PRECISION POINT DIAGNOSTICS Advanced Intestinal Barrier Assessment

A "Targeted" Approach to Wellness

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PATIENT INFO	
NAME:	John Doe
REQUISITION ID:	DAO211470002
DOB:	12/8/1991
SAMPLE DATE:	4/20/2021
RECEIVE DATE:	4/21/2021
DRAFT DATE:	7/7/2022

CLINIC INFO

RESEARCH & DEVELOPMENT
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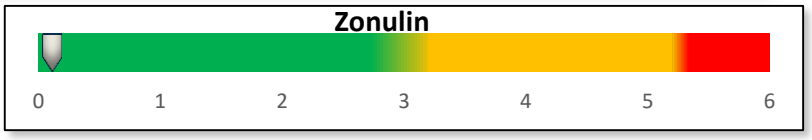
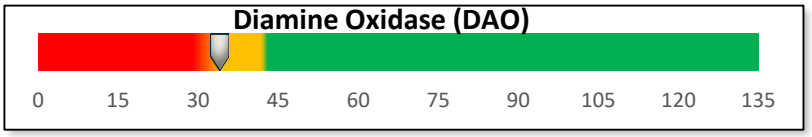
ADVANCED INTESTINAL BARRIER ASSESSMENT (PLASMA) | 1/2

0.11
Normal Range: < 3.19 ng/ml
NORMAL

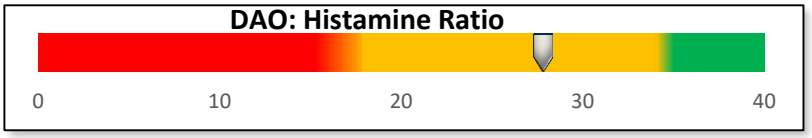


34.00
Normal Range: > 42.9 ng/mL
LOW



1.22
Normal Range: < 1.2 ng/mL
NORMAL

27.82
Normal Range: > 34.0 ng/mL
BORDERLINE LOW



A high DAO-to-Histamine ratio suggests that there is sufficient DAO present to degrade any free histamine.

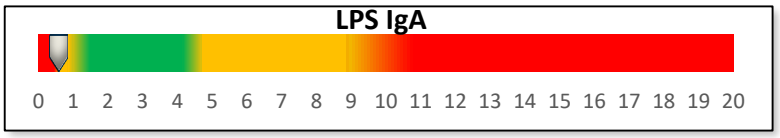
Conversely, a low DAO:Histamine ratio may be more indicative of histamine intolerance.

This test has been developed and its performance characteristics determined by Precision Point Diagnostics. It has not been cleared by the U.S. Food and Drug Administration.

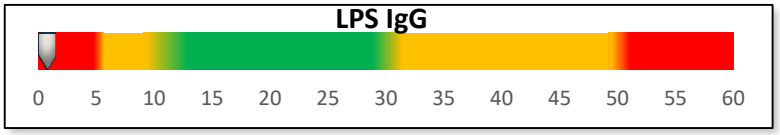
PATIENT NAME:	John Doe	REQUSITION	DAO211470002	DRAFT DATE:	7/7/2022

ADVANCED INTESTINAL BARRIER ASSESSMENT (PLASMA) | 2/2

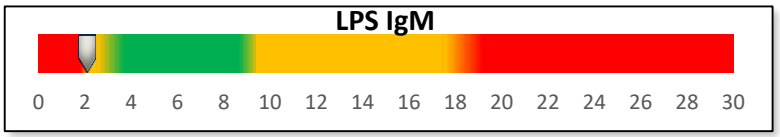
0.58
Normal RANGE: 0.83-4.47 µg/mL
LOW



0.59
Normal RANGE: 9.09-31.5 µg/mL
LOW



2.11
Normal RANGE: 2.5-9.4 µg/mL
BORDERLINE LOW



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PRECISION POINT DIAGNOSTICS

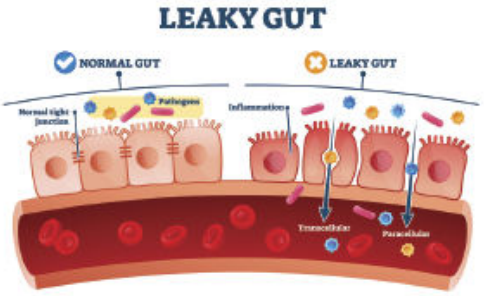
ADVANCED INTESTINAL BARRIER ASSESSMENT

Imbalances in Zonulin, Histamine, DAO and LPS are associated with intestinal permeability, often referred to as, "leaky gut."

When the gut barrier is weakened, a person is more vulnerable to food antigens, toxins, and unfriendly microbes. A leaky gut tears down the body's defenses and opens up the system to increased inflammation. There are many possible causes of damage to the GI lining and subsequent leaky gut.

Common causes of intestinal permeability are bacterial overgrowth, food sensitivities including gluten sensitivity, antibiotics, PPI inhibitors, stress, food additivies, NSAIDs, and alcohol consumption.

Reducing inflammation and healing the GI lining can help restore the GI barrier and normalize Zonulin, DAO, histamine, and LPS.



High Zonulin

High plasma zonulin is associated with intestinal permeability. Zonulin is a protein that leads to the break-down of tight gap junctions in the GI lining. These junctions are critical for a healthy barrier against the outside world.

When the gut barrier is weakened, a person is more vulnerable to food antigens, toxins, and unfriendly microbes. A leaky gut tears down the body's defenses and opens up the system to increased inflammation.

Increased levels of zonulin may be a contributing factor in the development of celiac disease, autoimmune disorders, insulin dependent diabetes, multiple sclerosis and rheumatoid arthritis. Higher zonulin levels have been reported in patients with active celiac disease compared to non-celiac patients.1-3 Zonulin levels elevate 2-5 years before diabetes, autoimmune conditions, and allergies. Zonulin may therefore be an early marker of disease processes.

Histamine Intolerance

Histamine Intolerance - Histamine intolerance can develop when a person has abnormal levels of histamine and the histamine degrading enzyme, diamine oxidase (DAO).

Typical symptoms of histamine intolerance are headache, diarrhea, migraine, general inflamed, circles under the eyes and runny nose.

Histamine intolerance might be more obvious with specific food triggers leading to asthma and arrhythmia, hypotension, urticaria, and dysmenorrhea. When DAO or histamine is imbalanced, the main focus of treatment is to increase DAO, reduce histamine, and heal the gut.

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PRECISION POINT DIAGNOSTICS

High Histamine

Anaphylaxis	Dizziness	Affected locomotion	Sneezing
Painful menstruation	Congestion	Stomach Ache	Reproductive
Circadian rhythm	Runny nose	Itching	Issues
High blood pressure	Arrhythmia	Cramps	Diarrhea
Shortness of breath	Nausea, vomiting	Abnormal	Flush
Body temperature	Hives	heart rate	Gas
changes	Memory Loss	Headache	Low muscle tone

Histamine

Histamine balance is a critical factor in patients with allergic and gastrointestinal symptoms. Neither too high, nor too low of a level of Histamine is desirable. Histamine was first discovered in its role in anaphylactic allergy. A specific allergen can trigger the degranulation of mast cells, subsequently releasing histamine. This can lead to severe, life-threatening symptoms. When the gut barrier is weakened, a person is more vulnerable to food antigens, toxins, and unfriendly microbes. A leaky gut tears down the body's defenses and opens the system up to increased inflammation.

Classic symptoms of high histamine are tachycardia, headache, flushing, urticaria, pruritis, hypotension, bronchospasm, and cardiac arrest. However histamine can have far-reaching impacts and lead to many atypical symptoms because it binds cells throughout the body- in the gastrointestinal tract, respiratory tract, skin, cardiovascular system, and central nervous system, among others.

Gut permeability can also increase histamine. Leaky gut activates T cells and triggers degranulation of histamine-containing mast cells. In addition to histamine made in the body, we consume histamine in varying amounts in foods.

After extreme histamine exposure, as in anaphylactic shock, levels of both diamine oxidase and histamine will be elevated. Low histamine levels may cause fatigue or depression. Alterations of histamine have been noted in sleep-wake disorders such as narcolepsy, as well as other neurological and psychiatric diseases. Brain levels of histamine are decreased in Alzheimer's and low histamine has been seen in cases of convulsions and seizures.

High Histamine Foods

Very High: Aged or fermented foods: kimchi, yogurt or kefir, kombucha, aged cheese, alcohol of any kind, vinegar, and cured meat. Fish and seafood, especially canned or smoked fish.

Medium: Spinach, eggplant, mushrooms, tomatoes, canned vegetables, dried fruit, avocados, strawberries, papaya, pineapple, and leftovers.

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DAO

Diamine Oxidase (DAO) is histamine's vital counterpart and the primary enzyme responsible for keeping histamine levels in check. DAO degrades extracellular histamine and is mainly produced in the microvilli of the small intestine. When diamine oxidase is low it means the patient cannot properly break down Histamine. Histamine-N-methyltransferase (HNMT) is the secondary enzyme involved in Histamine break down.

Low Diamine Oxidase is associated with headaches, fatigue, hives, any allergy symptom, dysmenorrhea, estrogen dominance, arrhythmia, inflammation, arthritis, and certain neurologic conditions such as multiple sclerosis. Symptoms of low DAO are essentially identical to symptoms of Histamine excess because they are two sides of the same coin.

Low levels of DAO correlate with poor mucosal integrity and indicate poor gut function. Atrophy of the microvilli can cause low DAO. Patients suffering from diseases like urticaria, Crohn's, or celiac disease are reported to show low DAO activity in serum or plasma. Low DAO can also be a trigge for depression or anxiety. Low Diamine Oxidase in plasma can be used to diagnose Histamine intolerance. Individuals with an inability to break down Histamine may seem to "react to everything," or improve on anti-histamines. Those with anaphylactic reactions often have lower DAO activity. Following a Histamine-free diet can result in a significant reduction, or even disappearance, of symptoms within a few weeks.

Many medications inhibit DAO or damage the gut lining, reducing DAO production. Alcohol and its degradation product, acetaldehyde, are inhibitorsof DAO.

DAO: Histamine Ratio

The DAO: Histamine Ratio helps detect even (insert) subtle imbalances between Histamine and DAO levels. Even if the DAO enzyme level is normal, symptoms can occur when Histamine is high. A low ratio indicates that there may not be enough of the DAO enzyme relative to the amount of Histamine in the body.

Treatments to normalize DAO or Histamine will also improve this ratio.

High LPS

An elevated Lipopolysaccharide (LPS) reaction indicates intestinal permeability or "leaky gut". Lipopolysaccharide is the immunogenic portion, as well as the major constituent, of the outer cell membrane of gram-negative bacteria. LPS is a bacterial endotoxin made by bacteria in the body.

When Lipopolysaccharides are high in the blood, it means they are passing not only between intestinal cells, but also directly through the cells, potentially causing neuroinflammation and brain injury. When LPS is absorbed into the blood stream it can elicit a strong immune response.

Elevated levels may be associated with bacterial infection, food sensitivities, chronic inflammation, autoimmune conditions, digestive disorders, and neurological conditions.

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Low LPS

There is clinical importance to having a low immune reaction to LPS antibodies. Since there will always be some LPS present, there should be an immune response recorded. When a patient tests on the low end of the spectrum for an immune response for LPS IgG, LPS IgA and LPS IgM, this is a good indication that their immune system is not functioning as it should. When there is a low response this means immunoglobulin levels go down and bacterial levels stay up. Ongoing gut pain and flairs persist, as patients can no longer fight infections as they should and the higher level of bacteria in the gut causes irritation.

Conditions associated with low LPS antibodies are IBS, Crohns Disease and Colitis.

Conditions Associated with Elevated Levels of LPS

Shock	Type 2 Diabetes	Obesity
Multiple Organ Dysfunction	Alzheimer's	Mood and Appetite Disorders
	Autoimmunity	
Depression	Infertility	Cognitive Decline
Anxiety	Hypogonadism	Anorexia
Sepsis	Leptin Resistance	Parkinson's
Atherosclerosis	Chronic Constipation	Chronic Pain

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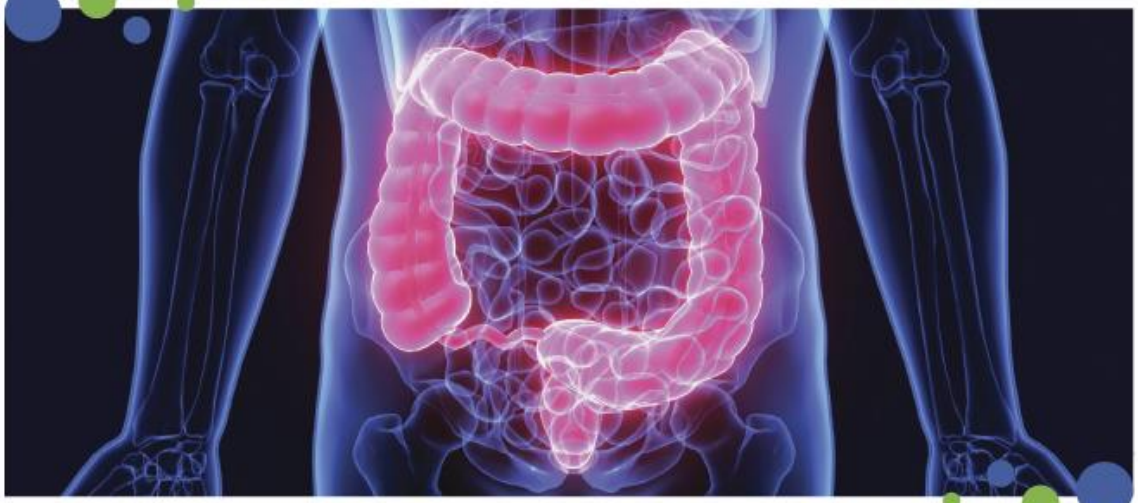
ANALYTES	LOW LEVELS
Zonulin	Low Zonulin is not clinically significant.
DAO	Low DAO is a result of atrophied microvilli demonstrating gut permeability. This will also result in an inability to degrade Histamine creating sensitivity and symptoms associated with histaminosis. See High Histamine for treatment.
Histamine	Low levels can be associated with fatigue, depression and certain types of schizophrenia. Histidine (sp) and accessory amino acids can be given to raise levels.
DAO: Histamine	A high ratio shows that the gut lining is in balance between its ability to make and degrade histamine.
LPS IgA, IgM, IgG	Low LPS Antibodies are associated with an immune system that is chronically worn down. IBS and IBD can both be a result of an infection that was chronic and that has resulted in little to no immune reserve. Immunoglobulins are an excellent intervention. Adequate Vitamin A and D as well as adequate protein can also help to increase levels. Assume there is a long-term infection that has decreased levels and consider antimicrobials such as Berberine and Garlic as well.



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ANALYTES	HIGH LEVELS
Zonulin	Possible bacteria, yeast, gluten. Treatment: • Treat dysbiosis with garlic, oregano, and with berberines from Goldenseal or Oregon grape. • Immunoglobulins sourced from colostrum, egg, or serum because immunoglobulins block Zonulin from binding to tight junctions • Remove wheat/gluten.
DAO	DAO will increase initially to compensate for higher levels of histamine from dysbiosis and/or immune dysregulation of foods. It is a compensatory response due to challenge of Histamine. Treat by lowering Histamine. Higher levels may also just be due to healthy microvilli and a robust production.
Histamine	Increased levels are secondary to antigens causing mast cell degranulation. Also, certain bacteria can create histamine and certain foods are higher in histamine. Treatments to increase DAO: Oral DAO, Omega 3 fatty acids, Vitamin C, Copper and b6 as cofactors, and Sacchromyces. Treatments to lower histamine: Oral DAO, SAMe to increase methylation of Histamine, or B5 to acetylate Histamine. Other therapies for degranulation of mast cells or histamine producing cells include: Quercetin, Vitamin C, and Omega 3 fatty acids. Other therapies to decrease degranulation of mast cells or histamine producing cells include: Quercetin, Vitamin C and Omega 3 fatty acids.
DAO: Histamine	When the ratio is low it means there is not enough Diamine Oxidase to degrade histamine. See Histamine section above for treatment.
LPS IgA, IgM, IgG	This indicates that the immune system is actively fighting bacterial overload. Treatments include antimicrobials to lower bacterial load. Berberine and Garlic are suggested as well as immunoglobulins to suppport the immune system.
LPS High IgM: Low IgG	A high IgM with a Low IgG means there was poor seroconversion to a matured response to LPS. Antimicrobial therapies and immunoglobulins will support improvement in these areas. Toxicity can block seroconversion from IgM to IgG. Detox may be warranted.

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REFERENCES

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