IPA test

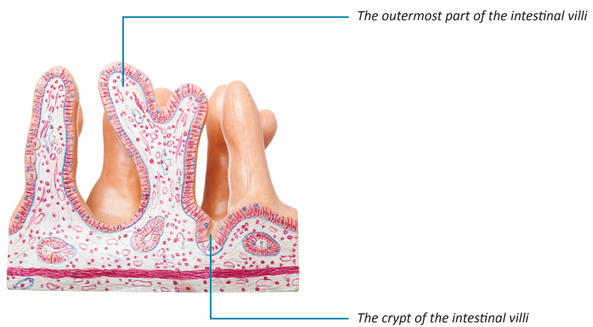
The theory behind the IPA test has been comprehensively reviewed, and by evaluating the past 30 years scientific literature, it is now possible to obtain a more in-depth understanding about intestinal function. The IPA test differs from other intestinal permeability tests in that it analyses five types of sugar and their correlative enzymes as opposed to only two types. With two sugars you are getting perhaps just two fifths of the clinical picture.

The IPA test provides an indication as to whether a patient suffers from one or more of the following clinical conditions: reduced absorption capacity; increased gastrointestinal permeability; inflammation; or lactose and sucrose intolerance – knowledge not previously obtainable from the two sugar tests. The test is carried out following the ingestion of a sugar solution containing the five different types of sugar: mannitol, sucrose, lactose, raffinose and cellobiose. The concentrations of the different sugars are identifiable in urine. The levels or their mutual ratios indicate whether the above clinical conditions are prevalent.

Intestinal function

The intestine has the paradoxical double function of being an absorbing organ as well as a barrier against permeation of toxic compounds and macromolecules. Both of these functions can be disturbed by various mechanisms such as inflammation, oxidative stress, dysbiosis, bacterial overgrowth and food reactions[1]. This may result in localised symptoms such as flatulence, rumbling tummy, stomach pain/cramps, constipation, diarrhoea or general discomfort as well as more systemic problems such as fatigue[2], eczema[1] and joint pain[3]. Therefore, a precise assessment of intestinal function is very useful in relation to creating an individualised treatment protocol. Intestinal absorption mechanisms are rather complex; roughly speaking, around three pore sizes are found in the intestinal mucosa. The smallest pores are located in the outermost part of the intestinal villi, the largest pores are located in the crypt (bottom) of the intestinal villi, and the medium-sized pores are located in between the other pores. These pores are made of tight junction proteins and regulate the molecular transport and absorption. Small molecules such as monosaccharides are transferred via the small pores, whereas larger molecules such as disaccharides can only be transported via the larger pores[4]. This basic knowledge serves as the evidence-based foundation for the test and explains how it is possible to extract valuable data about intestinal integrity and functionality from the concentrations of the sugar molecules in a simple urine sample.

Image showing the intestinal microvilli



The test is relevant for patients with the following symptoms and clinical conditions:

- *Irritable bowel syndrome, including bloating, rumbling and flatulence*
- *Constipation and diarrhoea*
- *Nutrient deficiency*
- *Fatigue*
- *Eczema*
- *Migraine*
- *Coeliac disease and Crohn's disease*
- *Food allergy and intolerance*
- *Rheumatoid arthritis, joint and muscle pain*
- *Ankylosing spondylitis*
- *Reiter's syndrome*
- *Schizophrenia and autism*

Possible causes of increased intestinal permeability:

- *NSAIDs*
- *Antibiotics*
- *Intestinal tract infections*
- *Bacterial overgrowth and dysbiosis*
- *Food reactions*
- *Chemotherapy and radiation damage*

Sample collection

The test kit contains the above-mentioned sugar mixture as well as the other collection components. The sugar mixture is dissolved in a glass of water to be drunk before bedtime. During the night and the following morning, the urine is collected in the measuring cup enclosed, and the contents are measured at least 8 hours after ingestion of the sugar solution. Approx. 20 ml is transferred to a test tube and sent to Nordic Laboratories for further analysis.

