bowel, but is slow; the second is rapid and efficient, but occurs only together with glucose. Therefore, fructose in excess of glucose (called 'free fructose') is potentially malabsorbed. This occurs if the fructose transporter is inefficient, or if fructose meets bacteria before absorption because of rapid transit along the small bowel or SIBO. Breath hydrogen testing is the only validated assessment method, using a dose that replicates a high dietary intake,[15] typically 35 g. A positive result does not require complete dietary elimination but advice to restrict intake to manage gastrointestinal symptoms.

Other sugars

Glucose is tested if SIBO is suspected, as glucose is rapidly absorbed and only causes a rise in breath hydrogen if it meets bacteria in the small bowel before absorption. The sugar alcohol or polyol, sorbitol, is rarely requested. It is always slowly absorbed, but breath testing can identify when it is minimally absorbed. Sucrose (cane sugar) is a disaccharide that requires sucrase in the small intestinal brush border in order for it to be split into glucose and fructose. Sucrose breath testing is rarely performed, as malabsorption is extremely uncommon. It should only be tested after a negative glucose breath test.

How are the tests reported?

Qualitative reporting

Standard reports state that malabsorption of the sugar is 'present', 'not present' or the test is 'uninterpretable' due to inadequate hydrogen (or methane) production or to technical issues such as a high baseline hydrogen production. Criteria vary across laboratories; a cut off that is too low may detect false positives whereas a cut off that is too high creates false negatives. A rise in breath hydrogen of at least 10 ppm above baseline for two consecutive readings provides a reasonable indication of malabsorption.[15]

Semiquantitative reporting

Patients want to know how severe their malabsorption is so they can determine if they can tolerate small amounts of sugar without symptoms. Standard reporting provides no guidance. With a lactulose baseline test, a mathematical interpretation of results is possible to yield semiquantitative results. This can be calculated by comparing the 'area under the curve' (calculated by the trapezoidal rule) for hydrogen production after fructose or lactose with that after lactulose, for which the entire 15 g dose is malabsorbed (*Figure 2*). The results can then be expressed semiquantitatively as nil, small degree or convincing malabsorption. This can theoretically guide the degree of dietary restriction, although this has not yet been studied.

Reporting of symptoms during the test

Symptoms that develop during the test, such as bloating, pain or diarrhoea, are usually recorded. Some laboratories report symptoms for 12–24 hours after the test. Symptoms during testing are now considered of marginal interpretive value as the specificity is low and in the patient's diet it may be the cumulative combination of FODMAPs that cause symptoms.

How should the results be interpreted?

Malabsorption is not an abnormal state. However, malabsorption offers an opportunity for treatment; reducing the intake of that sugar may reduce the troublesome functional gut symptoms.

What is the next step?

All patients with functional gut symptoms undergoing breath tests should receive dietary advice, preferably by a dietician with training in the low FODMAP diet. The tests do not determine

Time (mins)	0	20	40	60	80	100	120	140	160	180
Lactulose	0	0	6	10	12	19	27	45	68	48
Fructose	0	4	18	29	38	47	63	41	36	22
Lactose	0	0	1	6	9	10	6	0	0	0

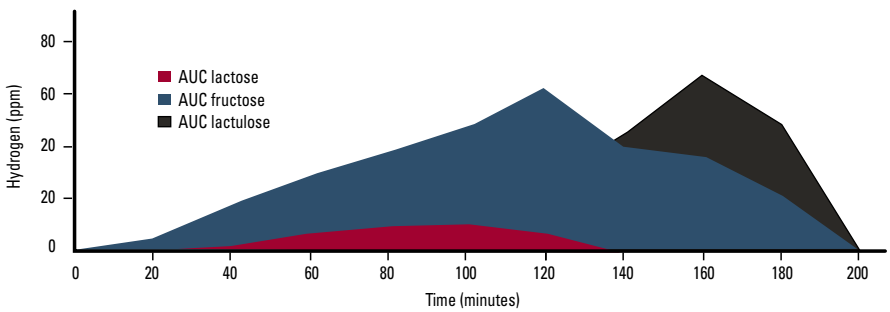

Figure 2. Example of semiquantitative reporting of results
AUC = area under the curve
AUC for fructose and lactose as a proportion of the AUC for lactulose reveals that 100% of the ingested fructose and 14% of the ingested lactose were malabsorbed, ie. convincing fructose malabsorption and small degree of lactose malabsorption

whether dietary change is worthwhile – it only guides the dietician in designing the diet.

