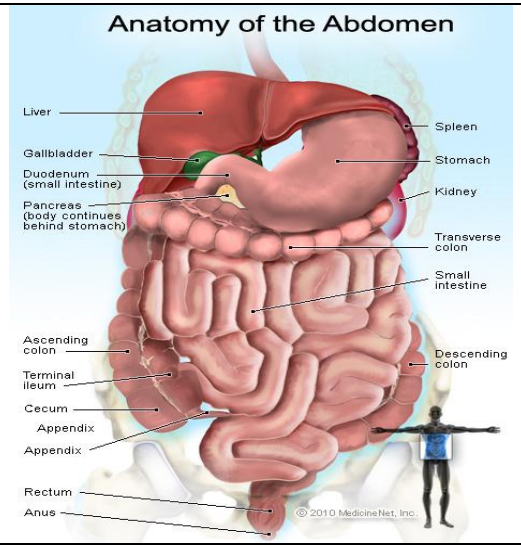
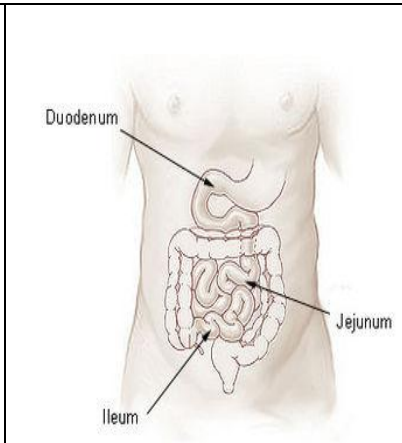
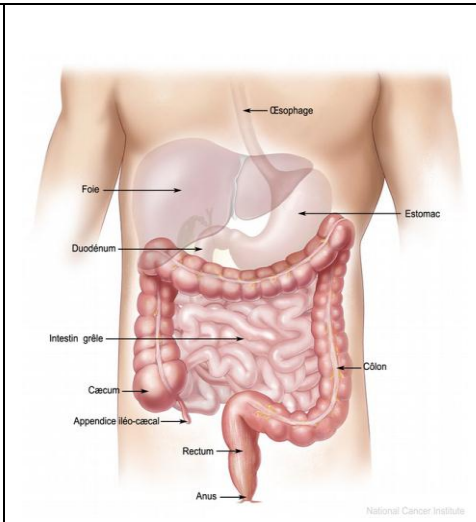
CLINICAL APPLICATIONS : Basic principles of "Hydrogen/Methane Breath-Testing"







Intestine (gut, bowel):

- small intestine
  - duodenum
  - jejunum
  - ileum
- large intestine
  - caecum
  - colon
  - rectum

GAS PRODUCTION

1. **Normally when fasting and at normal rest conditions, H2 is not present in human breath.**
2. **But when some substances are not digested, fermentation take place**
3. **When some bacteria (called anaerobic bacteria) digest food, they produce acids, water and gases (fermentation)**
4. **The major gases produced by these bacteria include, hydrogen (H2), methane (CH4) and other small concentrations of aromatic gases.**
5. **These gases are absorbed and diffused into the blood stream, trough the vascular system from the site of their digestion.**
6. **By this way they are conducted to the lungs for blood gas purification.**
7. **Gases diffuse across the capillary membrane into the alveoli in the lung.**
8. **From the alveolus they will appear in the expired alveolar gas from where they can be measured.**

So, if either H2 or CH4 are produced biologically, it tells us that some food substance is somewhere exposed to some bacterial fermentation

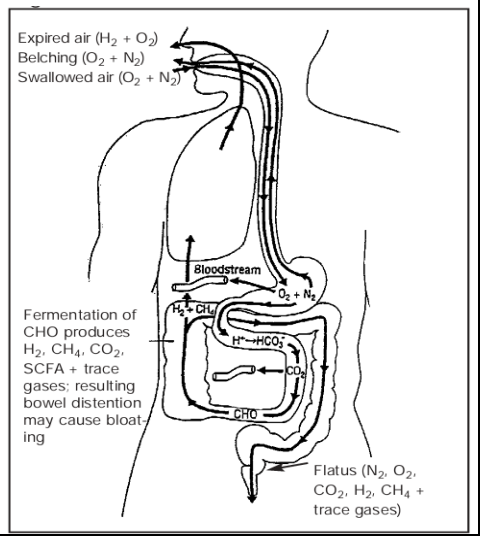
BACTERIAL ACTIVITY

In small intestine:

1. Most of the bacteria contained into the food are killed by the acidity of the stomach.
2. Therefore Small intestine usually contain few bacteria, these are normally limited to the colon
3. But in some conditions, called "bacterial overgrowth", bacteria will exist in high concentrations in the small intestine.
4. Their presence in that area can interfere with the absorption of some vitamins and other essential foodstuffs, so it is important to diagnose the conditions, because they can lead to nutritional deficiencies and severe diseases.

In the colon

1. Colon usually has a high bacterial-count.
2. Colon is concerned with conserving water and salt by reabsorbing them from the luminal contents.
3. Fiber, very popular in breakfast cereals, is not digested in the small intestine, so to digest it undergoes bacterial fermentation in the colon. Amounts of starch (10-20% of foods like legumes) escape digestion in the small intestine and are broken down in the colon, thus, adding to the efficiency of energy production by such food-stuffs.
4. Short-chain fatty acids (SCFA) produced by that process are absorbed in the colon, and are beneficial to health reducing colonic acidity (pH) and favorize bacterial colonization.
5. Thus, fermentation in the colon is normal, and it is even important.
6. Gases which are produced in the colon are reabsorbed and equilibrated with the blood leaving that digestion area.



MEC manufacture breath-testing instrumentation since 1985 offering the ability to measure Hydrogen (H2), Methane (CH4) and even Carbone dioxide (C02) from a single exhaled alveolar sample gas contained in a sample bag, syringes or other breath collector bags as well as Software for methodology which adds reliability to the breath test and helps clinicians to properly diagnose patients.

Advantages of H2 breath testing

These tests offer **simple and safe alternatives** compared **to more invasive procedures** such **as blood gas analysis** and **biopsies** for obtaining aspirates for culturing.
Besides being accurate and non-invasive, H2-BTs have other advantages such as: **lack of toxicity, low cost of equipment , low cost of daily operation, low cost of substrates and easy accessibility to clinical practice…**

1. The breath-H2 test is a simple non-invasive procedure which is **readily accepted by patients and clinical staff** (9), and which has greater reliability and acceptability than the blood test, and biopsy according to most reports in the literature (1,4-8)
2. **The lower dose** (ie: lactose 1g/kg BW of substates) usually used does not cause discomfort and explosive symptoms like diarrhea frequently seen by some malabsorbers or intolerants who are given the large dose 2g/kg BW required for the blood test (9).
3. **False-positive breath-tests are rare**, and usually caused by improperly doing the test, allowing the subject to smoke, to sleep to exercise or to eat shortly before or during the test (11) . ….**Most of false positive can be avoided by the use of proper methodology and well defined guidelines**.
   Remark : Bacterial overgrowth (from the colon retrograde into the small intestine) can also produce a false-positive breath-test, but it is usually preceded by an elevated fasting breath-H2 level and the response is seen soon after the sugar is ingested (within 20-30 minutes).
4. **False-negative results with the breath-test is well below that seen with the blood test** (1,4,5) False-negative results are reported to be from 5-15% of all lactose malabsorbers (12,14) due to a variety of causes.
   Many of the false-negative reports can be avoided by measuring methane in addition to hydrogen (15) because some methanogenic flora which convert partially colonic H2 to CH4...

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External links

International Association for Breath Research (IABR)
Journal of Breath Research

CLINICAL APPLICATIONS

DESCRIPTION OF H2-BREATH TESTS

- **Breath testing provides qualitative and quantitative diagnostic information**
  (i.e. the degree of response to a lactose challenge, which can be called Lactose Malabsorption **LM** or Lactose Intolerances **LI** , depending on severity of lactose maldigestion)

- **MEC Breathing test technology brought by MEC LACTOTEST 102 ™ and MEC LACTOTEST 202 ™ provides clinicians and physicians with a convenient, user-friendly and accurate and reliable diagnostic assessment of carbohydrate maldigestion and bacterial overgrowth of the small intestine.**

Hydrogen / Methane Breath Test is a painless and non-invasive test which helps to easily diagnose the following gastrointestinal disorders.

1. **Glucose-H2-Breath Test**
   is commonly used to determine **Small Bowel/Intestinal Bacterial Overgrowth (SIBO)** which means too many bacteria growing in small intestine, which can cause similar symptoms to food intolerance.

2. **Lactose H2 Breath test**
   is often used for detecting **Lactose intolerance**, or body's ability to properly process lactose, a sugar found in dairy products and dissociated by **Lactase enzyme**

3. **Fructose H2 Breath test**
   is commonly used for detecting **Fructose Intolerance** or body's ability to properly process fructose, a sugar found in many fruits and vegetables.

4. **Sucrose (saccharose) H2 Breath test**
   is commonly used for detecting **sucrose intolerance** or sucrase-isomaltase deficiency

5. **d-Xylose H2 Breath test**
   is commonly used for intestinal malabsorption or **Celiac disease** and appears by eating foods with **gluten**, immune system responds by damaging the small intestine.

6. **Lactulose H2 Breath test**:
   1 is often used for measurement of **Intestinal Transit Time ITT**, important baseline test to assess how long it takes food to pass through digestive system.
   2 is commonly also used to determine **Small Bowel/Intestinal Bacterial Overgrowth (SIBO)** which means too many bacteria growing in small intestine, which can cause similar symptoms to food intolerance.

7. **Sorbitol H2 Breath test**
   is often used to verify body's ability to properly process sorbitol, a sugar found in some fruits and artificial sweeteners.

8. **Xylitol H2 Breath test**
   is not sufficiently absorbed by many people so that, not infrequently, irritable bowel symptoms can be triggered by food containing xylitol

9. **Etc……**

Principals of optimal tests interpretations are consisting in analyzing the relationships between:
Patient documentation … select right indications….Substrate…gas exhalations…gas levels and time-dependence…related physiologic symptoms.
Each breath test starts with an initial measurement in the fasting state (basal value) prior to the patient having been administered a test substance.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also the exact documentation about symptoms. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

2. **The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.**

   - The symptoms that may occur during a test are not at all limited to **intra-gastrointestinal symptoms** such as: **hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…
   - But also frequently, the patient experiences **extra-intestinal symptoms** such as **fatigue, dizziness, headache or heartburn** (see figure 2).

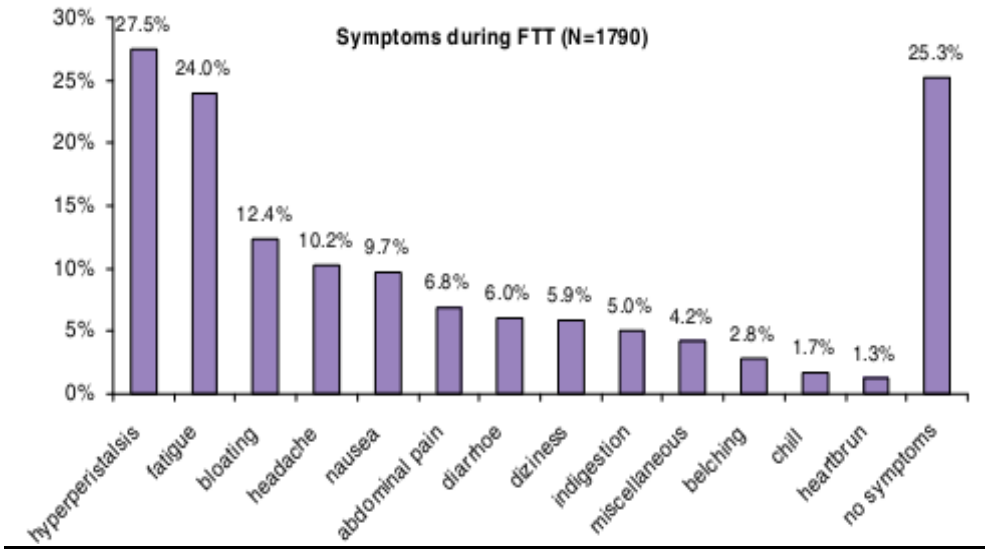


figure 2

INTERPRETATION

The interpretation of H2 BT results is based on three crucial factors:

- H2 and CH4 exhalation levels, appearance of symptoms and the time-dependent changes of these two factors during the test period.

Example of a negative breath test

- Only if both **criteria apply (lack of H2) and (lack of symptoms)** normal findings should be diagnosed (see figure 3).
- If there is no malabsorption of the test substance, there is **no significant increases in hydrogen levels**, i.e. readings vary **by less than 5 ppm above or below the basal value, (which must be less than 10ppm) and there are no symptoms.**

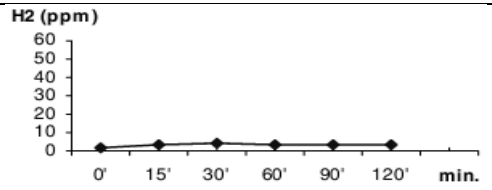
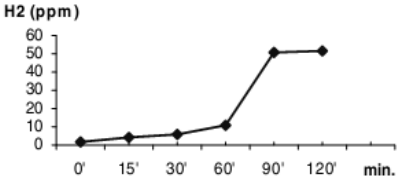


Figure 3. Negative breath test.
Test result: no H2 increase, no symptoms.
Interpretation: normal findings.

