

# Leaky Gut: Mechanism, Measurement or Misdiagnosis?

Paper 09 · Editorial concept paper · Created 15 October 2026

**Abstract.** Intestinal permeability is a real physiological property and is altered in certain diseases. The popular term 'leaky gut' becomes misleading when a measurable process is transformed into a universal diagnosis without standardized testing or validated causal interpretation.

## The real scientific object

The intestine regulates transport across an enormous epithelial surface. Tight junctions, epithelial integrity, mucus and immune structures contribute to different pathways of passage. Disease states including celiac disease and active intestinal inflammation may affect permeability; experimental stressors and medications may do so as well. That reality should neither be denied nor exaggerated into a theory that all chronic conditions begin with intestinal leakage.

## One name, several measurements

Permeability can be measured with specific orally administered probes, tissue-based methods or other specialized techniques, with interpretation shaped by the intestinal segment and experimental protocol. Serum concentrations of compounds proposed as 'barrier biomarkers' do not automatically measure the same phenomena. Widely marketed zonulin assays have drawn methodological criticism regarding molecular specificity, making confident clinical inference especially problematic.

## Correlation does not assign the direction

An inflamed intestine can become more permeable because of disease. Increased permeability might also contribute to inflammatory exposure in certain contexts. Both statements can be true. To prove that permeability causes a particular condition, temporal data or well-characterized intervention evidence must distinguish it from the possibility that permeability is downstream of infection, diet, drugs or inflammation.

## The Institute's proposed contribution

Instead of asking whether a person has 'leaky gut,' ask four more precise questions: Which barrier component is abnormal? What is crossing it? Does the resulting exposure have a demonstrated consequence? Would changing that specific transport process improve clinically relevant function? This turns a diffuse wellness claim into a sequence of falsifiable hypotheses.

## What should not be inferred

Bloating, fatigue, rash, anxiety and food intolerance have numerous explanations. A patient cannot be diagnosed with increased intestinal permeability from that symptom mixture alone. Neither can unvalidated supplements be described as 'sealing the gut' merely because they affect markers in cell cultures. The scientific opportunity is substantial, but it begins with measurement discipline.

## A measurement problem disguised as a disease debate

Arguments about 'leaky gut' often conflate three different propositions: intestinal permeability exists; intestinal permeability is altered in some disorders; and increased permeability is a major causal explanation for a broad variety of nonspecific illnesses. The first is a physiological fact, the second is supported in defined settings, and the third cannot be accepted without much more precise evidence. Separating them removes false polarization between those dismissing barrier biology and those treating permeability as a universal root cause.

## Biomarker specificity matters

A commercially available assay may produce a number with considerable precision while measuring something other than the molecule named in its marketing. Critiques of commercial zonulin testing illustrate this danger. Even an analytically valid test can have poor clinical validity if the same abnormal result appears in many conditions or does not predict response to intervention. For public-facing medical research the distinction between analytic validity, clinical association and clinical utility is essential.

## Concrete research alternatives

The strongest useful questions would concern specified patient groups, validated intestinal permeability methods, symptom trajectories and mechanistically linked mediators. It may be valuable to ask whether barrier changes precede a flare or follow it, or whether restoration of barrier function accompanies improvement in an inflammatory condition. A causal interpretation remains premature if multiple interventions change diet, microbiota, sleep and inflammation simultaneously. An interesting hypothesis deserves a study structure capable of being wrong.

## Selected scientific reading

1. [Camilleri M. Leaky gut: mechanisms, measurement and clinical implications in humans. Gut. 2019;68:1516–1526.](#)
2. [Kovacs P, Heiker JT. Blurring the picture in leaky gut research: shortcomings of zonulin as a biomarker. Gut. 2021.](#)

---

**Editorial status:** Conceptual scientific essay, not peer reviewed. Not original clinical data, a treatment protocol or medical advice. Selected readings are not a systematic review. Evidence and interpretation should be assessed independently.