Fructose and lactose are only two of six types of FODMAPs that need to be considered as symptom triggers. The sugar polyols, sorbitol and mannitol, can be breath tested, although the usefulness of this has not been formally examined. Fructans and galacto-oligosaccharides are universally malabsorbed, therefore breath tests are pointless. These carbohydrates need to be considered in the design of the diet in addition to the outcomes of fructose and lactose breath tests. The aim of testing helps achieve the least restrictive diet that achieves symptom control.

Figure 3 depicts the process that should be taken once breath tests are completed. Specialist dietician input is vital. Research investigating these dietary carbohydrates continues with foods composition still being tested. Breath test results help tailor the diet so fructose and lactose are only restricted if the tests have shown malabsorption. A 4 week dietary trial should be sufficient to improve symptoms in the majority of patients. Tolerance levels can then be tested in order to assess how strict the approach needs to be long term for symptom control.

Authors

Jacqueline S Barrett PhD, BSc(Biomed)(Hons), MNutrDiet, is Senior Lecturer and dietician, Gastroenterology Department, Alfred Hospital and Central Clinical School, Monash University, Melbourne, Victoria. jacqueline.barrett@monash.edu

Peter R Gibson MD, FRACP, is Professor and Director of Gastroenterology, Alfred Hospital and Central Clinical School, Monash University, Melbourne, Victoria.

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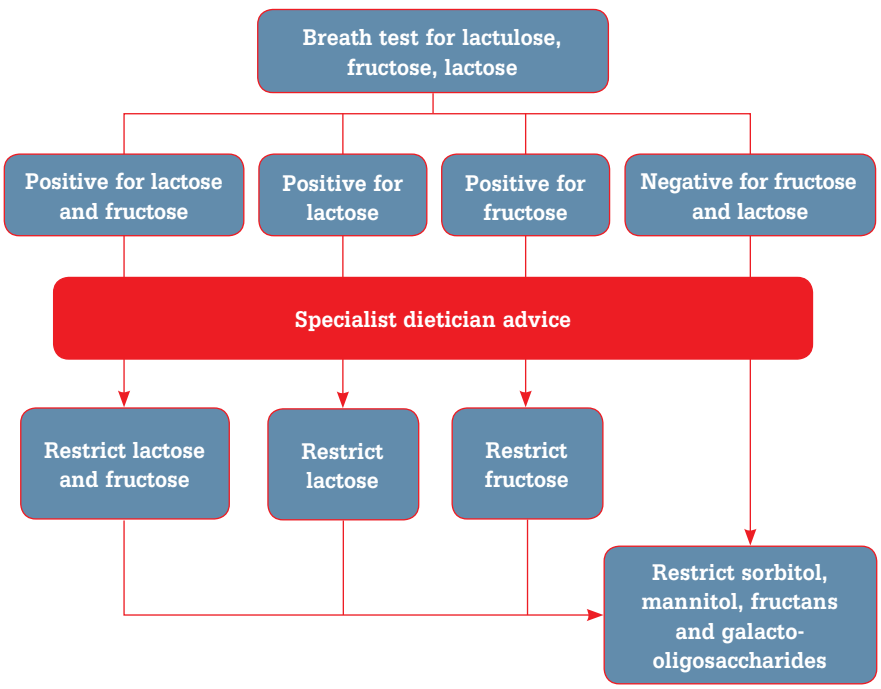

Figure 3. How to manage the patient following breath testing
Breath test outcomes for fructose and lactose assist the dietician in determining whether fructose and/or lactose need to be restricted for symptomatic relief, but regardless of results, dietician advice is required to consider other nontested carbohydrates as potential symptom triggers

correspondence **afp@racgp.org.au**