Leaky Gut Testing: The BHL #110

Leaky Gut – also known as intestinal permeability – describes a condition in which the lining of the small intestine becomes damaged, causing undigested food particles, toxic waste products, and bacteria to penetrate and enter the bloodstream. These foreign substances invading the bloodstream can cause autoimmune responses, including inflammatory and allergic reactions. These agents can cause local and systemic reactions associated with a broad range of diseases.

In addition to leaky gut’s role in “letting the bad things in” it also the culprit for keeping out the good; in the form of damaged cells which cannot adequately produce the substances necessary to aid in digestion of nutrients. A failure in the quality of nutrient intake is at the root of a myriad of health problems, including those which impact hormone balance and brain function.

Common Conditions Related to Leaky Gut

- Chronic constipation, diarrhea, or gas
- Weak immune system
- Headaches
- Excessive fatigue
- Depression or anxiety
- Skin rashes and problems such as acne or eczema
- Brain fog, memory loss
- Arthritis or joint pain

Leaky gut can be caused by damage from autoimmune reactions, such as gluten (gliadin) intolerance which destroys the mucosal layer, opens up tight junctions, and increases permeability. It can also be damaged by bacterial toxins related to Small Intestinal Bacterial Overgrowth (SIBO), which also contributes to intestinal barrier inflammation. Additionally, leaky gut can be caused by food sensitivities with the immune system activity in which white blood cells mount attack on undigested food particles. Stress - chronic and acute - will also contribute to a general lack of healthy gut balance.

How Does a Leaky Gut Affect Health?

If the tight junctions between cells get loose, larger proteins, microorganisms, and their components and toxins, can enter the bloodstream. Inflammation and an aberrant immune response are primary concerns with increased intestinal permeability, with numerous other problems to be considered.

- Inflammation can result from an immune response, infection, toxins and other substances that leak through the tight junctions and

Permeability of Intestinal Barrier
Demonstrated by penetration of lactulose and mannitol

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Kidneys: Urinary Excretion

- Low L/M Ratio: Normal
- No or low increased permeability
- High L/M Ratio: Abnormal
- Suggests increased intestinal permeability

Lactulose (L)
Mannitol (M)

Cells lining small intestine
Blood vessel

into the body. Tight junctions are dynamic structures involved in transport of water and electrolytes across the intestinal epithelium. The inflammation can be local (in the digestive tract) and cause problems such as abdominal discomfort, diarrhea, constipation and poor absorption of nutrients. The inflammation can also become systemic and affect various organs and organ systems. Local inflammation can also exacerbate the disruption of the tight junctions.

- Aberrant immune response that can mistake foreign proteins that have leaked through for self-proteins and result in autoimmune response.
- Exposure to allergens leading to autoimmune response and aggravation of existing allergenic functions.
- Chronic irritation to the gut lining leads to maldigestion and malabsorption of critical nutrients. Deficiencies result in a wide array of systemic problems.
- Chronic leaky gut can lead to an increased burden on hepatic detoxification systems. This can deplete important nutrient co-factors and increase toxic reactions.
- Increased passage of undigested food particles leads to the development of food allergies.
- Chronically impaired permeability affects the bowel’s barrier and immune function, leaving the body more susceptible to toxic substances and bacterial translocation.
About the Lactulose-Mannitol Urine Test

Leaky Gut can be assessed through the Lactulose/Mannitol test. The two different sized sugar molecules are excreted in the urine which reflects absorption from the gut and is a reliable representation of gut permeability. The smaller molecule (mannitol) freely crosses the gut barrier and is a general measure of small intestinal surface area; while the larger molecule (lactulose) is thought to only cross through the small intestine if pores are enlarged or cells are damaged.

To assess intestinal permeability, lactulose and mannitol excretion is recovered in urine. Variations in transit time in the intestine and renal clearance are normalized through the use of a ratio calculation which reflects the proportion of large to small sugars. This ratio is the researched criteria for assessing suspected intestinal permeability. It is important to note that the accuracy of the results is dependent on patient adherence to test preparations and instructions as well as normal renal function.