Example of a positive breath test with symptoms

- In general, **an increase in hydrogen concentrations of more than 20 ppm above the basal value** is **considered to be as positive test result** (significant H2 increase).
- A **significant H2 increase and the appearance of symptoms**, both occurring at **about 60 min** after starting the test, are diagnosed as an intestinal intolerance of the test substance (see figure 4).
- Generally, it should be possible to measure the maximum increase at the earliest after 60 or—even better—after 90 min as it takes that long until the non-absorbed proportion of the test substance has arrived in the large intestine.

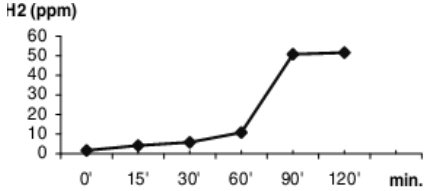


- **symptoms** - - + + + + + + +

Figure 4. Positive breath test and symptoms.
Test result: H2 increase and symptoms, both after 60 min.
Interpretation: intestinal **intolerance** of the test substance

Example of a positive breath test without symptoms

- If there is a significant H2 increase after 60 min but clinical complaints (symptoms) are lacking, a **malabsorption** of the test substance (instead of an intestinal intolerance) has to be diagnosed (see figure 5).
- Generally we recommend the term **'intolerance'** if positive breath test results occur together with symptoms in contrast to the term 'malabsorption', indicating a positive breath test but no appearance of symptoms.
- If the value rises more than 10 ppm but less than 20 ppm above the basal value, the test result is considered as **'borderline positive'**. Again it needs to be taken into consideration, at what time this borderline H2 increase occurs. **An increase of more than 10 ppm above the basal value within 30 min is seen as indicative of a test substance-dependent small intestinal bacterial overgrowth syndrome (SIBOS).** There are essentially two possibilities for this particular H2 profile:

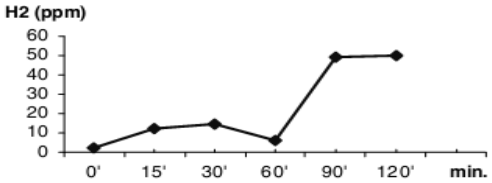


- **symptoms** - - - - - - - -

Figure 5. Positive breath test without symptoms.
Test result: H2 increase after 60 min, no symptoms.
Interpretation: malabsorption of the test substance but **without intolerance.**

Example of a positive breath test

a. The curve shows a dual-peak profile (see figure 6)
   i.e. **an H2 increase in the first 30 min is followed by a drop in the H2 concentration, which is once more followed by an H2 increase after 60 min**. **This indicates that there is a SIBOS with a still intact function of the ileo-cecal valve** and that the bacteria in the small intestine are able to metabolize the test substance.
   The second peak (after 60–90 min) a test substance-dependent SIBOS and intact ileo-cecal valve has to be diagnosed. :
   1. If there is no discomfort during the test, a malabsorption of the test substance with test substance- dependent SIBOS **with intact ileo-cecal valve** would need to be diagnosed.
   2. If the clinical complaints only occur during the first 60 min and disappear relatively quickly afterwards, this would indicate that the complaints were caused by the overgrowth in the small intestine rather than by the malabsorption of the test substance in the large intestine.



- **symptoms** - - - - - - - -
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Figure 6. Breath test curve with dual-peak profile.
Test result: H2 increase within 30 min, drop of H2 level, second H2 peak after 60 min.
Interpretation: malabsorption/intolerance (depending on appearance of symptoms) with SIBOS and intact ileo-cecal valve.

The positive breath test

b. **The curve shows an early increase (before 60 min) that remains at least 20 ppm above the basal value without a drop in theH2 concentration until the 90th minute**. This curve has a quasi dual-peak shape without a 'valley' between the first and the second peaks (see figure 7). In such a case, the assumption is that stool from the large intestine (cecum) has 'flown back' into the small intestine (terminal ileum) via the ileo-cecal valve. This is not a particularly rare occurrence because, in the case of malabsorption due to fermentation, a great deal of pressure can be produced in the cecum. **The ileo-cecal valve is extended and becomes 'leaky'**. What is less well known is the fact that there is antiperistaltic movement in the cecum in order to 'knead through' the mashed food. **During this process, the contents of the large intestine flow back into the small intestine if the ileo-cecal valve leaks**, which results in bacterial overgrowth in the terminal ileum while the rest of the small intestine has not yet been overgrown with bacteria. Such cases are referred to as **'backwash ileitis'**. As a situation such as this is almost always associated with complaints, an means that a major part of the test substance could not be absorbed, and is therefore fermented in the large intestine (malabsorption). If, during the test, the subject experiences discomfort, an intestinal intolerance of the test substance with intestinal intolerance of the test substance with backwash ileitis would need to be diagnosed. If the patient does not complain of discomfort during the test, he needs to be examined in order to establish whether he is sensitive to palpatory pressure applied on the right lower abdomen at the intersection between the small and the large intestines. If there is no sensitivity to palpatory pressure and if the H2 level shows an image as in figure 7, the correct diagnosis should be 'malabsorption of the test substance with reflux of bowel content via the ileo-cecal valve without backwash ileitis'.

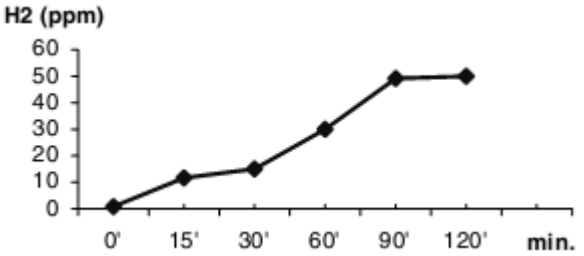

Figure 7. Breath test curve with early increase.
Test result: H2 increase within 60 min, no drop until 90th min and appearance of symptoms.
Interpretation: intestinal intolerance and backwash ileitis.

Others examples ……..

External links

Identification of Patients With Diabetic Gastroparesis by Hydrogen Breath Testing
http://www.testbreath.com/resources/h-diabetic.htm
Carbohydrate Malabsorption
diabetic.htmhttp://www.gastrolab.com.au/carbohydrate-malabsorption.html
Bacterial Contamination of the Small Intestine as an Important Cause of Chronic Diarrhea and Abdominal Pain: Diagnosis by Breath Hydrogen Test
http://www.testbreath.com/resources/bacterial_contamination.htm
BREATH TESTING IN INTESTINAL DISACCHARIDASE DEFICIENCY AND BACTERIAL OVERGROWTH OF THE SMALL INTESTINE
http://www.testbreath.com/resources/h-intestinal.htm

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1. The Glucose- H2/CH4-Breath Test

(SIBO) Small intestinal bacterial overgrowth is common in intestinal failure.

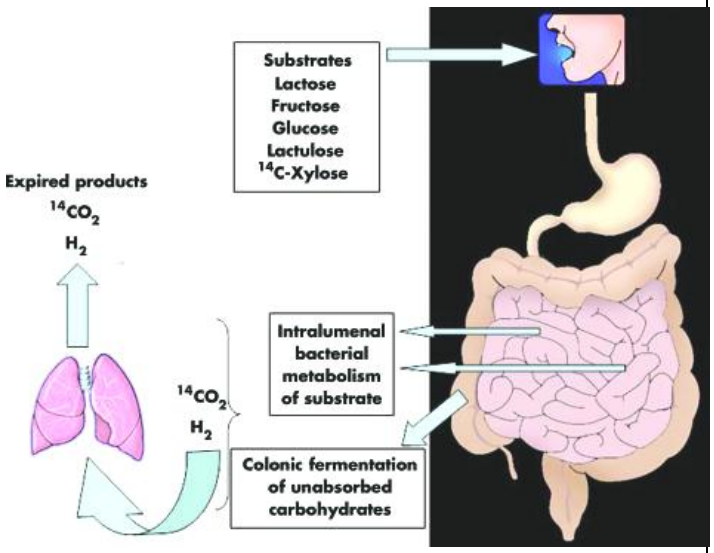
- **Its occurrence relates to alterations in intestinal anatomy, motility, and gastric acid secretion.**
- **Its presence may contribute to symptoms, mucosal injury, and malnutrition.**
- **Relationships between bacterial overgrowth and systemic sepsis are of potential importance in the intestinal failure**
- **The management of patients with bacterial overgrowth remains, for the most part, primarily empiric and comprises antibiotic therapy and correction of any associated nutritional deficiencies.**

1. **The Glucose-H2-Breath Test** is commonly used to determine **(SIBO) Small Bowel/Intestinal Bacterial Overgrowth** which means too many bacteria are growing in small intestine. This can cause similar symptoms as food intolerance and has to be related to **patient symptoms like diarrhea, gas, cramping or bloating etc …**

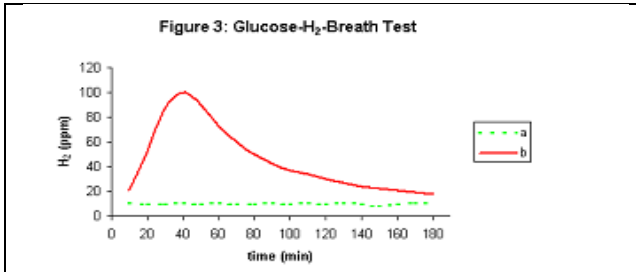
2. **Bacteria are ordinarily not present in significant numbers within the small intestine**, where digestion and absorption of sugars take place. Therefore, when a challenge dose of substrate (eg. Glucose) is ingested, the **level of H2 and sometimes CH4 in exhaled alveolar air will rise significantly** within one to two following hours depending on the intestinal transit time.

3. Hydrogen breath tests aids in the diagnosis of **(SIBO) Small Intestinal Bacterial Overgrowth which provides a framework for understanding (IBS) Irritable Bowel Syndrome** patients.

4. In this case the types of gas produced by bacteria in the digestive tract are an important factor in this understanding.



Schematic drawing showing the principles behind breath tests.



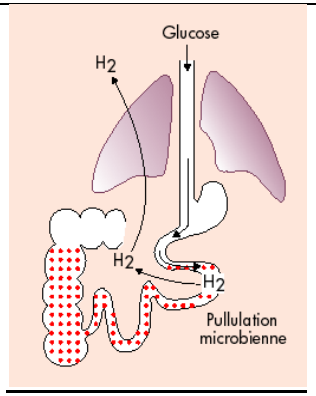
Plots of H2-concentration in breath over time after ingestion of glucose may therefore have the following shapes and has to be related to patient symptoms of diarrhea, gas, cramping or bloating

a) **Normal.**

- Glucose is rapidly and completely absorbed in the small intestine and therefore does not arrive at the large intestine (Colon)

b) **Pathologic.**

- Glucose in the small intestine produce bacterial colonization and fermentation combined with hydrogen production is called **SIBO "Small intestinal bacterial overgrowth".**
- The glucose-H2-breath test is applied for diagnosing bacterial overgrowth of the small intestine, sometimes in combination with galactose-H2-breath test also for the diagnosis of **glucose/galactose malabsorption** or intolerance
- The test is also considered for the diagnosis of **exocrine pancreas insufficiency**



Patient preparation

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four **(4) weeks of a colonoscopy** (intubation, anesthesia, etc).
- Patients should not take **antibiotics** or **antimicrobials** within **3 to 4 weeks** prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid **laxatives,** stool softeners or stool bulking agents **one (1) week** prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- **STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST**

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.(10ml/Kg BW with max of 250 ml)
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure, methodology with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the Bacterial Overgrowth Breath Test:

- There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort from ingestion of glucose including diarrhea, gas, cramping or bloating with a max duration of 12 H

Implementation of the glucose-H2-breath test:

Substrate	Dosage	Readings (min)	Positive Delta	Remark
Glucose Adults	25 g in 250 ml water (max. 50 g)	0–15–30–60–90–120	>10 ppm	• ***Remark*** *: Usually the so-called cut-off value (**Delta**), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)*
children	1 g/kg BW in 10 ml water/kg BW (max. 25 g)	0–15–30–60–90–120	>10 ppm	

- i.e After an overnight fast as above mentioned, 25 g glucose, dissolved in 250 ml of water, is orally administered. Alveolar gas (deep end expiratory breath) is sampled immediately before substrate intake, and thereafter every 0–15–30–60–90–120 and eventually 150 and 180 minutes.

RESULT INTERPRETATION

- If H2-concentration ascends by more than **Delta = 10 ppm**, then bacterial overgrowth of the small intestine must be assumed. Sensitivity and specificity of the glucose-H2-breath test, however, are only in the order of 60 to 90% or 75 to 100%, respectively. Nevertheless the test went its way for want of better alternatives.

SYMPTOMS

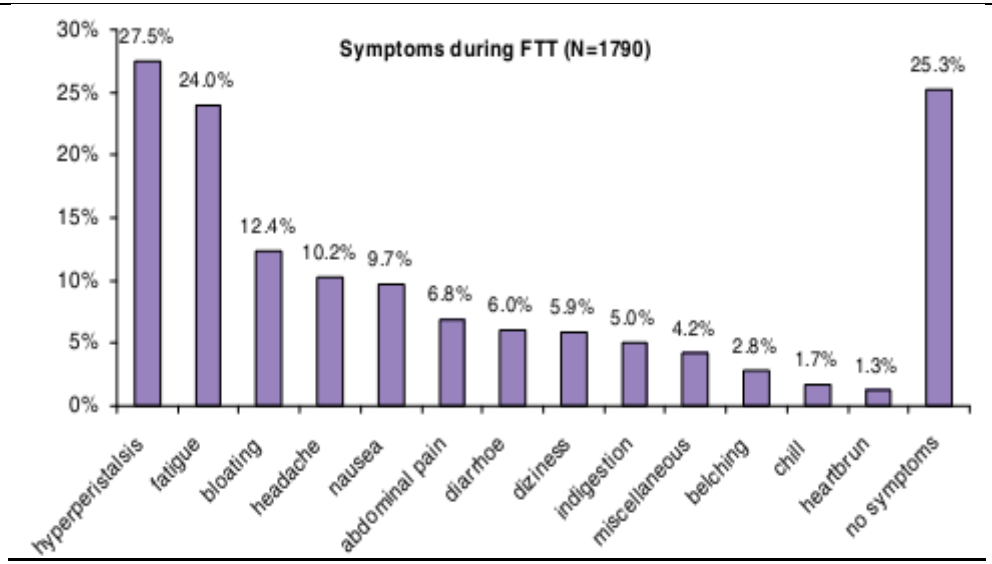
1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).