Test result

Below follows a presentation of the various markers measured in the IPA test and a description of the intestinal digestion and absorption of each type of sugar molecule as well as a description of the types of clinical conditions to consider, in case the levels measured are too high or one or more mutual ratios are imbalanced

Mannitol level – a measure of intestinal absorption capacity
Mannitol is a sugar alcohol of small molecular size which, under normal conditions, is absorbed in the upper part of the small intestine through the epithelial cells via the small pores in the brush borders (passive diffusion). It will then be traceable in the urine[5]. When the absorption of mannitol is suboptimal, it will not be found in the urine. This is an indication of reduced absorption capacity and hence the intestinal uptake of important nutrients is hindered, which could ultimately lead to a deficiency in vitamins and minerals[6,7].

Cellobiose level – a measure of intestinal permeability
Cellobiose is a disaccharide consisting of two glucose molecules. Cellobiose is not hydrolysed by the enzymes in the gastrointestinal tract. Under normal conditions, it will therefore be practically untraceable in the urine. Instead, it will pass through to the large intestine, in which it serves as a substrate for the intestinal flora. However, if cellobiose is found in the urine sample, this means that the sugar has been absorbed through the paracellular tight junctions. This reflects damage to the intestinal mucosa and a resulting increased intestinal permeability, which could ultimately lead to increased absorption of unwanted toxic substances and molecules[5].

Sucrose level – a measure of gastric permeability
Sucrose is a disaccharide consisting of glucose and fructose, also known as white table sugar. It is readily hydrolysed by the small-intestinal brush border enzyme sucrase (in the duodenum). Under normal conditions, sucrose is not traceable in urine. However, if sucrose is detected in the sample, it may be due to increased passive gastric absorption caused by irritation or mucosal inflammation[4,8,9].

Raffinose/mannitol ratio – a measure of damage to the small intestine
Raffinose is a trisaccharide consisting of galactose, fructose and glucose. Raffinose is not hydrolysed by the enzymes in the gastrointestinal tract. Under normal conditions, it will be untraceable in urine, since it will pass directly through to the large intestine, in which it serves as a substrate for the intestinal flora. However, if raffinose is absorbed via passive diffusion, it will be traceable in urine and be an indication of reduced capacity in the tight junctions and possible intestinal inflammation[10]. As mentioned above, mannitol is a small sugar molecule, the absorption of which is limited in cases of intestinal inflammation or damage, as in coeliac disease or Crohn's disease[11]. A high raffinose/mannitol ratio is an indication of damage to the epithelial tissue in the duodenum[12].

Lactose/raffinose ratio – a measure of lactose intolerance
Lactose is a disaccharide which is hydrolysed to galactose and glucose in the small intestine (primarily the jejunum) by the brush border enzyme lactase. Therefore, under normal conditions, lactose will not be identifiable in the urine. However, if lactose is identified in the urine the level of lactase in the small intestine is not sufficient to hydrolyse lactose optimally and the patient is likely to have increased intestinal permeability. A high lactose/raffinose ratio is an indication of lactose intolerance[12].

Sucrose/raffinose ratio – a measure of sucrose intolerance
The ratio between sucrose and raffinose is interpreted analogously to the lactose/raffinose ratio. A high sucrose/raffinose ratio is an indication of low activity of the enzyme sucrase in the small intestine (primarily the duodenum) and of sucrose intolerance. With a decreasing ratio, intestinal damage may be observed more distally[12].

Interpretation patterns

Experience from research and clinical use of the IPA test shows that it may be important to be aware of certain patterns in the results. The patterns are shown below.

