

TOP GUT HEALTH BIOMARKERS — CLINICAL MEANING & INTERPRETATION

Your Weekly Newsletter

by Dr. Nick Sieveking

April 7, 2026



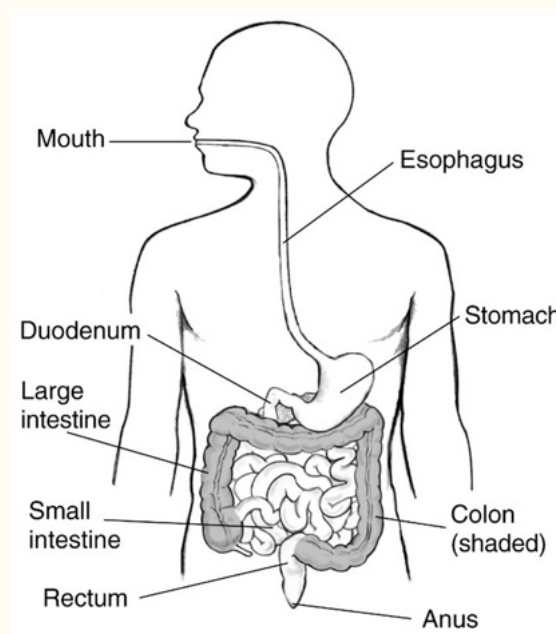
Your Gut: More Than Just Digestion

Your gastrointestinal (GI) tract—from mouth to anus—is approximately 30 feet long and has an internal surface area of roughly 30 m² (~320 ft²).

That makes it one of the largest interfaces between your body and the outside world.

Your gut is not just a digestive tube. It functions as:

- A selective filter → absorbs nutrients, vitamins, and water
- A defense barrier → prevents toxins and pathogens from entering circulation
- An immune organ → houses ~70% of your immune system



The Gut Barrier: Tight Control Matters

Think of your gut lining as a highly selective filter.

- **Zonulin** regulates the tightness of junctions between intestinal cells

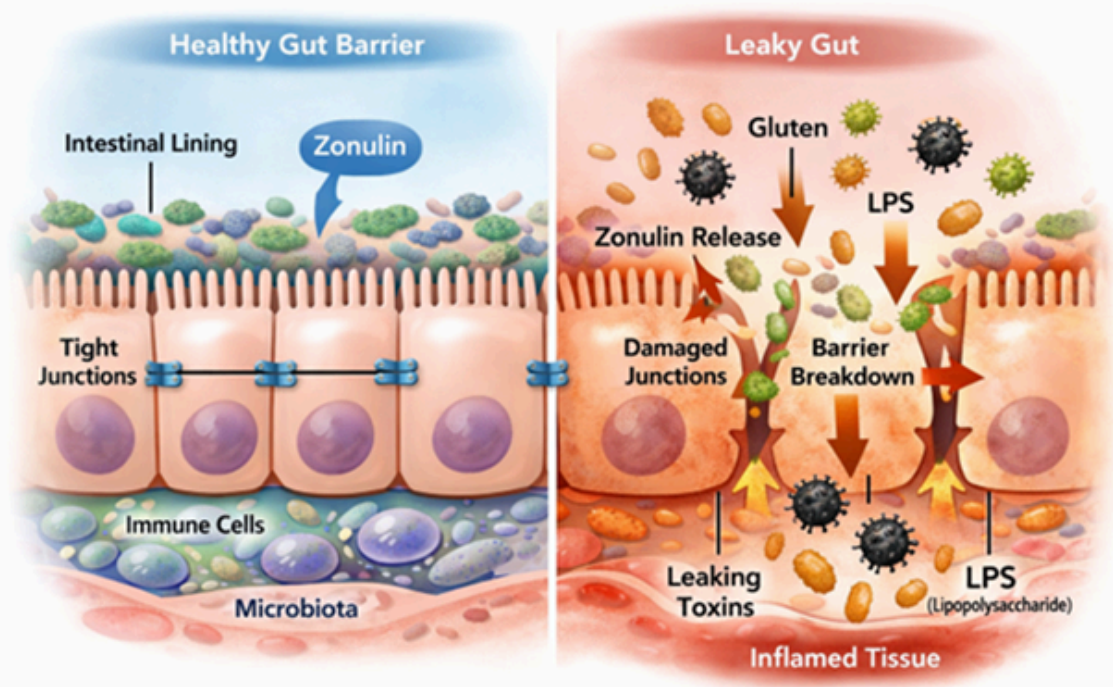
- When functioning properly → only beneficial molecules pass through
- When dysregulated → junctions loosen