Internet Notes :

- **Small bowel bacterial overgrowth syndrome (SBBOS),** or **small intestinal bacterial overgrowth (SIBO)**, also termed **bacterial overgrowth**; is a disorder of excessive bacterial growth in the small intestine. Unlike the colon (or large bowel), which is rich with bacteria, the small bowel usually has less than 10^4 organisms per milliliter.[1] Patients with bacterial overgrowth typically develop symptoms including nausea, bloating, vomiting and diarrhea, which is caused by a number of mechanisms.
- The diagnosis of bacterial overgrowth is made by a number of techniques, with the gold standard diagnosis being an aspirate from the jejunum that grows in excess of 10^5 bacteria per millilitre. Risk factors for the development of bacterial overgrowth include the use of medications including proton pump inhibitors, anatomical disturbances in the bowel, including fistulae, diverticula and blind loops created after surgery, and resection of the ileo-cecal valve. Small bowel bacterial overgrowth syndrome is treated with antibiotics, which may be given in a cyclic fashion to prevent tolerance to the antibiotics.

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External links

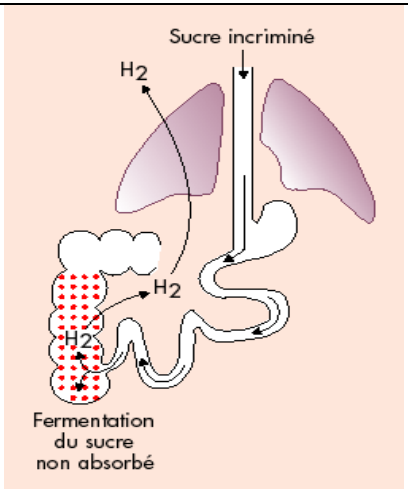
2. Lactose- H2/CH4-Breath Test

Lactose.

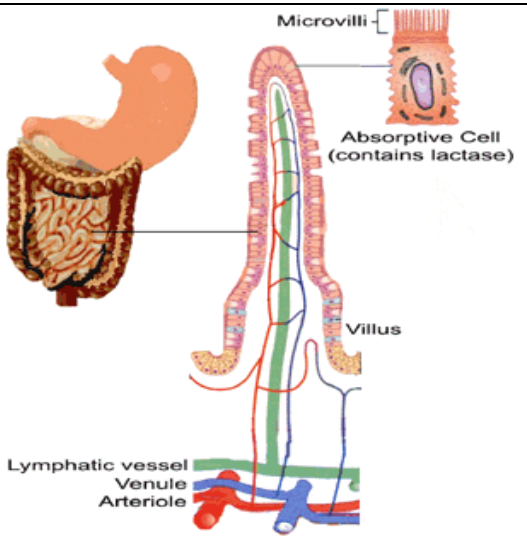
- **Lactose** is a **disaccharide**, a sugar found in dairy products and during digestion lactase (an enzyme) splits it to form **galactose** and **glucose**, which are absorbed in the small intestine, Lactose is the natural sugar in milk. It is also found in milk products, such as cheese and ice cream, and processed foods, such as bread, cereal, and salad dressing.

Lactose-H2-Breath Test

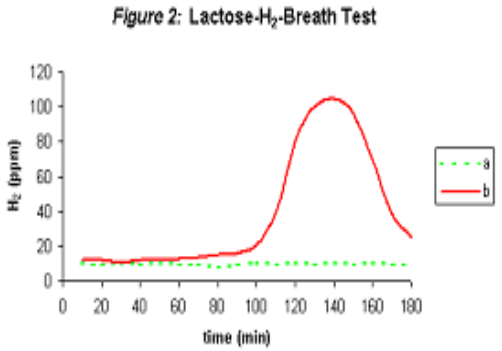
- This test is often used for **detecting Lactose intolerance**, or body's ability to properly digest lactose**. Lactase** is the enzyme needed to digest lactose. Many people, particularly those of African, Native American, or Asian background, normally have low levels of lactase, (the enzyme needed to digest lactose), after childhood. Also, as people age, their enzyme levels decrease. As a result, over time people may experience increasing amounts of digestion symptoms after eating food containing lactose.



Fermentation of non absorbed sugar (Lactose)



Lactase: enzyme found in microvilli cells of small intestine that hydrolyzes lactose.



Plots of H2-concentration in breath over time after ingestion of lactose may therefore have the following shapes:

a) Normal.

- **Lactose is split into galactose and glucose** and then **completely absorbed** in the **small intestine.**
- In normal fermentation by anaerobic microorganisms therefore proceeds either not until the large intestine or not at all.

b) Pathologic

- **Without lactase** the test **substance is neither split into the monosaccharide nor absorbed in the small intestine.**
- Therefore the substrate is fermented to form hydrogen in the large intestine "colon". There this hydrogen is absorbed through the intestinal wall and then dissolved into the bloodstream, released into the lungs through the capillary blood vessels surrounding the alveoli and finally expired.
- The lactose-H2-breath test is used for the **diagnosis lactase deficiency** and therefore of **lactose malabsorption LM** or **lactose intolerances LI** , which is highly abundant all over the world.

Optimal preparation of the patient before H2/CH4 BREATH –TESTS

- Patients should not be tested within **four (4) weeks of a colonoscopy or barium enema**, which is a diagnostic test (contrast material called barium into the rectum)
- Patients should not take **antimicrobials** and should try to avoid **bismuth preparations within 3 to 4 weeks** prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid **laxatives**, **stool softeners or stool bulking agents one (1) week** prior to the test.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or boiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda, cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING completely **12 HOURS** BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Proceed to Normalized Breath-Gas Measurements

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest **normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique**. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix for more info

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc…… see appendix for more info

Potential Complications of the Lactose Breath Test:

- Normally there are very few potential serious complications during the 3-hour testing. Patients may feel minor discomfort from ingestion of lactose including diarrhea, gas, cramping or bloating. ..See symptoms

Implementation of the lactose-H2-breath test:

Substrate	Dosage	Readings (min)	Positive	Remark
Lactose				*Remark: Usually the so-called cut-off value (**Delta**), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference D exceeds this critical value, a certain metabolic anomaly must be assumed)*
Adults	1 g/kg BW in 10 ml water/kg (max 50 g in 250 ml water)	0–15–30–60–90–120a	>20 ppm	
children	1 g/kg BW in 10 ml water/kg BW (max. 25 g)	0–15–30–60–90–120a	>20 ppm	

After an overnight fast as above mentioned, 1g/kg (maximum 25g) lactose, dissolved in 10 ml /kg BW of water, are orally administered for diagnosing lactase deficiency.
Alveolar gas (deep end expiratory breath) is sampled immediately before substrate intake and 30, 60, 120 and 150 minutes after substrate ingestion.

RESULTS

We recommend a cut-off value or (Delta = 30 ppm) for distinguishing patients with lactase deficiency and normal. Sensitivity and specificity are then in the range of 90 to 96%. If additional symptoms like abdominal pain are reported, lactose intolerance may be assumed.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

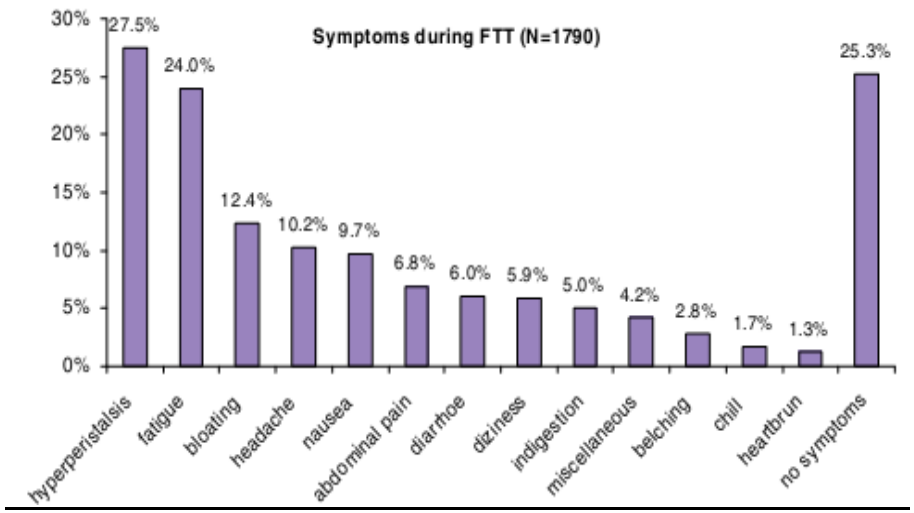


figure 2

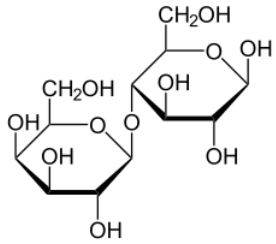
PREVALENCE of lactose intolerance in adults of various ethnic groups various ethnic groups (see appendix)

TABLE 1. Incidence of lactose intolerance in adults of various ethnic groups [5, 23]	
Ethnic group Lactose intolerant	***(%) of prevalence***
African Blacks	***95-100***
Orientals	***90-100***
North American Blacks	***65-75***
Mexicans	***70-85***
Mediterraneans	***60-80***
Jewish Descent	***60-70***
Middle Europeans	***10-20***
North American Caucasians	***10-20***
Northern Europeans	***1-10***

Internet Notes :

http://en.wikipedia.org/wiki/Lactose_intolerance#cite_note-NDDIC-0

Lactose intolerance, also called **lactase deficiency**[1] or **hypolactasia**, is the inability to digest and metabolize lactose, a sugar found in milk. It is caused by a lack of lactase, the enzyme required to break down lactose in the digestive system, and results in symptoms including abdominal pain, bloating, flatulence, diarrhea, nausea and acid reflux.
Most mammals normally become lactose intolerant when they are young but some human populations have developed lactase persistence, in which lactase production continues into adulthood. It is estimated that 75% of adults worldwide show some decrease in lactase activity during adulthood.[2] The frequency of decreased lactase activity ranges from 5% in northern Europe through 71% for Sicily to more than 90% in some African and Asian countries.[3]



Lactose (disaccharide of β-D-galactose & β-D-glucose) is normally split by lactase.

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External internet links

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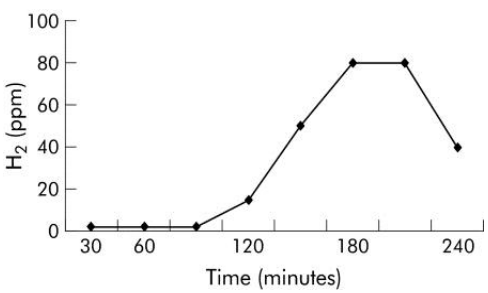
3. The Fructose- H2/CH4-Breath Test

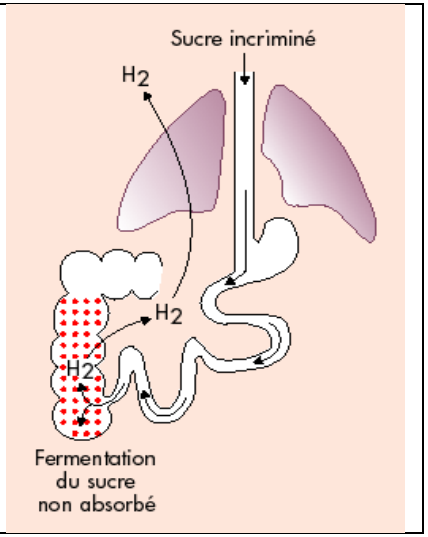
The Fructose-H2-Breath Test is detecting **Fructose Intolerance** and is used for the diagnosis of **fructose-malabsorption** or body's ability to properly process fructose. Fructose is a sugar found in many fruits and vegetables and is naturally present in **onions, artichokes, pears, and wheat. It is also used as a sweetener and in some soft drinks and fruit drinks.**

Deficiency of the subunit of the "enzyme aldolase" in the liver or the small intestinal mucosa.

Important : The test is absolutely contraindicated for patients with hereditary fructose intolerance.
In this case the application of this diagnostic tool would be life-threatening. (The abundance of this metabolic anomaly is of the order of 1:10 000 to 1:15 000. Symptoms are a hyperglycaemic shock after intake of food containing fructose (fruits, milk products containing saccharose, sweets etc.) in infancy, metabolic disorders accompanied by vomiting, fever and dystrophy, hepatomegalia and hepatic malfunctions. Diagnosis is possible on the basis of a deficiency of the subunit of the enzyme aldolase in the liver or the small intestinal mucosa.)



Schematic drawing of hydrogen breath tests (fructose with or without sorbitol and lactose) indicating carbohydrate malabsorption.



PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

!!!! Potential Complications of the Fructose Breath Test:

- Normally there are very few potential serious complications during the 3-hour testing. Patients may feel minor discomfort from ingestion of fructose including diarrhea, gas, cramping or bloating.
- ***Important : The test is absolutely contraindicated for patients with hereditary fructose intolerance.*** *In this case the application of this diagnostic tool would be life-threatening. (The abundance of this metabolic anomaly is of the order of 1:10 000 to 1:15 000. Symptoms are a hyperglycaemic shock after intake of food containing fructose (fruits, milk products containing saccharose, sweets etc.) in infancy, metabolic disorders accompanied by vomiting, fever and dystrophy, hepatomegalia and hepatic malfunctions. Diagnosis is possible on the basis of a deficiency of the subunit of the enzyme aldolase in the liver or the small intestinal mucosa.)*

Implementation of the fructose-H2-breath test:

Substrate	Dosage	Readings (min)	Positive	Remark
Fructose				*Remark : Usually the so-called cut-off value (**Delta**), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)*
Adults	25 g in 250 ml in 10 ml BW water (max. 25 g)	0–15–30–60–90–120a	>20 ppm	
children	1 g/kg BW in 10 ml water/kg BW (max. 25 g)	0–15–30–60–90–120a	>20 ppm	

(*) The test is absolutely contraindicated for patients with inherited fructose intolerance

After a nocturnal fasting period as above explained, 25 g of fructose, dissolved in 250 ml of water, are orally administered. Breath samples are taken immediately before and 45, 90, 135 and 180 minutes after substrate intake.

RESULT: If H2-concentration ascends by more than Delta = 20 ppm, then fructose malabsorption must be assumed.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

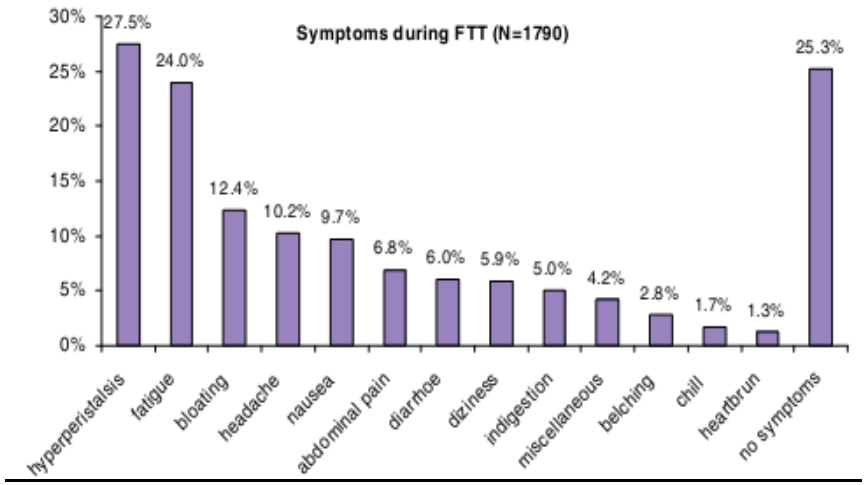
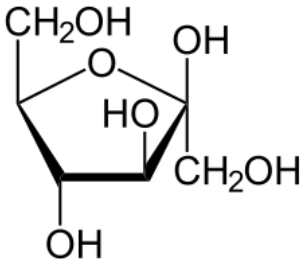


figure 2

Internet Notes :

Fructose malabsorption, formerly named "dietary fructose intolerance," is a digestive disorder[1] in which absorption of fructose is impaired by deficient fructose carriers in the small intestine's enterocytes. This results in an increased concentration of fructose in the entire intestine.
Fructose malabsorption is found in up to 30% of the population of Western countries and Africa.[2] Some estimates for Asia seem to be considerably lower but are still at 10% of the population.[2]
This condition is common in patients identified to be suffering symptoms of irritable bowel syndrome, although occurrence in these patients is not higher than occurrence in the normal population. Conversely, patients with fructose malabsorption often fit the profile of those with irritable bowel syndrome.[3] A small proportion of patients with both fructose malabsorption and lactose intolerance also suffer from celiac disease.
Fructose malabsorption is not to be confused with hereditary fructose intolerance, a potentially fatal condition in which the liver enzymes that break up fructose are deficient.
Fructose intolerance may refer to:

- Fructose malabsorption, a digestive disorder of the small intestine in which the fructose carrier in enterocytes is deficient
- Hereditary fructose intolerance, a hereditary condition caused by a deficiency of liver enzymes that metabolise fructose



Internet scientific References

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12. ^ Skoog SM, Bharucha AE (2004). "Dietary fructose and gastrointestinal symptoms: a review". *Am. J. Gastroenterol.* **99** (10): 2046–50. doi:10.1111/j.1572-0241.2004.40266.x. PMID 15447771.

13. ^ [a] [b] [c] Shepherd SJ, Gibson PR (2006). "Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management". *Journal of the American Dietetic Association* **106** (10): 1631–9. doi:10.1016/j.jada.2006.07.010. PMID 17000196.
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External internet links

1. Fructose Malabsorption at the food intolerance network -- Society for Public Health
2. Fructose Malabsorption -- Practical Gastroenterology
3. Low FODMAP Diet
4. Excess Fructose Content of American Foods
5. Ledochowski M, Widner B, Bair H, Probst T, Fuchs D (2000). "Fructose- and sorbitol-reduced diet improves mood and gastrointestinal disturbances in fructose malabsorbers". *Scand. J. Gastroenterol.* **35** (10): 1048–52. doi:10.1080/003655200451162. PMID 11099057.
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4. Sucrose (saccharose) H2/CH4-Breath Test

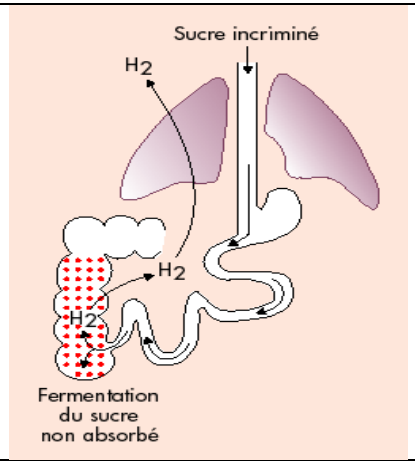
- **Sucrose** is the organic compound commonly known as **table sugar** and sometimes called **saccharose**
- Sucrose-H2-Breath Test is commonly used for detecting **sucrose intolerance** or sucrase-**isomaltase deficiency.** Sucrose is split to form **glucose** and **fructose** in the **small intestine.**

In normals

- These monosaccharide are **completely absorbed in small intestine**, without attaining the large intestine, therefore substrates does not reach the colon and **there is no production of H2** and **there are no symptoms during all the test**

In Pathology

- In **case of bacterial overgrowth in the small intestine** hydrogen production by fermentation competes with absorption and metabolisation, We can see a **first peak** and then a second peak for the sucrose reaching the colon
- if sucrose is not completely absorbed in small intestine, it will reach the colon where fermentation will create a peak of H2 there is **sucrose malabsorption** if there are no symptoms and there is **sucrose intolerance** if there are symptoms



PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the Bacterial Overgrowth

There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort from ingestion of sucrose including diarrhea, gas, cramping or bloating.

Implementation of the sucrose-H2-breath test:

Sbstrate	Dosage	Readings (min)	Positive	Remark
Sucrose (or Saccharose) Adults	25 g in 250 ml in 10 ml BW water (max. 25 g)	0–15–30–60–90–120a	>20 ppm	*(remark : Usually the so-called cut-off value (**Delta**), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)*
children	1 g/kg BW in 10 ml water/kg BW (max. 25 g)	0–15–30–60–90–120a	>20 ppm	

For diagnosing sucrose intolerance after overnight fast, 1 g/kg (maximum 25 g) sucrose, dissolved in 100 ml of water, are orally administered. Breath is sampled immediately before and 30, 60, 120, and 150 minutes after substrate intake.

RESULT: The cut-off value for distinguishing patients with sucrose intolerance from normals is D = 20 ppm.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

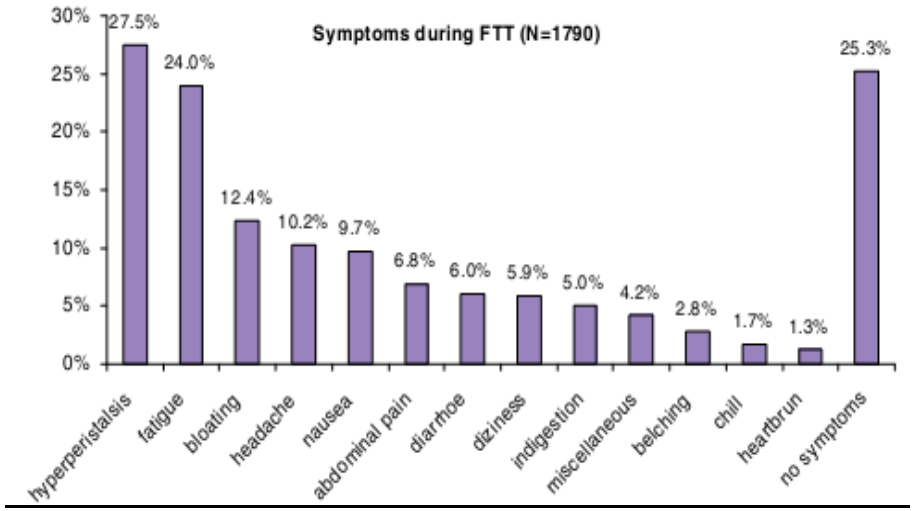
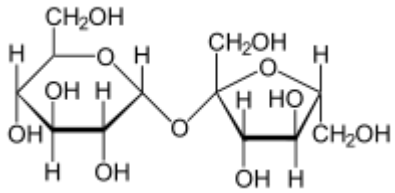


figure 2

Internet Notes :

Sucrose (or Saccharose) **intolerance**, also called **congenital sucrase-isomaltase deficiency** (CSID)[1] **Sucrase-isomaltase deficiency**,[2] is the condition in which sucrase, an enzyme needed for proper metabolization of sucrose, is not produced in the small intestine. It is more common among the Inupiat.[3]	 Sucrose

Internet scientific References

1. ^ Sander P, Alfalah M, Keiser M, *et al.* (January 2006). "Novel mutations in the human sucrase-isomaltase (SI) gene that cause congenital carbohydrate malabsorption". *Hum. Mutat.* **27** (1): 119. doi:10.1002/humu.9392. PMID 16329100.
2. ^ Baudon JJ, Veinberg F, Thioulouse E, Morgant G, Aymard P, Charritat JL (April 1996). "Sucrase-isomaltase deficiency: changing pattern over two decades". *J. Pediatr. Gastroenterol. Nutr.* **22** (3): 284–8. doi:10.1097/00005176-199604000-00010. PMID 8708882.
3. ^ Meier RJ, Draper H, Milan F (January 1991). "Pedigree analysis of sucrose intolerance among Native Alaskans". *Arctic Med Res* **50** (1): 8–12. PMID 2021397.

External internet links

- http://www.csidinfo.com/
- http://www.orphan-europe.com/sucrase_mangel_gb.html
- http://www.sucraid.net/
- http://en.wikipedia.org/wiki/Sucrose_intolerance#cite_note-pmid16329100-0

5. d-Xylose H2/CH4-Breath Test (Gluten Enteropathy)

- The D-xylose-H2-breath test is used for diagnosing and management of intestinal malabsorption e.g. **coeliac disease.**
- **Celiac disease is genetic. (autoimmune disease)** destruction of the villi,
- **In normals D-xylose ($C_5H_{110}O_{5)}$ is absorbed in duodenum and upper jejunum** (but less rapidly than glucose and galactose).
- Unlike glucose the test does not discriminate between bacterial overgrowth and malabsorption in the small intestine.
- **Celiac disease appears by eating foods with gluten, immune system responds by damaging the small intestine**. Gluten is a protein in wheat, rye and barley. It is found mainly in foods but may also be in other products like medicines, vitamins and even the glue on stamps and envelopes.
- Celiac disease affects each person differently**. Symptoms may occur in the digestive system, or in other parts of the body**. One person might have diarrhea and abdominal pain, while another person may be irritable or depressed. Irritability is one of the most common symptoms in children. Some people have no symptoms.
- **Blood or urinary D-xylose test can help clinicians to diagnose coeliac disease. Clinician may also need to take biopsy and examine a small piece of tissue from small intestine**.

- But H2-breath test with D-xylose is a useful and **practical test for the screening and follow-up of celiac disease and is simpler and more reliable** than the blood or urinary D-xylose test and certainly for biopsy

- Pancreatic diseases

PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the Bacterial Overgrowth:
There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort including: pain, diarrhea, gas, cramping or bloating.