BioHealth’s Lactulose-Mannitol Testing

- **Peak Excretion Measurement:** We’re testing peak excretion and representing the “suspected intestinal permeability” interpretation based on the ratio at this time point. The ratio is in place to account for variations in gastric emptying, intestinal transit, renal clearance, and incomplete urine recovery which are factors that affect the lactulose and mannitol equally.

- **Test Method:** Advanced testing methodology of liquid chromatography–mass spectrometry (LC-MS) has advantages over enzymatic methods given the large analyte concentration range. LC-MS has high accuracy, the ability to detect a broad range of concentrations, and minimal interferences.

- **Convenient Collection Process:** Using a pre/post baseline challenge 4-hour collection - following literature guidelines to capture peak excretion times - instead of a pooled collection - eliminates the need for bulky urine collection containers and inconvenient collection experiences. There is also an easy to use vacuum pressure collection device that eliminates the need for messy pipette transferring and reduces contamination and bacterial growth by reducing sample exposure to air.

- **Simple Interpretation:** Results are explained clearly through the Lactulose-Mannitol Ratio guideline that is well established in research and clinical communities.

Interpretation

Listed below are basic interpretation guidelines for lactulose and mannitol. (See sample report on last page).

- Elevated lactulose to mannitol ratio (L/M ratio) – Elevation of the L/M ratio can occur because of increased absorption of lactulose in higher proportion to mannitol. This scenario indicates a loss of tight junction integrity and leaky gut. Severity of leaky gut is rated as mild, moderate or high:
  - Mild - L/M ratio greater than 0.03 up to 0.07
  - Moderate - L/M ratio greater than 0.07 up to 0.10
  - High – L/M ratio greater than 0.10

**NOTE:** An elevated L/M ratio could occur too from low mannitol absorption. However, in this situation the lactulose would be normal.

- Low mannitol with normal lactulose – this can occur from loss of the absorptive surface of the epithelial cells. Tight junctions may still be intact. Ratio between lactulose/mannitol may be elevated, despite lactulose levels in the urine being normal.

Basic Scenarios

1. The higher the level of lactulose, indicates the higher level of leaky gut and damage to the tight junction found between epithelial cells. A leaky gut often leads to increased food reactions, e.g. allergies or sensitivities, inflammation, joint and muscle pain, headaches and fatigue.

2. The higher level of lactulose/mannitol ratio generally correlates to high lactulose absorption and advanced leaky gut. Similar symptoms to that of high lactulose apply as well. However, it is possible to have a high lactulose/mannitol ratio if the mannitol itself is very low.

3. Low mannitol indicates poor function of the absorptive surface of the epithelial cell. It is possible to have poor epithelial surface function, but normal tight junction integrity. Poor absorption can lead to weight loss, poor growth, hair loss, diminished skin and nail integrity and vitamin and mineral deficiencies.

Considerations

There are many things that can cause damage or disruption to the intestinal barrier. Listed here are some common considerations when evaluating an abnormal Intestinal Permeability Test:

- **Acute or chronic infections** – Bacteria and/or parasites can lead to damage of the intestinal barrier. Giardia, for example, damages the epithelial cells leading to poor absorption of nutrients, whereas Clostridia difficile carrier releases toxins that severely damage tight junctions leading to leaky gut.

- **Food allergies/sensitivities** – Consuming foods that trigger inflammation in the digestive system can lead to leaky gut and/or poor absorption. A well-known example is Celiac disease. For people with Celiac disease, the consumption of gluten triggers adverse immune reactions to the epithelial cells compromising nutrient absorption. In severe situations, leaky gut may occur through breakdown of the tight junction as well.

- **Lifestyle** – Consuming unhealthy foods and drinks, e.g. processed, high sugar, trans-fats, alcohol, caffeine can all lead to irritation along with epithelial surface. The consumption of a diverse amount of plant-based foods, organic and healthy fats has a restorative and health promoting influence on the digestive system.

- **Drugs/ Antibiotics** – Overuse of certain pharmaceutical drugs can lead to disruption of the intestinal barrier. For example, antibiotics can lead to depletion of normal intestinal bacteria which themselves promote a healthy gut. The overdose of medications like Ibuprofen (non-steroidal anti-inflammatory drug, NSAID) can lead to irritation and epithelial cell damage.
• **Stress** – Increased stress, whether from emotional/mental or physical factors, can lead to depletion of normal immune function in the digestive system. With the loss of immune protection there is increased potential for opportunistic infections such as invasive candida.