This leads to increased intestinal permeability (“leaky gut”).

What Happens When the Barrier Breaks Down

When the gut becomes permeable:

- Bacterial toxins (especially LPS) enter circulation
- Undigested food particles cross into the bloodstream
- The immune system becomes chronically activated



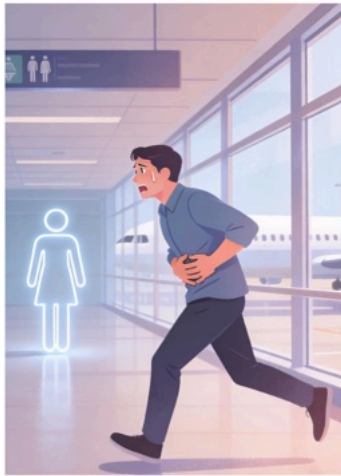
These drive systemic inflammation, immune dysregulation, and metabolic disruption.

Key Biomarkers That Tell Us Our Gut Barrier Has Been Breached

- **LPS Antibodies** (IgA, IgG, IgM) → chronic exposure to endotoxin driving inflammation
- **Zonulin** → marker of intestinal permeability
- **Secretory IgA** (sIgA) → gut immune function; the gut is under attack
- **Diamine Oxidase** (DAO) → gut lining dysfunction + impaired histamine breakdown
- **8-OHdG (8-hydroxy-2'-deoxyguanosine)** → cellular damage + active Gut inflammation
- **F2-Isoprostanes** → significant membrane damage + active inflammation
- **Calprotectin** → intestinal inflammation marker

Clinical Consequences of a Compromised “Leaky” Gut

1. Chronic Inflammation	Elevated inflammatory cytokines Increased hs-CRP Joint pain / Fibromyalgia Bone loss (Osteopenia) Muscle loss (Sarcopenia)
2. Autoimmune / Allergic Conditions	Hashimoto's, Rheumatoid Arthritis, Lupus Frequent respiratory infections (sinus, ear, bronchial) Increased allergies (rhinitis, asthma, food allergies) Higher autoimmune risk (celiac, thyroid disease)
3. Metabolic Dysfunction	Insulin resistance Weight gain and visceral fat Fatty liver disease
4. Cardiovascular Disease	Endothelial dysfunction Atherosclerosis progression Hypertension Stroke
5. Neurologic Effects	Brain fog Cognitive decline Memory loss Neurodegeneration (e.g., Alzheimer's) Depression / mood changes Autism Insomnia
6. Skin Conditions	Acne Rosacea Eczema
7. Hormonal Imbalance	Estrogen metabolism disruption
8. Gastrointestinal Symptoms	Bloating, diarrhea, cramping pain IBS-type symptoms Food sensitivities (gluten, dairy, soy, corn, etc.)
9. Advanced Associations	Colorectal cancer Advanced liver disease Accelerated cellular aging Solid tumors



Bottom Line

Your gut is central to inflammation, immunity, metabolism, and overall health.

When the barrier is intact → health is stable.

When it is compromised → disease processes begin to develop.

If you don't measure it, you're guessing. Biomarkers allow us to understand what is happening at the level of the gut barrier.

[Our Top Biomarkers We Check at Ageless Solutions](#)

1. Anti-LPS Antibodies (Lipopolysaccharide Antibodies)

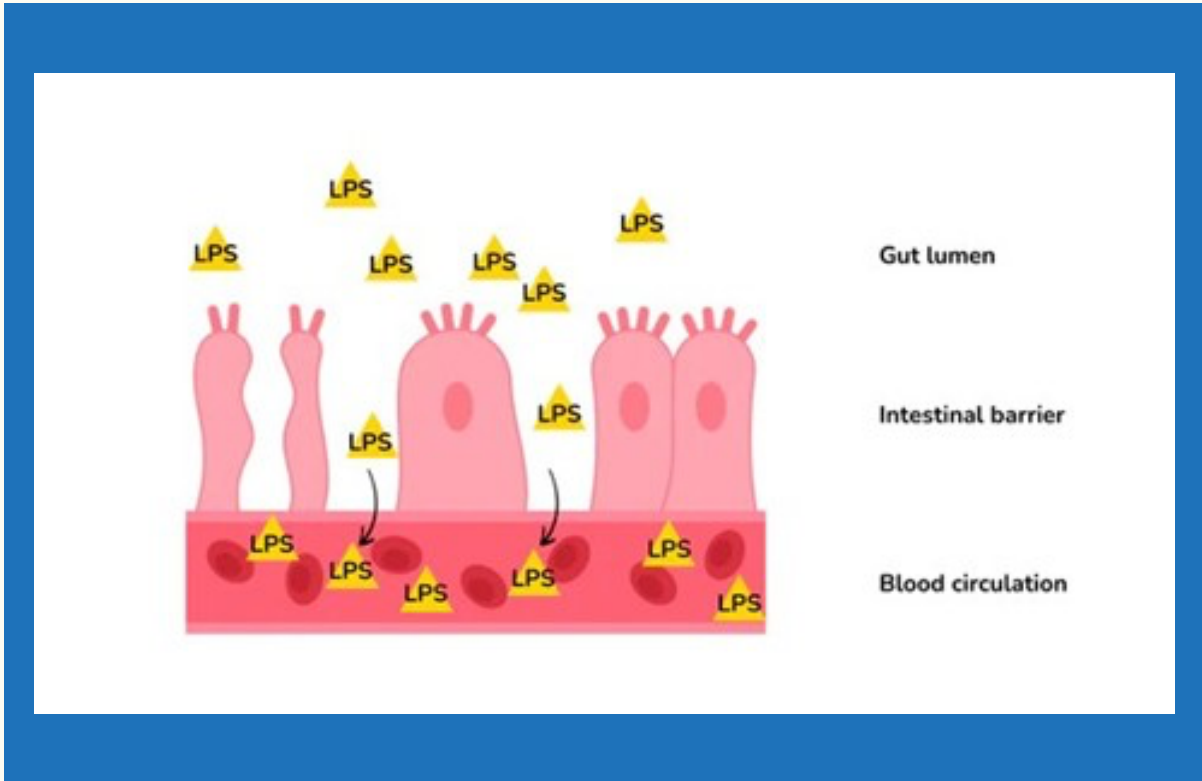
What it is

- **Blood test** measuring antibodies against LPS (lipopolysaccharide)
- LPS = endotoxin from Gram-negative bacteria
 - Normal: stays inside the gut
 - Problem: becomes harmful when it enters the bloodstream
- How LPS enters the bloodstream: through damage to the gut lining ("leaky gut"), allowing toxins to pass into circulation.

Common causes of gut barrier breakdown

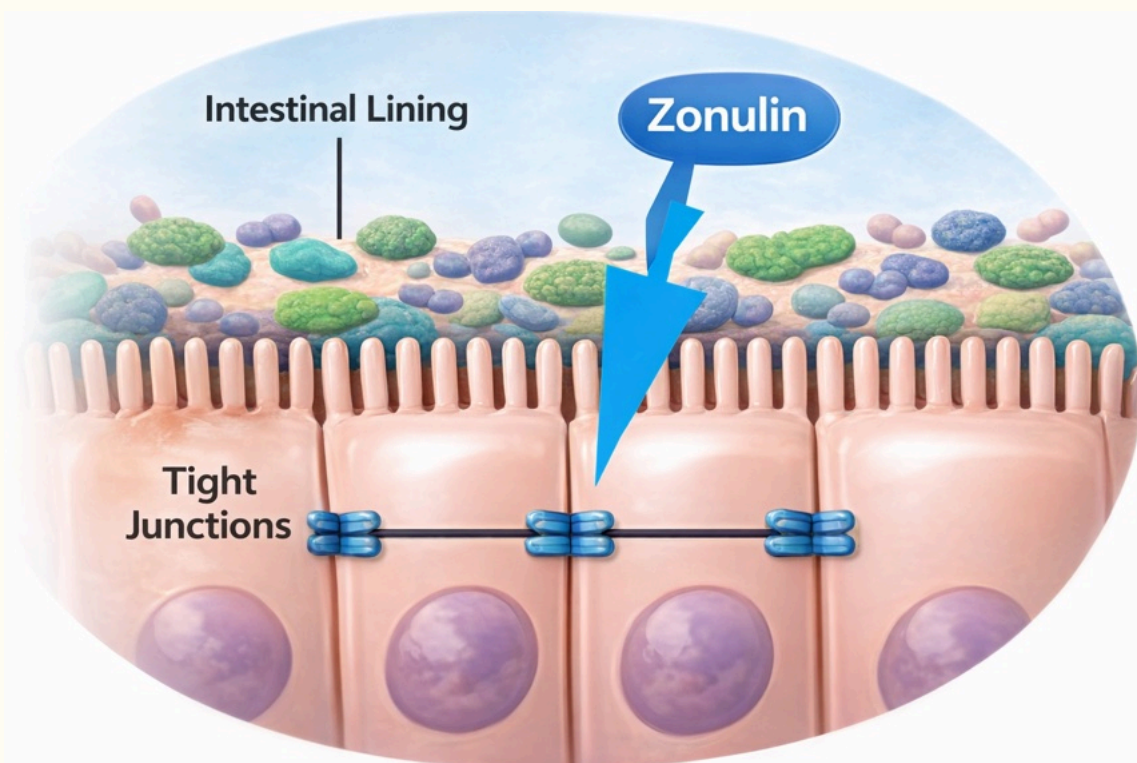
- High-fat, high-sugar Western diet (especially saturated fats)
- Gut dysbiosis and SIBO
- Acute or chronic GI infections (bacterial, viral, parasitic)

- Chronic intestinal inflammation (IBD, celiac disease)
- Alcohol use
- Medications (NSAIDs like Advil, chemotherapy)
- Physical stress (shock, major surgery, extreme endurance)
- Long-term antibiotic use
- Stress, malnutrition, chronic inflammation



Treatment: (see “Treatment Strategy”)

2. Zonulin



What it is

- Blood test

- A regulatory protein controlling tight junctions between intestinal cells of the gut lining => the “gatekeeper” of gut permeability
- Prevents “Leaky Gut”
- Normal serum levels: 20-40 ng/mL

Physiologic role

- Controls selective passage of:
 - Nutrients and molecules
 - Antigens (immune sampling)
 - Immune cells
- Plays a key role in immune system training and tolerance
- 👉 Elevated zonulin = increased gut permeability (“leaky gut”)

What causes tight junction breakdown

- Dietary triggers: gluten/gliadin (even in some non-celiac individuals), ultra-processed foods, additives
- Gut conditions: dysbiosis, SIBO, infections (bacterial, viral, parasitic)
- Inflammatory disorders: celiac disease, IBS, Crohn’s, ulcerative colitis
- Autoimmune diseases: type 1 diabetes, rheumatoid arthritis, multiple sclerosis, lupus -->
- Metabolic dysfunction: obesity, insulin resistance, type 2 diabetes, metabolic syndrome, fatty liver -->
- Alcohol use (direct mucosal injury)
- Medications/toxins: NSAIDs (Advil), antibiotics, PPIs (e.g., Prilosec), chemotherapy
- Nutrient deficiencies: vitamin B, zinc, vitamin A, glutamine,



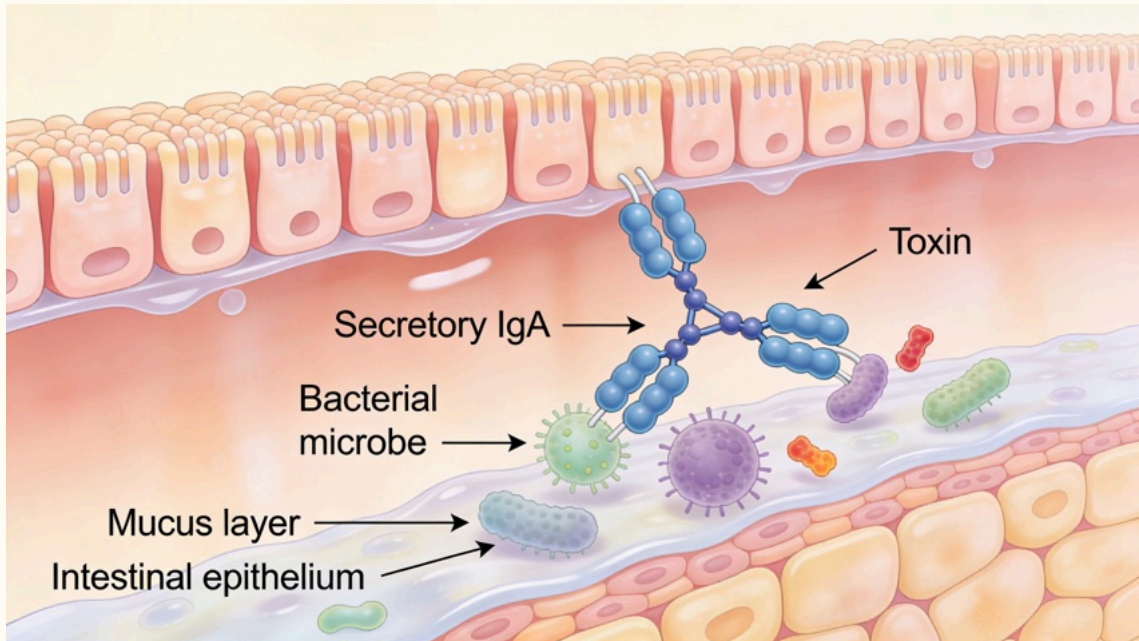
- Environmental toxins: pesticides, herbicides, heavy metals, mold (mycotoxins)
- Chronic stress: cortisol-mediated barrier disruption
- Untreated food sensitivities/allergies: gluten, dairy, soy, corn, etc.

Treatment → See “Treatment Strategy” section

3. Secretory IgA (sIgA)

What it is

- **Stool or Saliva test**
- The primary immune antibody of mucosal surfaces (gut + respiratory tract)
→ your first-line defense
- Functions:
 - Binds microbes and toxins
 - Prevents pathogen attachment
 - Maintains microbiome balance
- Produced by plasma cells in gut-associated lymphoid tissue (GALT)



Interpreting sIgA Levels

Low sIgA (<500 µg/g)

→ Immune exhaustion / suppression

Common causes of **low** sIgA

- Chronic stress (cortisol-mediated suppression)
- Nutrient deficiencies (vitamin A, D, zinc, poor diet)
- Chronic infections or dysbiosis (Candida, parasites, SIBO)
- Long-standing gut inflammation (celiac disease, Crohn's, ulcerative colitis)
- Autoimmune and chronic inflammatory states
- Genetic IgA deficiency
- Medications: corticosteroids, antibiotics, PPIs (Prilosec), NSAIDs (Advil), oral hormones
- Malnutrition

Clinical consequences of **low** sIgA

1. Gut effects

- Increased GI infections (bacterial, fungal, parasitic)
- Dysbiosis and overgrowth (e.g., Candida)
- IBS-type symptoms (bloating, pain, altered bowel habits)
- Increased intestinal permeability ("leaky gut")
- Food sensitivities (gluten, dairy, soy, corn, etc.)

- Increased risk of IBD in some patients
2. Immune / allergy
- More frequent respiratory infections (sinus, ear, bronchial)
 - Increased allergies (rhinitis, asthma, food allergy)
 - Higher autoimmune risk (celiac, thyroid disease)
3. Systemic effects
- Chronic low-grade inflammation:
 - Fatigue
 - Joint pain
 - Skin issues
 - In chronic disease states (diabetes, liver disease), associated with worse outcomes

High sIgA (>2000 µg/g)

→ Active immune stimulation

Suggests

- Infection
- Antigen overload
- Food reactions
- Dysbiosis / SIBO

Clinical consequences of **high** sIgA

- Gut immune system is overactive and reacting to luminal triggers
- Inflammatory bowel disease (Crohn's, ulcerative colitis)
- Gluten-driven or antigen-driven inflammation
- Chronic infection or microbiome imbalance

Symptoms

- Bloating, abdominal pain
- Diarrhea, urgency, food-triggered flares

Systemic effects

- Fatigue, brain fog, joint aches, poor sleep
- Increased risk or worsening of autoimmune disease
- Ongoing barrier damage → worsening "leaky gut"

Advanced associations

- Seen in some cases of colorectal cancer and advanced liver disease (as part of broader gut barrier dysfunction)

Treatment

→ See "Treatment Strategy" section

4. Diamine Oxidase (DAO)

What it is

- **Blood test**
- Enzyme produced by intestinal lining cells (enterocytes)
- Responsible for breaking down histamine from food
- Prevents excess histamine from entering circulation

Interpreting DAO Levels

Normal: ≥ 10 U/mL

Low DAO (<10 U/mL)



→ Histamine intolerance

Common causes

- Genetic variants (reduced DAO production/function)
- Intestinal damage or inflammation:
 - Celiac disease, non-celiac gluten sensitivity
 - IBD, infections, carbohydrate malabsorption
- Medications:
 - NSAIDs (Advil), certain antidepressants
 - Blood pressure medications, antibiotics
- Alcohol use (impairs DAO + damages mucosa)
- Nutrient deficiencies (B6, copper, vitamin C, zinc)
- Hormonal influences (estrogen fluctuations: cycle, pregnancy, contraceptives)
- Gut dysbiosis with histamine-producing bacteria

Symptoms

- Flushing

- Headaches / migraines
- Anxiety
- Tachycardia (palpitations)
- IBS-like symptoms (bloating, pain, gas)



Clinical Consequences of Low DAO (“histamine intolerance”)

1. Gut
 - Bloating, abdominal pain, gas
2. Skin / allergy-like
 - Flushing, itching, rashes, nasal congestion
3. Neurologic
 - Migraines, dizziness, brain fog
 - Insomnia / sleep disturbance
4. Cardiovascular
 - Palpitations, tachycardia
5. Systemic
 - Chronic fatigue
 - Fibromyalgia-like pain
 - ADHD-like symptoms

High DAO

- Rarely clinically significant

Treatment

→ See “Treatment Strategy” section

5. 8-OHdG (8-hydroxy-2'-deoxyguanosine)

What It Is

- Measured in **Urine** or **Blood**
- Marker of oxidative DNA damage
 - a “chemical scar” left on DNA after damage from reactive oxygen species (ROS)
- Reflects direct cellular injury, including damage to the intestinal lining and mitochondria

- (ROS = *unstable oxygen molecules that damage DNA, proteins, and cell membranes*)

Interpreting 8-OHdG Levels

- Reported as ng/mg creatinine
- Optimal (first morning sample): ~0–5.2 ng/mg
- 👉 **High levels** = increased oxidative stress and DNA damage
→ associated with aging, cancer risk, and chronic disease

Causes of Elevated 8-OHdG

Lifestyle & environmental

- Smoking (including secondhand exposure)



- Chronic stress (elevated cortisol)
- Alcohol use
- Poor diet (low in fruits/vegetables, high in processed foods)
- Environmental toxins:
 - Air pollution, radiation
 - Heavy metals, pesticides, industrial chemicals
- Excessive intense exercise (transient increase)
(moderate exercise lowers levels over time)

Clinical Consequences of Elevated 8-OHdG

- Chronic diseases:
 - Cardiovascular disease
 - Diabetes
 - COPD
 - Kidney disease
- Chronic inflammation and infections
- Certain cancers

- Aging (accumulated oxidative stress and reduced DNA repair)

Treatment

→ See “Treatment Strategy” section

6. F2-Isoprostanes

What It Is

- **Urine** or **Blood** test
- Gold-standard marker of lipid peroxidation
 - measures oxidative damage to cell membranes
- Formed when free radicals attack lipids in cell membranes
- Reflects damage to:
 - Cellular membranes
 - Mitochondria
 - Neurons
- Indicates direct injury to intestinal lining cell

(Free radicals = unstable molecules from sources like pollution, smoking, and radiation that damage cells)

Interpreting F2-Isoprostanes

- Reported as ng/mg creatinine
- Normal: ≤ 1.0 ng/mg

👉 Elevated levels = increased oxidative damage to cell membranes

Causes of Elevated F2-Isoprostanes

Lifestyle & environmental

- Smoking (including secondhand exposure)
- Poor diet (high processed/red meat, low antioxidants)
- Sedentary lifestyle, excess body weight (increased BMI, waist circumference)
- Alcohol use
- Environmental toxins:
 - Air pollution, radiation
 - Heavy metals, pesticides, industrial chemicals

Medical & metabolic

- Obesity, metabolic syndrome, type 2 diabetes
- Cardiovascular disease:
 - Coronary artery disease
 - Peripheral artery disease
 - Post-operative atrial fibrillation
- Certain cancers and precancerous states

Treatment: (see “Treatment Strategy”)

7. CalProtectin (Intestinal Inflammation Marker)

What it is

- **Stool** test
- Protein released by activated white blood cells (neutrophils)
- Marker of active inflammation in the gastrointestinal tract
- Reflects direct immune activity in the gut lining
- Helps distinguish:
 - Inflammatory conditions (IBD)
 - vs. Non-inflammatory conditions (IBS)

Interpreting CalProtectin Levels

- Reported as $\mu\text{g/g}$ stool
- Normal: $<50 \mu\text{g/g}$
- Borderline: $50\text{--}120 \mu\text{g/g}$
- Elevated: $>120 \mu\text{g/g}$

👉 Higher levels = greater intestinal inflammation

Causes of Elevated CalProtectin

Gastrointestinal inflammation

- Inflammatory bowel disease (Crohn's disease, ulcerative colitis)
- Infectious colitis (bacterial, viral, parasitic)
- Celiac disease (especially active/untreated)
- Diverticulitis

Medication-related

- NSAIDs (Advil, ibuprofen)
- Some antibiotics

Other contributors

- Gastrointestinal bleeding
- Colorectal polyps or cancer
- Severe food intolerances or antigen-driven inflammation

Clinical Significance of High CalProtectin

1. Gut-specific inflammation

- Active mucosal inflammation and immune activation
- Correlates with disease severity in IBD
- Useful for monitoring response to treatment

2. Differentiation tool

- High calprotectin → think inflammatory disease (IBD)
- Normal calprotectin → more consistent with IBS or functional disorders

3. Symptom of Elevated Calprotectin

- Diarrhea
- Abdominal pain
- Urgency
- Blood or mucus in stool

Low / Normal Calprotectin

- Suggests no significant intestinal inflammation
- Helps rule out IBD in symptomatic patients

Treatment: (see “Treatment Strategy”)

Final Markers: Food Antibodies & Immune Reactivity

These last markers help us understand how your immune system is reacting to food—and whether your gut barrier has been compromised over time.

8. IgE Food Allergies (Immediate Reactions)

- Blood test
- IgE antibodies drive true food allergies
 - rapid, immediate reactions

Key concept:

- A healthy gut barrier prevents IgE formation
- When the barrier breaks down:
 - Food particles enter circulation
 - Immune system reacts
 - IgE antibodies develop

👉 Leads to:

- Immediate allergic reactions
- Ongoing inflammation that can further damage the gut

9. IgG Food Antibodies (Delayed Sensitivities)

- Blood test
- Reflect immune exposure to foods, not true allergies

Key concept:

- Develop more easily when the gut barrier is compromised

👉 Typically associated with:

- Delayed, low-grade inflammation
- Symptoms that are harder to link to specific foods:
 - Bloating
 - Fatigue
 - Brain fog

Important: IgG reflects recognition, not always pathology—but in the right clinical setting, it can signal ongoing immune activation.

10. IgA Antibodies (Local vs Systemic Immunity)

Two critical measurements:

Stool IgA (Secretory IgA)

- Reflects what’s happening in your gut right now
- Your most important functional gut immune marker
- Shows real-time immune response to microbes and food antigens

Blood IgA (Serum IgA)

- Reflects whole-body immune activity
- Used in diagnosing conditions like celiac disease

👉 Simple way to think about it:

- Stool IgA = current gut activity
- Blood IgA = systemic immune response (what's already spilled over)

Bottom Line

- A healthy gut barrier prevents abnormal immune reactions to food
- When the barrier breaks down:
 - Food antigens cross into circulation
 - Immune responses develop (IgE, IgG, IgA)
 - Inflammation increases
 - The cycle continues

👉 These markers help us identify where you are in that process—and how to reverse it

Treatment Strategy: The 4 R's of Gut Restoration

“To heal the gut, we remove what’s harming it, replace what’s missing, rebuild healthy bacteria, and repair the gut lining so it can function properly again.”

Remove → Replace → Reinoculate → Repair

1. Remove (Eliminate the Triggers)

- **Dietary irritants:**

Ultra-processed foods, added sugars, alcohol, and common triggers (gluten/dairy if sensitive)



- **Pathogens & overgrowth:**

SIBO, Candida, parasites, Helicobacter pylori, dysbiosis

→ Often require short-term antibiotics or antifungals

- **Lifestyle & medications:**
NSAIDs, smoking, excess alcohol, chronic stress, poor sleep

2. Replace (Restore Digestion)

- **Replenish deficiencies:**
Stomach acid, bile acids, pancreatic enzymes
- **Short-term digestive support (when indicated):**
Bitters, enzyme blends, HCl (supervised use)
- **Nutrition foundation:**
Nutrient-dense foods to support enzyme production and absorption

3. Reinoculate (Rebuild the Microbiome)

- **Probiotics & fermented foods:**
Evidence-based probiotics, kefir, yogurt, sauerkraut, kimchi
- **Prebiotic fibers (as tolerated):**
Inulin, GOS, partially hydrolyzed guar gum, resistant starch
→ Adjust for SIBO/IBS sensitivity
- **Long-term diet strategy:**
Diverse plant fibers, polyphenol-rich foods, reduced ultra-processed intake

4. Repair (Heal and Seal the Gut Lining)

Goal: Restore barrier integrity, reduce inflammation, and support regeneration

- **Core nutrients:**
L-glutamine, zinc (zinc carnosine), vitamins A & D, omega-3s
- **Soothing botanicals:**
Aloe (inner fillet), DGL licorice, slippery elm, marshmallow root
- **Mucosal support compounds:**
Colostrum, N-acetyl-glucosamine, targeted probiotics/postbiotics
- **Foundational inputs:**
Adequate protein, micronutrient repletion, anti-inflammatory diet
- **Address root drivers:**
Chronic stress (HPA axis), sleep deprivation, metabolic dysfunction

SPECIAL PROMO:

--Through April 17, 2026--

We can't stress enough the importance of checking systemic inflammation. Take advantage of our limited time offer for a **FREE hs-CRP** test at **Ageless Solutions**.

Make Appointment

STAY TUNED!

Be on the lookout for next week's newsletter, "*The Ageless Solutions Approach to Hair Loss.*"

[Newsletter Archives](#)



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