Implementation of the xylose-H2-breath test:

Substrate	Dosage	Readings (min)	Positive	Remark
D-Xylose Adults children	25 g in aqueous solution in 250 ml water 5-g D-xylose	0–15–30–60–90–120a,b	>20 ppm	*Remark : Usually the so-called cut-off value (Delta), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference D exceeds this critical value, a certain metabolic anomaly must be assumed)*

After overnight fast, for determining xylose absorption, 25 g D-xylose in aqueous solution are administered. The faster the substrate is absorbed, the smaller is the amount of the substrate, which arrives at the colon and can be fermented there to form hydrogen. Breath is sampled immediately before and 45, 90, 135 and 180 minutes after substrate intake.
Results : The cut-off-value for distinguishing patients with intestinal absorption deficiencies from normal is Delta = 20 ppm.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

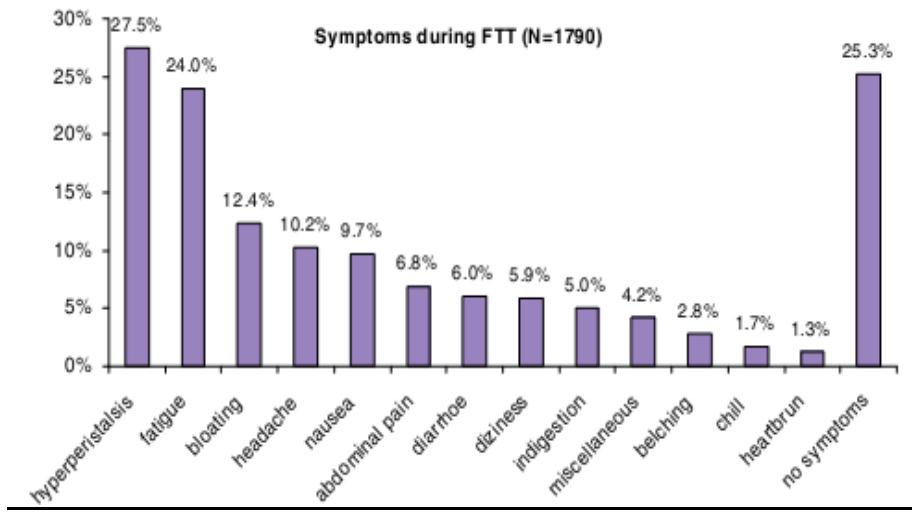


figure 2

Internet scientific References

***D-xylose* kinetics and hydrogen breath tests in functionally anephric patients using the 15-gram dose. *J Clin Gastroenterol.* 2000 Jul;31(1):55-9.**
Craig RM, Carlson S, Ehrenpreis ED.
Source
Department of Medicine, Northwestern University Medical Center, Chicago, Illinois 60611, USA.
Abstract
*Malabsorptive evaluation in renal failure is difficult because most absorptive testing requires urinary collections. Kinetic analysis of **d-xylose absorption and d-xylose breath testing** were performed in an effort to establish an effective absorption test in functionally anephric patients. We studied 13 fasting renal failure patients with no diarrhea or symptoms suggesting malabsorption on two separate nondialysis days after they received 15 g oral d-xylose on day 1 and 10 g IV on day 2. Serum collections were used to calculate the kinetic rate constants and extent of d-xylose absorption. **After the oral d-xylose, end expiratory breaths were collected every 15 minutes for 3 hours and were analyzed for H2 with gas chromatography**. Five subjects also allowed upper endoscopy and duodenal biopsy. The mean absorption rate constant (Ka) and bioavailability (F) were similar to published values for normal subjects using the 15-g dose (0.936 min(-1); range, 0.227-1.96; and 74%, range 46-99, respectively). Of the patients, 12 had normal 1-hour serum d-xylose concentrations (>20 mg/dL). There was no clear inverse correlation between the rate constant for absorption or bioavailability and peak breath hydrogen or the area under the curve for breath H2 versus time. Using 15 g oral d-xylose, mean bioavailability and absorption rate constants are normal in functionally anephric patients with no clinical evidence of malabsorption. Three patients had elevated breath peak H2 concentrations, but there was no clear inverse correlation between bioavailability and the breath H2 values. A 1-hour serum dxylose concentration >20 mg/dL may be considered normal in this patient group, similar to patients with normal renal function.*
PMID:10914778[PubMed - indexed for MEDLINE]

Hydrogen breath test with D-xylose for celiac disease screening is as useful in the elderly as in other age groups.
http://www.ncbi.nlm.nih.gov/pubmed/11680597
Casellas F, Sardi J, de Torres I, Malagelada JR.
Source
Department of Pathology, Hospital General Vall d'Hebron, Barcelona, Spain.
Abstract
Up to one fifth of celiac disease patients are diagnosed after the age of 60. The hydrogen breath test with D-xylose as substrate (xylose-BT) has proved useful for the diagnosis of adult celiac disease. Our aim was to determine the potential influence of age-related intestinal mucosal changes on the reliability of this test. We reviewed the results of the xylose-BT in 50 patients with clinical celiac disease in whom the diagnosis was confirmed by histology. A control group of 53 patients with various diarrheal disorders and without jejunal mucosal atrophy at biopsy was similarly studied. Both celiac patients and controls were divided into adults (age < or = 60 years) and elderly (age >60 years). Seven of the 50 celiacs and 8 of the 53 controls were in the elderly category (P = NS). In the celiac disease group, no differences were observed between the elderly and adult patient subgroups for basal H2 excretion (22.4 +/- 42 vs 9.7 +/- 11 ppm), delta increase (56 +/- 43 vs 53 +/- 36 ppm), or area under the curve (7,452 +/- 5,546 vs 6,739 +/- 5,951 ppm x min). The false negative rate was similar for celiac adult (7/43) and elderly (2/7, P = ns) patients. Sensitivity of the xylose-BT was 0.83 in adults and 0.71 in the elderly, and specificity 0.51 in adults and 0.50 in the elderly. In conclusion, the results of the xylose-BT in celiac patients are not influenced by age. The xylose-BT is as valuable a tool for the screening of celiac disease in the elderly as it is in younger patients.
PMID:11680597[PubMed - indexed for MEDLINE]

Follow-up of celiac disease with D-xylose breath test.
http://www.ncbi.nlm.nih.gov/pubmed/8888728
Casellas F, De Torres I, Malagelada JR.
Source
Digestive System Research Unit, Hospital General Vall d'Hebron, Barcelona, Spain.
Abstract

Hydrogen breath tests (H2-BT) are commonly used to diagnose carbohydrate malabsorption. Specifically, the H2-BT with D-xylose has been shown to be as valid as the traditional urinary test for the recognition of intestinal malabsorption. We have now investigated the H2-BT with D-xylose in the follow-up of patients with celiac disease. Seventeen patients with celiac disease established clinically and confirmed by jejunal biopsy were studied. H2-BT was performed before and after treatment with a gluten-free diet for at least five months. Alveolar breath samples were obtained before administering orally 25 g of D-xylose and thereafter at 30 min intervals for 5 hr. Samples were analyzed for H2 by chromatography. Simultaneously, the 5-hr urinary excretion of D-xylose was determined by colorimetry. Gluten removal significantly decreased the H2 delta change (from 56.5 +/- 5.9 ppm to 32.2 +/- 8.8, P < 0.05). A similar decrease was observed in the area under the curve (P < 0.05). Conversely, urinary D-xylose excretion increased significantly (P < 0.05). Eleven of the 17 celiacs clinically improved after treatment. The H2-BT normalized in every patient who entered remission on the gluten-free diet, whereas the urinary D-xylose excretion remained abnormal in six of them. In the six nonresponder patients the H2-BT remained high in five, whereas urinary D-xylose excretion paradoxically normalized in 2. We conclude that H2-BT with D-xylose is a useful and practical test for the follow-up of celiac disease and is simpler and more reliable than the urinary D-xylose test.
PMID:8888728[PubMed - indexed for MEDLINE]

Potential usefulness of hydrogen breath test with D-xylose in clinical management of intestinal malabsorption.
http://www.ncbi.nlm.nih.gov/pubmed/8425444
Casellas F, Chicharro L, Malagelada JR.
Source
Digestive System Research Unit, Hospital General Vall d'Hebron, Autonomous University of Barcelona, Spain.
Abstract
Hydrogen breath tests (H2 BT) have been used extensively to investigate intestinal disaccharidase deficiencies. A potentially useful test for assessing intestinal absorptive function, the H2 BT with D-xylose (H2 BT-D-xylose), has received scant attention. We report here the results of our investigation of this test in 45 patients. Fifteen patients had proved malabsorption that was due to nontropical sprue in nine, and to lymphoma, Whipple's disease, or giardiasis in the remainder. Nine patients had small-bowel bacterial overgrowth secondary to either postsurgical sequelae or intestinal dysmotility. Twenty-one patients with irritable bowel syndrome and 21 healthy individuals served as control groups. All participants ingested 25 g of D-xylose, and alveolar breath samples were obtained thereafter at 30 min intervals for 5 hr. Breath H2 was measured by chromatography. Basal H2 production, peak change (delta) and area under the curve (AUC) were calculated. Simultaneously, 5-hr urinary excretion of D-xylose was measured by colorimetry and served as the reference test. In healthy individuals, D-xylose ingestion increased H2 production (delta = 5.8 +/- 1.4 ppm, P < 0.001). Changes were similar in patients with the irritable bowel syndrome. In contrast, the increase was of a much greater magnitude in the malabsorption group (delta = 49.9 +/- 7.2 ppm, P < 0.001 vs healthy controls). AUC analysis yielded comparable results. Test performance analysis showed that, in malabsorption the H2 BT-D-xylose had a sensitivity index of 0.86, which was identical to that of the urinary D-xylose test. Specificity was 1 and 0.95, respectively; and predictability 1 and 0.93, respectively.(ABSTRACT TRUNCATED AT 250 WORDS)
PMID:8425444[PubMed - indexed for MEDLINE]

External internet links

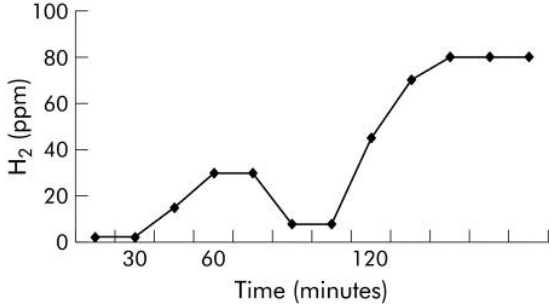
6. Lactulose- H2/CH4-Breath Test

- Lactulose is an **artificially synthesized disaccharide** composed of **fructose and galactose**, for which an **enzyme splitting it into the corresponding monosaccharide does not exist.**

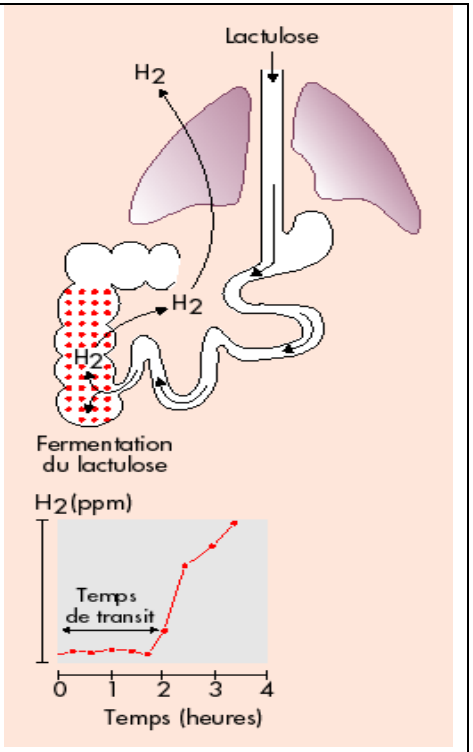
  1. **Lactulose H2 Breath test** is often used for measurement of **Intestinal Transit Time (ITT)**, important baseline test to assess how long it takes food to pass through digestive system.

  2. This test is also commonly used for **Small Intestinal Bacterial Overgrowth (SIBO)**

Plots of H2-concentration in breath over time after ingestion of lactulose may therefore have the following shapes:



A positive lactulose hydrogen breath test indicating small intestinal bacterial overgrowth with an easily detected early peak due to small bowel bacteria, clearly distinguishable from the later prolonged peak corresponding to the passage of the remaining lactulose into the colon.



a) Normal.

For want of a suitable enzyme lactulose is not split into the monosaccharides. Normally, bacterial overgrowth in the small intestine does not exist. At the end of the orocoecal transit time the test substance therefore arrives at the large intestine, where it is fermented to form hydrogen (or methane). Hydrogen (or methane, respectively) is absorbed through the intestinal wall and then dissolved into the bloodstream, released into the lungs through the alveolar blood capillary vessels surrounding the alveoli, and finally expired. (Alveolar gas)

b) Pathologic.

Because of pathology, bacterial overgrowth of the small intestine fermentation and production of hydrogen already starts in the small intestine.

The lactulose-H2-breath test is the most widespread non-invasive test for determining **orocoecal transit time**. It serves to investigate the residence time of certain food constituents, particularly carbohydrates, in the intestinal system.

PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the lactulose Bacterial Overgrowth

There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort from ingestion.

Implementation of the lactulose-H2-breath test:

Substrate	Dosage	Readings (min)	Positive (Delta)	Remark
Lactulose Adults children	10 g in 150 ml of water (adults) 3.34 g in isotonic soltn. (children < 6 months) 6.68 g in isotonic soltn. (children > 6 months)	0–15–30–60–90–120–150–180 0, 30, 60, 120, 150 0, 30, 60, 120, 150	<10 ppm >20 ppm	(non-H2-production; evaluation of transit time) **Not recommended on children** *Remark : Usually the so-called cut-off value (Delta), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)*

Children up to an age of six months ingest 3.34 g lactulose in isotonic solution (3.34 g/5 ml Duphar-Duphalaco-syrup), children older than six months (6.68 g lactulose/10 ml syrup). Adults are supplied with (10 g lactulose dissolved in 150 ml of water). Breath samples are taken immediately before and 30, 60, 120 and 150 minutes after substrate ingestion.