• **Candida** – Candida, and other yeast organisms, although commonly commensal to the digestive system, can lead to leaky gut through increased conversion to invasive forms. Candida, for example, produces hypha which are known to disrupt the tight junction between epithelial cells.

• **Chemical toxins** – There are various environmental chemicals that can lead to intestinal barrier disruption. One example is glyphosate, a common herbicide chemical. Glyphosate can lead to disruption of the healthy bacteria in the digestive system which leads to an increased potential for opportunistic bacteria and invasive candida.

### Related Testing

When leaky gut is discovered, there are well-established as well as modern approaches to treatment, with emphasis on lifestyle, diet, and supplementation with impactful nutrients, especially the amino acid L-glutamine, and botanicals such as cat’s claw bark extract and quercetin.

But to discover and address the cause of the leaky gut will make a dramatic difference in the speed of recovery and likelihood of remission. Some of the most common lab tests for identifying dysfunction and disease which drives intestinal permeability, include:

- Bacteria and yeast cultures
- Food allergy/sensitivity testing
- Parasite and pathogen testing on stool
- Small Intestinal Bacterial Overgrowth (SIBO) breath testing

### For Suggestion on Treatment Options for Leaky Gut, contact Client Services at 800-570-2000 or through biohealthlab.com.

### References


### Intestinal Permeability Test ( #$110$ )

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose Baseline</td>
<td>&lt;0.2</td>
<td>ug/mL</td>
</tr>
<tr>
<td>Mannitol Baseline</td>
<td>23.0</td>
<td>ug/mL</td>
</tr>
</tbody>
</table>

**Lactulose Result**

- **Result**: 65 ug/mL
- **Reference Range**: <= 42 ug/mL

**Mannitol Result**

- **Result**: 213 ug/mL
- **Reference Range**: 66 - 449 ug/mL

**Lactulose/Mannitol Ratio:**

- **Result**: 0.06
- **Reference Range**: <= 0.03

**INTERPRETATION**: Intestinal Permeability is suspected based on Lactulose/Mannitol Ratio result.

Baseline levels may be raised if patient did not adhere to dietary and fasting preparations. Lactulose is not expected to be present in the baseline sample and baseline mannitol should not exceed the post-drink mannitol result.

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**Traditional determination of laboratory ranges includes the central 95% of an apparently healthy population. Comparing results against additional intervals within these standard ranges allows for a more precise assessment of patient values. Yellow zones were established based on a study of the central 68th percentile within the healthy population and are not necessarily abnormal and should not be used as absolute cut-offs for patient diagnostic criteria. Results should always be interpreted in the context of other external diagnostic and clinical information specific to the patient.**

*The guidelines are for research purposes only.*
Interpretive Guidance

Intestinal Permeability can be assessed through the Lactulose/Mannitol test. The two different sized sugar molecules are excreted in the urine which reflects absorption from the gut and is a reliable representation of gut permeability. The smaller molecule (mannitol) freely crosses the gut barrier and is a general measure of small intestinal surface area; while the larger molecule (lactulose) is thought to only cross through the small intestine if pores are enlarged or cells are damaged (sometimes referred to as "leaky gut"). This can often occur in patients with celiac disease, patients with damage due to allergens, inflammation, pathogens, or NSAIDS.

To assess intestinal permeability, lactulose and mannitol excretion is recovered in urine. Variations in transit time in the intestine and renal clearance are normalized through the use of a ratio calculation which reflects the proportion of large to small sugars. This ratio is the researched criteria for assessing suspected intestinal permeability. It is important to note that the accuracy of the results are dependent on patient adherence to test preparations and instructions as well as normal renal function.

Lactulose: Rate of excretion is variable and dependent on diet and renal clearance.

Mannitol: Rate of excretion is variable and dependent on diet and renal clearance.

L/M Ratio: Intestinal permeability is measured as a ratio of lactulose and mannitol sugars excreted in urine (L/M ratio). Literature has established L/M Ratio normal cutoff is 0.03. Patients with values above 0.03 should be assessed for possible intestinal permeability.

References: