



What is the best available way to test for intestinal permeability?

The new screening test for intestinal permeability, using the protein biomarker **Zonulin**, has now become available. This is an important new development in clinical diagnosis and treatment planning. How does this new test compare to what has been available up to now?

There are many other tests that have been used to try to determine intestinal permeability. Unfortunately most of these tests are not validated for that purpose.

As an example, the well-known **lactulose/mannitol** test has been used, for the most part, for scientific research but not for clinical diagnosis. The test can be time consuming (6 hours, or more), relatively complicated to perform and difficult to interpret. It must be done under very tightly controlled conditions. One has to make sure that the patient is taking the sugars, that the urine is collected properly and sent to the lab immediately and that the right HPLC (High-performance liquid chromatography) is performed. In addition, it has a poor correlation with macromolecule permeability, the hallmark of “leaky gut” problems.

There are stool tests, such as the one for **alpha 1-antitrypsin**, that highlights a protein-losing enteropathy and is an indication of intestinal permeability or



“leaking”. However, this test is positive only in the most severe cases of intestinal hyperpermeability.

Intestinal toxemia & anaerobe overgrowth can be determined with the **Indican** (Opermayer) urine test. Normally there are low levels of this organic compound in urine. These levels increase with high protein diets or inefficient protein digestion. If there is inadequate digestion, putrefaction can occur in the colon. This is not a particularly sensitive test and is not suited for determining gut permeability.

Then of course, there are tests for **antibodies** against the components making up the tight junctions in the intercellular space between enterocytes, such as **occludin and ZO-1**. However, this kind of antibody response is not seen in most autoimmune diseases. For example, in celiac disease, the autoimmune response is not against the tight junctions, but against gluten. That is, there may be a change in tight junction functionality without an autoimmune response.

Damage to intestinal permeability or dysbiosis can be determined by testing **Bacterial Lipopolysaccharides (LPS)** through blood IgG, A and M. Normally these LPSs are not found in blood, but only in the intestine. Finding blood levels means there has been a significant tight junction barrier breach, allowing bacterial components, like LPS, to be absorbed. However, although there may be a very significant breach of the intestinal barrier, with clinical manifestations, it



may still be insufficient to permit enough LPS to be absorbed in a quantifiable manner.

The primary screening test, that determines tight junction damage is the level of serum **Zonulin**. It is easy to do, and actually tests for changes in the tight junctions. Changes in Zonulin levels are directly correlated to changes in intestinal permeability and the penetration of macromolecules through the intercellular intestinal barrier.

Clinically, how will the Zonulin test change patient treatment?

It is of the greatest importance to have a biomarker of intestinal permeability because it allows the clinician to say: There is a problem that, if fixed, may help manage this condition. For example, if the problem is due to bacterial contamination, the use of probiotics or other molecules will help fix the problem.

Most importantly, however, is prevention. There is ample evidence that regulation of **Zonulin** can prevent the onset of diabetes by years. It is also possible to predict increases in bowel inflammation by looking at gut permeability. Those with increased permeability are the most likely to have an increase in bowel



inflammation in the months that follow, while the ones that have a normal permeability do not.

There is also increasing evidence that **Zonulin** plays a role not only in control of the intestinal barrier, but also in control of the blood brain barrier. The entry of antigenic components past the gut and the brain barriers, as well as the role played by the microbiome, are now leading to a better understanding of the role played by the gut in diseases such as Multiple Sclerosis and Autism, and others.

Therefore, proper clinical assessment can be tremendously enhanced by a validated biomarker of gut permeability. The first of such protein biomarkers is **Zonulin**, which is now validated for simple dried blood spot testing and available for use.