Results : If the H2-content of breath increases by more than 20 ppm after having taken up 20g lactulose and compared to reference value, then carbohydrate malabsorption must be assumed.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

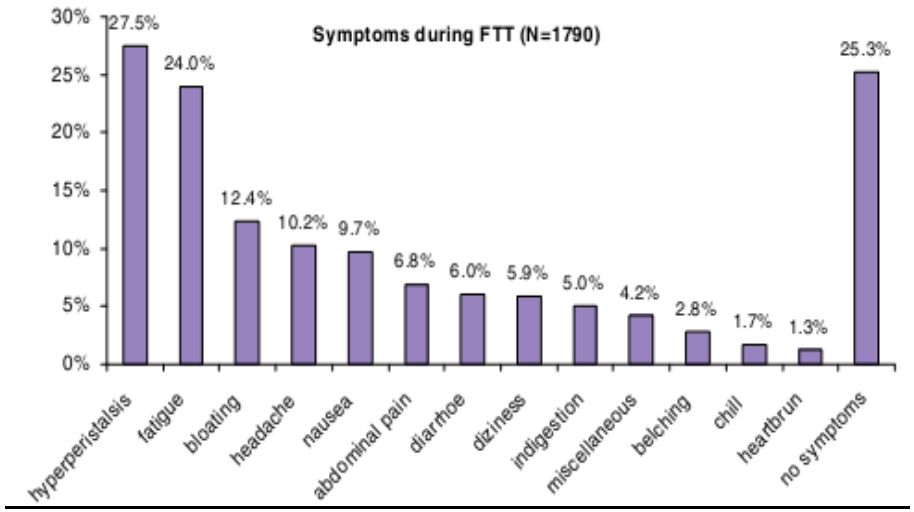


figure 2

Internet scientific References

Breath hydrogen response to lactulose in healthy subjects: relationship to methane producing status.

Source *D Cloarec, F Bornet, S Gouilloud, J L Barry, B Salim, and J P Galmiche Laboratoire d'Explorations Fonctionnelles Digestives, Hôpital Guillaume et René Laënnec, Nantes, France.*

Abstract

In order to assess the relationship between methane (CH4) producing status and the breath excretion of hydrogen (H2) in healthy subjects, breath CH4 and H2 were simultaneously measured for 14 hours after oral ingestion of 10 g lactulose in 65 young volunteers. Forty were breath CH4 producers and 25 were not. Statistically significant differences were observed between both groups, with lower values for CH4 producers recorded for the following parameters: fasting basal value of breath H2 (8.1 (4.9) v 5.2 (3.7) ppm, p less than 0.05), mouth-to-caecum transit time (68 (24) v 111 (52) min, p less than 0.005), and breath H2 production measured as area under the curve 13.1 (6.9) v 8.8 (3.8) 10(3) ppm/min, p less than 0.02). There was no significant correlation between individual production of breath H2 and CH4. These results indicate that the response to lactulose depends on breath CH4 producing status. In clinical practice, defining normal values of mouth-to-caecum transit time without knowledge of breath CH4 producing status may lead to misinterpretation of the H2 breath test.

Orocecal transit time and bacterial overgrowth in patients with Crohn's disease.

Castiglione F, Del Vecchio Blanco G, Rispo A, Petrelli G, Amalfi G, Cozzolino A, Cuccaro I, Mazzacca G.

Source

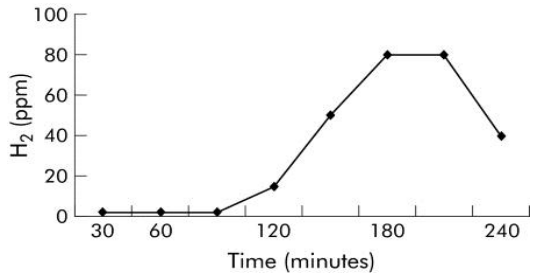
Cattedra di Gastroenterologia, Facoltà di Medicina, Università Federico II, Naples, Italy.

Abstract

Bacterial overgrowth is frequent in patients with Crohn's disease (CD) and can contribute to symptoms. Motility abnormalities can predispose to bacterial overgrowth. The hydrogen (H2) and methane (CH4) breath test is a sensitive and simple tool for the diagnosis of bacterial overgrowth and for the evaluation of orocecal transit time (OCTT). In this study, we investigated the prevalence of OCTT modifications and bacterial overgrowth in a series of consecutive adult patients with CD. In 43 healthy subjects and 67 patients with CD. we performed the lactulose breath test using a gas analyzer that offers the opportunity of measuring both H2 and CH4. Of the patients, 24 had undergone an ileocolic resection before the test with ablation of the ileocecal valve. At the time of the test 15 patients had active disease, whereas in 52 subjects the disease was quiescent. Fifty-seven patients and forty controls were evaluable for OCTT and bacterial overgrowth. In 10 patients and in 3 controls, no H2 or CH4 peak was recorded during the 8-hour test. Out of 57 patients, 13 (23%) were affected by bacterial overgrowth. The prevalence of bacterial overgrowth was higher in patients with previous surgery (30%) than in nonoperated patients (18%). In all patients with bacterial overgrowth, an antibiotic treatment induced a normalization of the test and an improvement of the symptoms. We observed a longer OCTT in the patients compared to controls, although this difference was not statistically significant (154 +/- 45 vs. 136 +/- 45 minutes). OCTT was significantly longer compared to controls in the 14 CD patients with previous ileocolic resection (180 +/- 53 vs. 136 + 45 minutes; p < 0.004). In conclusion, we found that a significant proportion of unselected patients with CD has bacterial overgrowth and prolongation of OCTT. We suggest that the modifications in OCTT in patients with CD can predispose to bacterial overgrowth. The lactulose breath test is a simple method that can be more widely used in patients with Crohn's disease. *J Clin Gastroenterol. 2001 Mar;32(3):274-5.*

External internet links

7. The Sorbitol-H2/CH4-Breath Test



Schematic drawing of hydrogen breath tests with or without sorbitol indicating carbohydrate malabsorption.

- For the **diagnosis of coeliac disease** occasionally also the H2-exhalation with breath after intake of the hexavalent alcohol sorbitol can be measured.
- Sorbitol is absorbed in the small intestine.
- **Sorbitol is an artificial sweetener**, very similar in appearance and with similar physical characteristics to both sucrose and dextrose sugars.
- However, **unlike the sugars, Sorbitol is not a carbohydrate**. Rather, Sorbitol is a **hexahydric alcohol**, or an **"alcohol sugar".** The chemical formula is $C_6H_{14}O_6$, which is similar to dextrose, except with 2 additional hydrogens atoms.
- Although sorbitol occurs in nature, it is manufactured commercially by the reduction of glucose (dextrose).

PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

- One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

- Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the Bacterial Overgrowth Breath Test:

There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort from ingestion of sucrose including diarrhea, gas, cramping or bloating.

Implementation of the sorbitol-H2-breath test:

Sbstrate	Dosage	Readings (min)	Positive		Remark
Sorbitol Adults children	12.5 g Sorbitolin 250 ml water **Not Yet on children**	0–15–30–60–90–120a,b	>20 ppm		Not on children

After a 12-hour fasting period (12.5 g sorbitol, dissolved in 250 ml of distilled water), are administered orally. During the fasting period and the test itself the individuals take only tea, coffee or tap water and refrain from higher physical activity. Breath sampling is taken immediately before and 30, 60, 120, 180 and 240 minutes after substrate intake

Results

Use a cut-off value of Delta = 10 ppm for distinguishing coeliac disease patients from normals.

Remark : Usually the so-called cut-off value (Delta), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

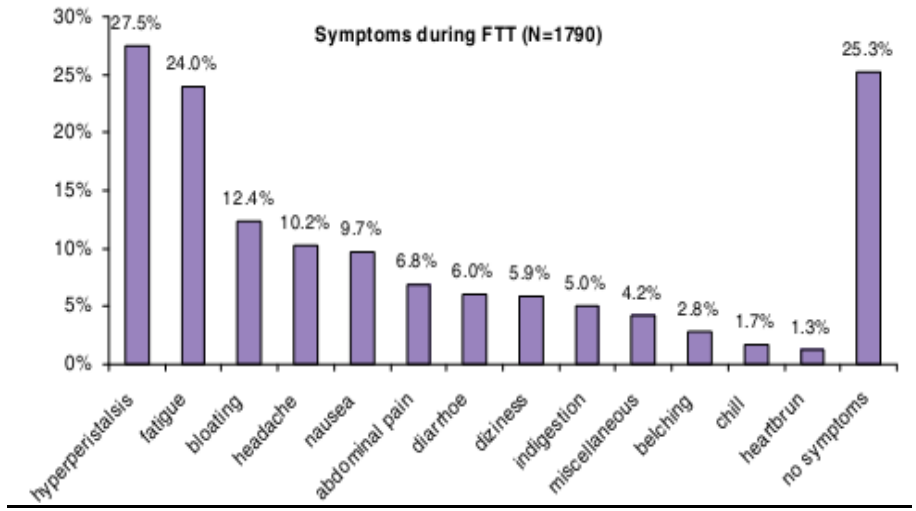


figure 2

Internet scientific References

Sorbitol H2-breath test versus anti-endomysium antibodies to assess histological recovery after gluten-free diet in coeliac disease.

Tursi A, Brandimarte G, Giorgetti GM.

Source

Emergency Department "L. Bonomo" Hospital, Andria, BA, Italy. antotursi@tiscali.it

Abstract

BACKGROUND:

Gluten-free diet plays a key role in treatment of coeliac disease, but it is difficult to evaluate its effect on improvement of villous architecture using sensitive non-invasive tests.

AIMS:

To compare sorbitol H2-Breath Test with antiendomysial antibodies in the follow-up of coeliac disease to detect histological recovery

METHODS:

A total of 38 consecutive patients with coeliac disease were studied. All underwent Sorbitol H2-Breath Test, antiendomysial and oesophagogastroduodenoscopy with multiple bioptic samples before diet and then 6, 12 and 18 months after gluten-free diet. Expiratory samples were collected before patients drank the test solution (5 g sorbitol in 150 ml tap water) and thereafter every 30 min for 4 hours. An increase in H2 concentration of > or = 20 ppm above fasting baseline was considered positive for sorbitol malabsorption. Antiendomysial antibodies were evaluated by the indirect immunofluorescent method.

RESULTS:

Antiendomysial antibodies were positive in 32/38 patients before gluten-free diet (84.21%), while they were positive in 20/34 (54.82%), 2/16 (12.5%) and 0/2 (0%) cases after 6, 12 and 18 months of gluten-free diet, respectively, no correlation being found with improvement of histological lesions (p = ns). As far as concerns sorbitol H2-Breath Test, maximal cut-off value (in ppm) decreased progressively and parallel to histological recovery during follow-up. Indeed, it decreased from a mean 63 ppm before diet to 35, 19 and 12 ppm, after 6, 12 and 18 months of gluten-free diet, with a stetistical difference being found before and after (p < 0.001). Likewise, the peak value (in minutes) appeared progressively later during follow-up, parallel to histological recovery. In fact, it appeared at a mean of 119 minutes before gluten-free diet, while it appears at a mean of 164, 195 and 219 minutes after 6, 12 and 18 months on gluten-free diet. A statistical difference before and after start of gluten-free diet was found also in this case (p < 0.001).

CONCLUSIONS:

Sorbitol H2-Breath Test is better than antiendomysial antibodies in revealing histological recovery in the follow-up of coeliac patients after the start of gluten-free diet due to its good correlation with histological damage. Moreover, it also appears to be able to detect dietary mistakes of the patients on gluten-free diet.

PMID:12643292 [PubMed - indexed for MEDLINE]

External internet links

6. Xylitol - H2/CH4-Breath Test

- **Xylitol is a sugar substitute** and, as such, is often **added to the so-called 'sugar-free' food** under the name **E-967**. The Xylitol tolerance test (XTT) is used to diagnose xylitol intolerance. Xylitol is not sufficiently absorbed by many people so that, not infrequently, irritable bowel symptoms can be triggered by food containing xylitol. In spite of this, the XTT is only carried out rarely. From a clinical point of view, the characteristics of xylitol are very similar to those of sorbitol.
- **Indications** for a xylitol tolerance test are suspected xylitol intolerance **(intolerance of chewing gum, boiled sweets, diabetic products etc.)** and borderline positive results in the fructose tolerance test or sorbitol tolerance test. We recommend giving a load of 12.5 g of xylitol dissolved in 250 ml of water. **This test is generally not yet carried out on children**.

PREPARATION

Optimal Patient Preparation Before H2/CH4 BREATH –TESTS

- Patients should not be tested within four (4) weeks of a colonoscopy or barium enema.
- Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
- Patients should avoid laxatives, stool softeners or stool bulking agents one (1) week prior to the test including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.

Foods and Drinks the Day Before the Test:

- **These foods and drinks are best:** Plain white bread, plain white rice, plain white potatoes, baked or broiled chicken or fish, water, non-flavored black coffee or tea. Salt may be used to flavor your food.
- **These foods and drinks should be avoided:** Beans, pasta, meats (steaks), fiber or bran cereals, soda (pop) cola drinks, butter or margarine and high fiber foods (whole grains).
- STOP EATING AND DRINKING 12 HOURS BEFORE THE TEST

The Day of the Test:

- DO NOT eat, drink, chew gum or tobacco, smoke cigarettes, eat breath mints or candy before or during the test.
- DO NOT sleep or exercise before or during the test.
- DO TAKE prescription medications with a small amount of water.
- DO BRUSH your teeth prior to the test.

Optimal exhalation procedure during H2/CH4 BREATH –TESTS

One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample: therefore we suggest normalizing Breath-test Gas Measurement with good established instruction procedure with proper expiration technique. Sample bags must be empty and no residual air may remains in the bag before patient exhalations ….see appendix

Optimal Preparation of equipments Before H2/CH4 BREATH –TESTS

Inappropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see appendix

Potential Complications of the Bacterial Overgrowth Breath Test:

There are very few potential serious complications during the 1-hour testing. In severe cases patients may feel minor discomfort from ingestion of **Xylitol** including diarrhea, gas, cramping or bloating.

Implementation of the Xylitol -H2-breath test:

Substrate	Dosage	Readings (min)	Positive Delta	Remark
Xylitol Adults children	12.5 g Xylitol in 250 ml water **Not Yet on children**	0–15–30–60–90–120a,b	>20 ppm	• Not on children • ***Remark*** *: Usually the so-called cut-off value (**Delta**), (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed)*

a. Additional reading after 45 min for evaluation of test substance dependent SIBOS.
b. Additional reading after 150 min and 180 min if slow transit time is suspected.

RESULT INTERPRETATION

- After an overnight fast as above mentioned, 12.5 g, **Xylitol** dissolved in 250 ml of water, is orally administered. Alveolar gas (deep end expiratory breath) is sampled immediately before substrate intake, and thereafter every 0,15,30,60,90,120,150 minutes.
- Readings of the H2 level should be taken at 0, 15, 30, 60, 90 and 120 min after the xylitol load. H2 levels of more than 20 ppm above the basal value indicate a positive test result, and should be interpreted according to the guidelines described in Appendix
- If H2-concentration ascends by more than **Delta = 20 ppm**, then bacterial overgrowth of the small intestine must be assumed. Sensitivity and specificity of the glucose-H2-breath test, however, are only in the order of 60 to 90% or 75 to 100%, respectively. Nevertheless the test went its way for want of better alternatives.

SYMPTOMS

1. The production of comparable and reliable results of **hydrogen breath tests does not just require a standardized implementation** of the breath test but also exact documentation about symptoms.

2. Apart from measured H2 levels, **it is above all necessary to establish the symptoms** that existed each time a measurement is taken.

3. The establishment of symptoms is essential for the interpretation of the test results and is of major importance for the clinical consequences.

4. The symptoms that may occur during a test are not at all limited to intra-gastrointestinal symptoms such as **: hyper-peristalsis, diarrhea, bloating, cramping, abdominal pain, gas, constipation, etc**…

5. But also frequently, the patient experiences extra-intestinal symptoms such as **fatigue, dizziness, headache or heartburn** (see figure 2).

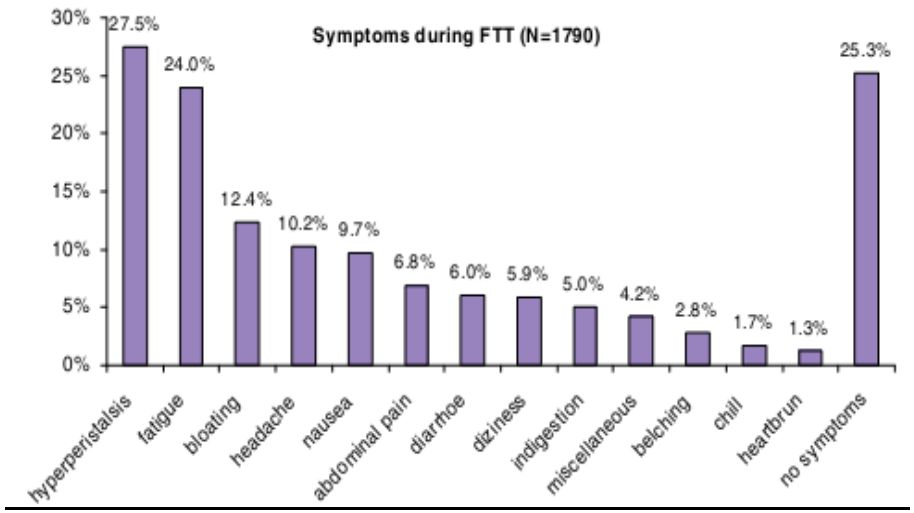


figure 2

Appendix 01 BREATH TEST IMPLEMENTATION (recommendations consensus Italy)

Methodology and indications of H2-breath testing in gastrointestinal diseases (H 2 -BREATHTESTING CONSENSUS CONFERENCE WORKING GROUP) Final statements from the First Rome Consensus Conference (H2-breath testing: methodology in adults and children) A GASBARRINI*, G. R. CORAZZA, M.MONTALTO*,G.GASBARRINI* & THEROME

Substrate	Challenge doses	Breath Sampling intervals [min]	(Delta) [ppm]	Interpretation of results
Lactulose Bacterial overgrowth	Children (< 6 months) 3.34 g in water Children (> 6 months) 6.68 g in water Adults 0.5 g /Kg body weight and max 10 g (15ml) in 150 ml of water (adults)	30,60,90,120,150,180, 30,60,90,120,150,180, 30,60,90,120,150,180,210,250	>20 >20 >20	Positive : Lactulose biphasic pattern in H2/CH4 levels , 2 peaks with an early increase of at least 12 ppm followed by a second much larger increase 20ppm after one hour. Two peaks may merge as an early plateau establish the symptoms that existed each time a measurement is taken
Lactulose Intestinal transit time	Children 0.5g /Kg body weight Adults 0.5g /Kg body weight and 10 g (15ml) in 150 ml of water (adults)	30,60,90,120,150,180, 30,60,90,120,150,180,210,250	>20	Normal mean time for Lactulose testing 70 to 75 min H2/CH4 rises min 3 ppm over the previous level for at least 3 successive time intervals establish the symptoms that existed each time a measurement is taken
Lactose malabsorbsion	Children 1 g/kg BW in 10 ml of water Adults 1 g/kg BW and max 20 g in 250 ml of water	30,60,90,120,150,180, 30,60,90,120,150,180,210,250 ,	>30	Positive if H2 increase of at least 20ppm over the lowest preceding value within the test period and/or CH4 levels increases by 12ppm over the baseline value within the test period establish the symptoms that existed each time a measurement is taken
D-Xylose Celiac disease	Children 1 g/Kg BW in 10 ml water Adults 25 g in 250 ml water	30,60,90,120,150,180, 30,60,90,120,150,180,210,250	>20	Increase of either H2 or CH4 levels 20ppm within 40-60 minutes suggests bacterial overgrowth. A later increase suggest impairment of intestinal capacity establish the symptoms that existed each time a measurement is taken
Saccharose (sucrose)	Children 2g/kg in 100 ml of water Adults 20 g in 250 ml of water	30,60,90,120,150,180, 30,60,90,120,150,180,210,250	>20	H2 level increase of at least 20ppm over the lowest preceding value within the test period . CH4 level increase of at least 12ppm within the test period establish the symptoms that existed each time a measurement is taken
Glucose Bacterial overgrowth	Children 1 g /Kg BW in 10 ml water Adults 1 g /Kg BW and max 25 g in 250 ml of water	30,60,90,120,150,180, 30,60,90,120,150,180,210,250	>10	Positive: Increase of at least 10 ppm breath H2/CH4 over the baseline value establish the symptoms that existed each time a measurement is taken
Fructose (*)	**Not yet evaluated on children** Adults 1g/kg 25 g max in 250 ml of water	30,60,90,120,150,180,210,250	>20	An increase of H2 or CH4 of 20ppm indicates a transport impairment establish the symptoms that existed each time a measurement is taken
Sorbitol	**Not yet evaluated on children** 0.25 g to 0.5 g /Kg Adults 12.5 g in 250 ml of water	30,60,90,120,150,180,210,250	>20	An increase after 60 min is normal . An increase of 20 ppm after with cramps indicates sensitivity to Sorbitol establish the symptoms that existed each time a measurement is taken
Fructose-Sorbitol	**Not yet evaluated on children** 12.5g fructose + 12.5g sorbitol in 250 ml water	30,60,90,120,150,180,210,250	>20	An increase after 60 min is normal . An increase of 20 ppm after with cramps indicates sensitivity to Fructose-Sorbitol establish the symptoms that existed each time a measurement is taken
Xylitol	**Not yet evaluated on children** 12.5 g in 250 ml water	30,60,90,120,150,180,210,250	>20	An increase after 60 min is normal . An increase of 20 ppm after with cramps indicates sensitivity to Xylitol establish the symptoms that existed each time a measurement is taken

(*) The test is absolutely contraindicated above all to children with suspected hereditary fructose intolerance and for patients with inherited fructose intolerance.

Guidelines for the interpretation of breath test results

- The interpretation of hydrogen breath test results is based on three crucial factors: H2 and CH4 exhalation level, appearance of symptoms and the time-dependent change of these two factors during the test period.
- Differences in the H2 concentration of 2–3 ppm during measurements taken in quick succession must be considered as random variation because the measuring uncertainty of the equipment is within this range. If, under the same trial conditions, the measured hydrogen values differ by more than 5 ppm, the device should be re-adjusted.
- The last column of the table presents "cut-off" or "threshold" values or **(Delta),** i.e. the minimum ascents of H2-concentration in breath after ingestion of test substance in comparison to the H2-concentration in breath when fasting, which indicate pathologic metabolic situations.

Methodology information

Appendix 01 bis BREATH TEST IMPLEMENTATION (recommendations concensus Austria)

Implementation of hydrogen breath tests.

*This is a summary overview of the parameters for the **Implementation and interpretation** of the most common hydrogen breath-tests. By Alexander Eisenmann1, Anton Amann2,4, Michael Said3, Bettina Datta1 and Maximilian Ledochowski1,4,5 (1 Department of Clinical Nutrition, Medical Hospital of Innsbruck, Austria2 Department of Anesthesia and General Intensive Care, Medical University of Innsbruck, Austria3 Department of Medicine, Military Hospital 2, Innsbruck, Austria4 Breath Research Unit of the Austrian Academy of Sciences, Dammstr 22, 6850 Dornbirn, Austria) E-mail: maximilian.ledochowski@tilak.at* Received 29 May 2008, in final form 2 July 2008 Published 24 July 2008 Online at stacks.iop.org/JBR/2/046002

Substrate	Dosage	Readings (min)	Positive		Remark
Fructose Adults children	25 g in 250 ml in 10 ml BW water (max. 25 g) 1 g/kg BW in 10 ml water/kg BW (max. 25 g)	0–15–30–60–90–120a 0–15–30–60–90–120a	>20 ppm >20 ppm		
Lactose Adults children	1 g/kg BW in 10 ml water/kg (max 50 g in 250 ml water) 1 g/kg BW in 10 ml water/kg BW (max. 50 g)	0–15–30–60–90–120a 0–15–30–60–90–120a	>20 ppm >20 ppm		
Glucose Adults children	50 g in 250 ml water (max. 50 g) 1 g/kg BW in 10 ml water/kg BW (max. 50 g)	0–15–30–45–60 0–15–30–45–60	>10 ppm >10 ppm		
Lactulose Adults children	10–20 g **Not Yet on children**	0–15–30–60–90–120–150–180	<10 ppm >20 ppm	(non-H2-production) (evaluation of transit time)	
Sorbitol Adults children	12.5 g Sorbitolin 250 ml water **Not Yet on children**	0–15–30–60–90–120a,b	>20 ppm		Not on children
Sorbitol/Fructose Adults children	12.5 g fructose +12.5 g sorbitol in 250 g water **Not Yet on children**	0–15–30–60–90–120a,b	>20 ppm		Not on children
Xylitol Adults children	12.5 g Xylitol in 250 ml water **Not Yet on children**	0–15–30–60–90–120a,b	>20 ppm		Not on children

a Additional reading after 45 min for evaluation of test substance dependent SIBOS.
b Additional reading after 150 min and 180 min if slow transit time is suspected.

Methodology information

Appendix 02

GUIDELINES and METHODOLOGY

ITALY

Methodology and indications of H2-breath testing in gastrointestinal diseases (H 2 -BREATHTESTING CONSENSUS CONFERENCE WORKING GROUP) Final statements from the First Rome Consensus Conference (H2-breath testing: methodology in adults and children)

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AUSTRIA

Methodology and indications: Implementation and interpretation of hydrogen breath-tests

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Appendix 03 :

Breath -Test PREPARATIONS

PATIENT PREPARATION PROCEDURE BEFORE H2/CH4 BREATH –TESTING

1. Depending from the type of breath tests measurements patient needs preparation procedure and should not be performed less than four weeks after therapy with antibiotics, bowel lavage or enteroscopy. Patients should not be tested within four (4) weeks of a colonoscopy.
2. Patients should not take antimicrobials and should try to avoid bismuth preparations (Pepto Bismol) within 3 to 4 weeks prior to administering the small intestinal bacterial overgrowth breath test.
3. One (1) week prior to the test Patients should avoid laxatives, stool softeners or stool bulking agents including: Colace, Milk of Magnesia, Ex-Lax, Metamucil or Citrucel.
4. Starting 24 hours before substrate uptake and during the test, beans, pies, larger amounts of apples, onions, leeks, garlic, cabbage, pickled cabbage bread fresh from the oven and other heavy food must not be taken in.
5. The patient should fast for at least 12 h Prior to the test,. During this time, he must not drink anything apart from water. In particular, he must be advised to avoid milk and/or fruit juice on the day prior to the test. The last meal on the day preceding the test should not be too ample and should ideally not consist of any fiber.
6. Before taking up the test meal with the substrate patients have to fast at least for12 hours. *(!!During this time and during breath sampling chewing gums must not be used because they usually contain sorbitol which may be fermented to form hydrogen in the intestinal system).* He must be informed to not eating breath mints or candy before or during the test
7. Starting at least 12 hours before the ingestion of the substrate the individuals must abstain drinking alcohol and avoid physical strain.
8. Twelve 12 hours prior to the test the patient should stop smoking. If, due to an oversight, the patient does smoke, it is still possible to conduct the test at a low basal H2 value (<5 ppm). If, repeatedly, increased basal H2 values are measured in a patient, it is recommended to measure the exhaled content of carbon monoxide (CO) to establish whether the patient did smoke shortly before the test.
9. Apart from vitamins, laxatives and antibiotics, medicines can be taken with pure water on the day of the examination.
10. During the test patient should not sleep or do exercises.
11. Wearers of dentures must not use an adhesive on the day of the test. The claim that it is contraindicated to brush the teeth prior to the breath test because most types of toothpaste contain sorbitol or xylitol is incorrect. In our sample we have never encountered problems due to patients' brushing teeth in the morning. In contrast, when patients fail to brush their teeth, increased basal H2 concentrations may occur and even distort the test result. Besides, carrying out the test on patients who did not brush their teeth beforehand is unpleasant for the patient and the staff involved.

MEASUREMENT PROCEDURE DURING H2/CH4 BREATH –TESTS

1. Alveolar air, i.e. the last part (about 150 ml), of one single expiratory action starting from normal respiratory level and tidal volume has to be collected. First immediately before (reference levels) and then in certain intervals for several hours after the intake of substrate or the test meal. Breath sampling intervals, as well as the amounts of substrates to be administered, are indicated in tables or monographs, respectively.
2. Evaluation of the measured data is based on the course of H2/CH4 concentrations **in exhaled gas** in dependence on time in comparison with the H2/CH4 concentration **in the inhaled air**. **(attention for ambient methanol, ethanol volatile gases who can influence zero settings of analyzers)**
3. Usually the so-called "cut-off" or "threshold" value (**Delta)**, (i.e. the difference of the maximum H2-concentration in breath a certain time after substrate intake minus the H2-concentration immediately before substrate intake), is used as the diagnostic criterion. If this difference Delta exceeds this critical value, a certain metabolic anomaly must be assumed.
4. Since the gastric residence times of any substrate scatter in a wide range even in normal and H2/CH4 production usually does not begin before the substrate has passed stomach and duodenum, breath sampling must not be finished, before the H2/CH4 concentration in breath has passed its maximum.

EQUIPMENT PREPARATION BEFORE H2/CH4 BREATH-TESTS MEASUREMENTS

1. Depending from the type of breath tests equipment check for appropriate preparation of the analyzers, installation stable temperature, zero setting, full-scale calibration, etc……see manuals …….maintenance procedure , Calibration procedure (span zeroing linearity) etc ….

Appendix 04 GLOSSARY OF USED TERMS

- **Absorption**: Transfer of final food components into the intestinal mucosa
- **Bacterial overgrowth:** Too high a concentration of bacteria (in the small intestine)
- **Deficiency:** Lack of a biologically active substance
- **Digestion:** Decomposition of (commonly high molecular) food components by secretions of salivary glands, stomach, liver, pancreas and small bowel acting together Disaccharidase deficiency: Want of disaccharidases (in the small intestine)
- **Disaccharidases:** Enzymes, which cleave disaccharides to form corresponding monosaccharides. E. g. the disaccharide lactose in the small intestine is split up by lactase to form the monosaccharides galactose and glucose, which are absorbed in this part of the intestine.
- **Disaccharides:** Products of coupling two monosaccharides with one another in such a way that the aldehyde or keto group of one of the monosaccharides forms a glycoside with an OH-group of the other monosaccharide. Examples: Saccharose, composed of glucose and fructose; lactose, composed of galactose and glucose; maltose and trehalose, composed of two glucose molecules. Apart from the identity of the monosaccharide components disaccharides differ from each other in ring size of the respective semiacetals (5- or 6-membered rings) and in the manner these rings are connected with each other (ˋ- or ß-glycosidic connection).
- **Fructose:** Hexose with a keto group (ketohexose) in position 2
- **Galactose:** Hexose with an aldehyde group (aldohexose)
- **Glucose:** Hexose with an aldehyde group (aldohexose)
- **Hexoses:** Monosaccharides with six carbon atoms. Examples: glucose, fructose, mannose, galactose, sorbose
- **Intolerance:**Incompatibility with lactose, fructose and some other substances used in connection with breath tests
- **Isomaltose:** Disaccharide from two glucose molecules formed by enzymatic degradation of starch or amylopectine
- **Lactose intolerance (hypolactasia):** Lactase deficiency (in the small intestine)
- **Lactulose:** Synthetic disaccharide of fructose and galactose, for which an enzyme splitting it into the corresponding monosaccharides does not exist. Test substance for determining orocoecal transit time by the corresponding H2-breath test
- **Malabsorption:** Disorder of absorption of final food products through the intestinal wall
- **Mannose:** Hexose with an aldehyde group (aldohexose)
- **Monosaccharides:** (Mostly) linear chains from several, mostly fife (pentoses) or six (hexoses) carbon atoms with one terminal aldehyde (─CHO-) group (aldoses) or a keto group in position 2 (ketoses), while the remaining carbon atoms except from hydrogen carry one ─OH-group each Oligosaccharides:Products of coupling two (disaccharides) or several (trisaccharides, tetrasaccharides etc.) monosaccharides with one another in such a way that the aldehyde or keto group of a monosaccharide forms a glycoside with an ─OH-group of a neighbouring monosaccharide
- **Optical activity:** All chemical compounds with one or more carbon atoms having four different neighbours (ligands) rotate the plane of polarised light either to the right or to the left, that is to say they are optically active, dextro-rotatory or lævo-rotatory. In view of the tetrahedral structure of such an asymmetric carbon atom the corresponding molecules exist in two different forms, the one being the mirror image of the other. These so-called optical isomers are found either in pure form, especially in their natural occurrences, or as an equimolecular mixture of both forms. Optical isomers the molecular symmetry of which corresponds with the molecular symmetry of that isomer of tartaric acid, which rotates the plane of polarised light to the right, are named D-isomers, those corresponding with the other optical isomer of tartaric acid L-isomers. (Small letters d and l characterise the real sign of rotating the plane of polarised light, which is not necessarily identical with the sign of molecular symmetry itself. In case of tartaric acid this coincidence was brought about by definition.)
- **Pentoses:** Monosaccharides with five carbon atoms. Example: xylose
- **Polysaccharides:** Products of coupling many monosaccharides with one another in such a way, that the aldehyde or the keto group of one monosaccharide forms a glycoside with an ─OH-group of a neighbouring
- monosaccharide. Examples: starch, cellulose
- **Sorbose**: Hexose with a keto group in position 2 (ketohexose)
- **Sugars:** Crystalline mono- or oligosaccharides, readily soluble in water and tasting sweetly; in the narrower sense the disaccharide saccharose or sucrose obtained from sugar cane or sugar beets
- **Sweeteners:** 1. Some water-soluble, sweetly tasting substances other than sugars, which are also fermented in the intestinal system forming H2 (or CH4) and therefore can be also used as test substances for H2 -(or CH4-)breath tests (mannitol, sorbitol) 2. Water soluble, synthetic chemical compounds, the sweetening power of which considerably exceeds that of saccharose, glucose, maltose and other natural sugars. Not suitable for performing H2-breathtests

Appendix 05 Questions about H2/CH4 Breath Testing

Improper preparation of equipment:
Inappropriate preparation of the analyzers, stable temperature, zero setting, full-scale calibration, etc… (to complete)
Sample bags not empty and sampled gas is contaminated by residual air remaining in the bag before patient exhalations …. (to complete)

Improper conservation of the sampled gas:
Containers, tabs, etc …must be air tight and not diffusing gasses (to complete)

Normalizing Breath-Gas Measurements:
One of the sources of error in trace-gas analyses is contamination of the alveolar gas sample with dead space air during its collection. The problem is minimized by properly using the sampling system or the to collect properly the alveolar sample. However, if they are not used according to instructions, or if the syringe is contaminated with room air during transfer of the sampler to **MEC LACTOTEST 102 ™** or **MEC LACTOTEST 202 ™** the H2 and/or CH4 in the sample may be diluted so that falsely low concentrations will be indicated. The other source of error is that sampled gas is not end expiratory gas (alveolar gas) but mixed gas contaminated with lung dead space gases.
Therefore **MEC LACTOTEST 102 ™ & 202** can be used to correct the analysis of trace breath-gases for such small contamination. It is based on the concept that carbon dioxide (CO2) is present in alveolar gas at a virtually constant concentration, (5% CO2) while it is essentially absent in room air. Therefore, if alveolar air is erroneously mixed with room air or if patient didn't exhale end alveolar gas, the concentration of CO2 will be reduced, as will that of any trace gases present in the sample. By knowing the degree to which the CO2 was diluted, it is possible to apply a correction to the analysis of the trace-gas as well, thus being able to calculate the true "alveolar gas" concentration of the sample which was contaminated.

Improper preparation of the patient:
The inappropriate choice or incomplete avoidance of food by the patient on the night before the test will provide a high, but gradually falling level of hydrogen (H2) and methane (CH4) on which the test will be superimposed. This is because the amount of fiber in the colon will be elevated at the beginning of the test, and will fall during the hours of the measurement. Even if H2 is produced from the challenge-dose of carbohydrate, it may not exceed the initial baseline level by enough to be classified as a positive test.

Sleeping:
Allowing the patient to sleep during the test will cause an increase in breath- hydrogen (H2) and methane (CH4). This probably has two causes. Hypoventilation, which is an inadequate rate of air turn-over in the lung, slows down the rate of hydrogen (H2) and methane (CH4) removal from the blood. Sleep also decreases motility, which slows down the movement of carbohydrates through the colon and allows a longer time for hydrogen (H2) and methane (CH4) production. Thus, intermittent sleeping during the test will interfere with its reliability and should not be allowed.

High Baselines:
High fasting levels (> 10ppm) of trace gases at the beginning of the test may suggest that the patient did not follow instructions for complete avoidance of carbohydrate and fiber the night before; but it also may suggest that the patient has small intestinal bacterial overgrowth (SIBO).

Small Intestinal Bacterial Overgrowth (SIBO):
Bacterial overgrowth exposes the complex sugars and other soluble carbohydrates in the small intestine to bacterial fermentation instead of allowing them to be hydrolyzed enzymatically and absorbed in the relatively sterile intestine. If bacteria are introduced into the small intestine, they can survive and thrive in the nutritionally rich environment. As indicated above the harsh, acid environment of the stomach kills most bacteria, so there is a low bacterial count in the proximal part of the intestine (the duodenum and the jejunum). However, in achlorhydria (lack of acid production in the stomach) bacteria may pass into the small intestine and colonize there. Alternately, conditions of intestinal hypomotility ("blind-loop" syndrome or other causes of "stasis") permit bacteria to invade the small intestine from the colon. These conditions permit an increase in bacterial count to over 105 (100,000) bacteria per milliliter (mL) of intestinal contents, which defines the condition called "bacterial overgrowth". The condition leads to symptoms similar to those for carbohydrate malabsorption. It also, destroys some vitamins, interferes with the absorption of fatty acids and competes for sugars and other foodstuff ordinarily absorbed in the jejunum. Thus, it is a serious digestive disturbance which can be treated effectively, but only if it is diagnosed.

Appendix 06

Other Breath Testing information, resources and articles

- The place for all things SIBO - Dr. Allison Siebecker
- Small Intestinal Bacterial Overgrowth in Patients With Lower Gastrointestinal Symptoms and a History of Previous Abdominal Surgery
- Methane on breath testing is associated with constipation, featured in Digestive Diseases and Sciences.

- Small intestinal bacterial overgrowth in irritable bowel syndrome: are there any predictors?
- Small intestinal bacterial overgrowth syndrome.
- Stability of human methanogenic flora over 35 years and a review of insights obtained from breath methane measurements.
- Website on "A Community for Irritable Bowel Syndrome Sufferers"
- Website on "Just IBS" Facts about Irritable Bowel Syndrome (IBS)
- YouTube Video of Breath-Hydrogen Tests posted by Gastroenterologists, P.C. in Cedar Rapids, Iowa
- Implementation and Interpretation of Breath-Hydrogen Tests
- IBS and Sugar Intolerance: What does Research Say? - About.com
- UC HEALTH LINE: New Breath Test Can Detect Tummy Troubles "Dr. Ralph Giannella, MD, and colleagues in the digestive diseases division are now offering hydrogen/methane breath testing at University Hospital to help patients discover whether they have bacterial overgrowth in their small intestines or are lactose or fructose intolerant."
- Normalization of lactulose breath testing correlates with symptom improvement in irritable bowel syndrome: a double-blind, randomized, placebo-controlled study:
- Hydrogen glucose breath test to detect small intestinal bacterial overgrowth: a prevalence case–control study in irritable bowel syndrome:
- Abnormal breath tests to lactose, fructose and sorbitol in irritable bowel syndrome may be explained by small intestinal bacterial overgrowth:
- Breath Hydrogen and Methane Responses of Men and Women to Breads Made with White Flour or Whole Wheat Flours of Different Particle Sizes:
- IBS subjects with methane on lactulose breath test have lower postprandial serotonin levels than subjects with hydrogen:
- Your digestive system and how it works:
- **www.gipath.com** GI Pathology is fully licensed and accredited by the College of American Pathologists, CLIA, and the states of California, Florida, Maryland, New York, Pennsylvania and Rhode Island.
- **www.hydrogenbreathtesting.com** Commonwealth Laboratories, Inc. is a state and federally licensed clinical laboratory located in Massachusetts. Physicians can contact this company for breath-testing kits for mail-in analysis.
- Specialists in Gastroenterology in St. Louis, MO **www.gidoctor.net**, Specialists in Gastroenterology or SIG, is a G.I. group in St. Louis, specializing in gastro intestinal conditions.
- "A New IBS Solution takes you through the historical evolution of conventional medicine's views on IBS in a way that can be easily understood.
  In addition, Dr. Pimentel presents a simple treatment protocol that will not only help you resolve your IBS symptoms, but will also prevent their recurrence." **A New IBS Solution Website**
- Irritable Bowel Syndrome website contains useful information for patients: http://www.irritable-bowel-syndrome.ws/sibo-breath-test.htm
- BrainTalk Communities - Online Support Groups for Patients http://braintalkcommunities.org/forums