↑ Lactose	↑ Raffinose	Secondary lactose intolerance due to inflammation. Suspected damage to the intestinal epithelium in the jejunum.
↓ Lactose	↑ Raffinose	Damage to the duodenum and ileum, but without lactose intolerance.
↑ Lactose	↓ Raffinose	Primary lactose intolerance (should be confirmed with a breath test or lactose challenge).
↑Sucrose	↑ Raffinose	Damage to the intestinal epithelium in the duodenum.
↑Sucrose	→ Raffinose	Damage to the gastric mucosa.
→Sucrose	↑ Raffinose	Damage to the intestinal epithelium in the ileum.
↑ Lactose/Raffinose	↑ Raffinose/Mannitol	Secondary lactose intolerance due to inflammation.
↑ Lactose/Raffinose	↓ Raffinose/Mannitol	Primary lactose intolerance due to genetic predisposition.
↓ Sucrose/Raffinose	↓ Lactose/Raffinose	Indicates distal damage to the small intestine.
↑ Sucrose/Raffinose	↑ Lactose/Raffinose	Indicates damage to the proximal part of the intestine or whether the entire intestine is impacted.
↑ Raffinose/Mannitol	↓→ Sucrose/Raffinose	Indicates distal damage to the small intestine.

↑ = high level or ratio ↓= low level or ratio → = normal level or ratio

Other relevant laboratory analyses

Based on the patient's symptoms and the results of the IPA test, it may be relevant to consider other tests in order to obtain a clearer picture of possible cause. Further specific treatment may then be initiated.

A comprehensive intestinal assessment from faeces
This test identifies imbalanced intestinal flora such as bacteria, fungus and parasites. It also provides information on pancreatic production of enzymes, and whether faecal protein and fat levels are too high, which may be an indication of low production levels of gastric acid and/or bile. Furthermore the test reveals any elevated inflammation markers related to micro-inflammation, Crohn's disease, colitis and levels of sIgA and short-chain fatty acids. This test combined with the IPA test provides a comprehensive overview of function throughout the gastrointestinal tract.

SIBO – Small intestinal bacterial overgrowth
This test is a breath test and determines the presence of bacterial overgrowth in the small intestine, based on the gas level in the exhaled air. Useful when possible inflammation has been detected with the IPA test.

Lactose intolerance
The gold standard breath test can be used as a further diagnostic tool after the IPA test has indicated lactose intolerance. The test determines the presence of lactose maldigestion based on gases measured in exhaled air.

Fructose intolerance
Can be considered when fructose maldigestion is suspected. The gold standard breath test determines the presence of fructose based on gases measured in exhaled air.

IgG Food intolerance
This test showing immune reactions to ingested food is an important consideration when intestinal permeability has been detected. It identifies IgG antibodies against foods and is valuable because identifying, and removing these foods from the diet, reduces toxic load and possible inflammation, in turn aiding the integrity of the intestinal barrier.

Gluten/gliadin IgA/IgG and tissue transglutaminase analyses
These tests reveal how the body reacts to the protein gliadin, typically found in wheat, rye and barley. This provides a basis for assessing whether the symptoms may be caused by coeliac disease or non-coeliac gluten intolerance. These are important screening tests irrespective of what the IPA shows, but even more pertinent with abnormal IPA results.

Organic acids
This test provides an insight into a wide variety of nutrition-related metabolic processes in the body, e.g. problems with detoxification, oxidative stress and, specifically, whether the patient has a dysbiosis (fungal and bacterial overgrowth in the small intestine). It is this dysbiosis which may be implicated in the function of the small intestine, and is therefore advisable if the IPA test reveals abnormalities.

Gene testing
Genetic testing is now possible, and is the advisable method when suspecting primary lactose intolerance and primary fructose intolerance. These tests are measured via a blood sample.

Contact us for more information
If you would like more information about our tests or have any other questions, then please feel free to give us a call or contact us by email. We are more then happy to help.

References

1. *Bjarnason, I., Macpherson, A. & Hollander, D. Intestinal Permeability: An Overview. Gatroenterol1 108, 1566–1581 (995).*
2. *Berstad, A., Undseth, R., Lind, R. & Valeur, J. Functional bowel symptoms, fibromyalgia and fatigue: a food-induced triad? Scandinavian journal of gastroenterology 8-9, 914–9 (2012).*
3. *Smith, M. D., Gibson, R. A. & Brooks, P. M. Abnormal bowel permeability in ankylosing spondylitis and rheumatoid arthritis. The Journal of rheumatology 12, 299–305 (1985).*
4. *McOmber, M. E., Ou, C.-N. & Shulman, R. J. Effects of timing, sex, and age on site-specific gastrointestinal permeability testing in children and adults. Journal of pediatric gastroenterology and nutrition 50, 269–75 (2010).*
5. *Juby, L. D., Rothwell, J. & Axon, A. T. Cellobiose/mannitol sugar test--a sensitive tubeless test for coeliac disease: results on 1010 unselected patients. Gut 30, 476–80 (1989).*
6. *Nieminen, U., Kahri, A., Savilahti, E. & Färkkilä, M. A. Duodenal disaccharidase activities in the follow-up of villous atrophy in coeliac disease. Scandinavian journal of gastroenterology 36, 507–10 (2001).*
7. *Heitlinger, L. A., Rossi, T. M., Lee, P. C. & Lebenthal, E. Human intestinal disaccharidase activities: correlations with age, biopsy technique, and degree of villus atrophy. Journal of pediatric gastroenterology and nutrition 12, 204–8 (1991).*
8. *Sutherland, L. R. et al. A simple, non-invasive marker of gastric damage: sucrose permeability. Lancet 343, 998–1000 (1994).*
9. *Wyatt, J. et al. Increased gastric and intestinal permeability in patients with Crohn's disease. The American journal of gastroenterology 92, 1891–6 (1997).*
10. *Lobley, R. W., Burrows, P. C., Warwick, R., Dawson, D. J. & Holmes, R. Simultaneous assessment of intestinal permeability and lactose tolerance with orally administered affinose, lactose and L-arabinose. Clinical Science 79, 175–83 (1990).*
11. *Dawson, D. et al. Changes in jejunal permeability and passive permeation of sugars in intestinal biopsies in coeliac disease and Crohn's disease. Clinical Science 74, 427–431 (1988).*
12. *Hessels, J. et al. Assessment of intestinal permeability: enzymatic determination of urinary mannito l, raffinose, sucrose and lactose on Hitachi analyzer. Clinical chemistry and laboratory medicine 41, 33–8 (2003).*

Nordic Laboratories

Nordic Laboratories was founded in 1998 with the goal to provide patients and practitioners with clear, reliable laboratory test results. Since then, we've become a leading European laboratory test distributor. We are completely independent and, as a result, are able to choose laboratory assessments from a wide range of suppliers, based on the individual quality and value of each test.

Our commitment to deliver the highest quality laboratory evaluations allows us to serve clients from Scandinavia to Spain, the US to the UK, Hong Kong, the Middle East, and South Africa.

Our clients receive their tests promptly and have access to the highly qualified members of the Nordic team, who can assist them with their order.

As a part of the Nordic Group of companies, we are intent on incorporating a functional medicine approach into modern medicine. This passion for health and sustainability is reflected in everything we do.

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IPA-analysis

(Intestinal permeability and absorption capacity)

Why settle for 2 sugars, when 5 makes life sweeter?

At Nordic Laboratories, we are innovative thinkers. We want to challenge laboratory science to offer testing that enables us to identify the causes of digestive conditions and thus help ensure that the best possible treatment can be implemented. Based on our review of the scientific literature from the past 30 years, we have arrived at the most comprehensive test for assessing intestinal permeability and absorption capacity.

The IPA test measures five types of sugar as opposed to the two types analysed in conventional permeability tests. Analytical results for five types of sugar provide additional knowledge of and insight into intestinal function – enabling you to offer individually optimised treatment protocols.

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