ELISA/ACT Biotechnologies LLC

LRA by ELISA/ACT[®] CLINICAL UPDATE #2

Gut Hyperpermeability

What is gut hyperpermeability ("leaky gut"), and why is it a problem?

The gut is a major, potential portal of entry into the body for foreign antigens. Only its intact mucosal barrier protects the body from foreign antigen entry and systemic exposure.¹⁻⁸

This mucosal barrier is made up of nonimmunological components (mucous coat, mucous membranes) working independently and in concert with the local mucosal immune system (secretory IgA, lymphoid elements in Peyer's patches). Its effective functioning is peripherally assisted by a competent immune system (especially IgA RES function), specific production, hepatobiliary functions (Kupffer cell activation/phagocytosis, hepatocyte function, bile production and elimination), a healthy/balanced population of hostfriendly microflora (roughly a 20-40/60-80 ratio of Gram negative to Gram positive with sufficient percent of Lactobacillus species), and optimal digestive processes (adequate HCI/pepsin and pancreatic digestive enzyme activity, optimal soluble fiber intake, low transit time).^{1,7,99-32}

When this barrier is sufficiently compromised in any way, it becomes hyperpermeable to foreign or gutderived antigens allowing them to "leak" through in sufficient quantities to be recognized as foreign, and elicit a local and/or systemic immune response, ultimately resulting in immediate and delayed-type hypersensitivities, immune complex formation, and deposition, inflammation, and tissue/organ pathology.

Antigens from the gut, particularly bacterial antigens, can also significantly impair systemic immunity and host defenses. ^{1-8,33-34}

Are there specific clinical conditions that are related to hyperpermeability of the gut?

There are numerous clinical conditions that are known to be associated with "leaky gut" and pathologic uptake of gut-derived antigens. They include such conditions as inflammatory bowel disease, enterocolitis, toxigenic diarrhea, eczema and dermatitis, psoriasis, malabsorption syndromes, allergies, asthma, autoimmune disorders, immunopathies, and AIDS. Therefore, reducing the permeability of the gut to foreign antigens is a primary preventive and therapeutic tool in the treatment of such conditions.^{1,7,33,35-48}

How does one know for sure if gut hyperpermeability is an underlying problem in any of these conditions?

On review of the medical literature related to gut hyperpermeability (its causes and related pathologies) and the pathologies of the various related clinical conditions, it is best to consider the leaky gut syndrome as an integral part of the disease process and to approach treatment with that in mind.

Direct testing for gut permeability can be done using various compounds such as isotopic tagged Cr-EDTA, polyethylene glycol (radiator fluid), and a combination of non-absorbable and non-metabolizable sugars such as lactulose and manitol. ⁴⁹⁻⁵⁴ Such testing methods, however, are not readily available (the lactulose/mannitol test is being done by a few labs) and have definitely not been perfected for detecting early or moderate hyperpermeability. There is no "gold standard" testing method yet developed.

The LRA by ELISA/ACT[®] is valuable as an indirect test for gut hyperpermeability and offers the advantage of revealing valuable clinical information regarding reactive foods and environmental substances.

Generally, the more permeable the gut, the more reactive the patient will be, i.e. the more substances will show up as strong or intermediate reactions. We

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consider 20 or more reactive substances strongly suggestive of an underlying gut hyperpermeability problem.

The LRA by ELISA/ACT is also a more sensitive tool for detecting early development of and trends toward increasing hyperpermeability. Regular retesting of your patient can tell you if their leaky gut problem is being reversed (your treatment is successful) or if it is continuing. If few to no new foods/chemicals are coming up reactive and the number of previously reactive foods/chemicals are lessening, the problem is being corrected. However, if your patient continues to show increasing reactivity to new foods/ chemicals as well as a failure to reverse the number of previous reactions, hyperpermeability may still be a continuing problem.

What causes hyperpermeability of the gut?

Generally, anything that stresses or disrupts the integrity and/or optimal functioning of any immediate or peripheral component of the intact mucosal barrier can initiate and/or promote increased permeability of the gut. Like all disorders, there is no "one cause" and often the patient presents with a history of a number of disruptive factors. Some of the most common factors include:

1) Prolonged distress:

distress Chronic has profound detrimental effects on the immune system by compromising defense and repair mechanisms and, most importantly, significantly reducing secretory IgA production. Also, distress compromises digestive functions through sympathetic overdrive leading to reduced blood flow to digestive organs, reduced peristalsis, and the production of toxic metabolites.55-60

2) Fiber-poor diet with a high intake of refined, highly process, nutrient-deficient, chemically contaminated foods known to promote disease.⁶¹⁻⁸⁵

Such a diet has a direct effect on the GI tract by:

a) promoting inflammation and cancerous changes in the gastric and intestinal mucosa. ^{61-71,75-76}

b) favoring dysbiosis (imbalance of microflora) and growth of pathogenic microflora.^{17,73-74}

c) encouraging the formation of various bowel toxicants (bile acid metabolites, procarcinogens, local inflammatory compounds).^{61-65,76}

d) increasing transit time (constipation) allowing greater putrefaction and prolonged contact of bowel mucosa to toxicants.^{31-32,66,77-80}

e) compromising digestion resulting in increased exposure of the intestinal mucosa to potentially antigenic macromolecules of poorly digested proteins and food remnants.⁸⁴⁻⁸⁵

3) Dysbiosis and presence of pathogenic microflora such as yeasts, Salmonella, Shigella, C. *difficile, Helicobactor pylori, Yersinia enterolytica*, Blastocystis hominis, Giardia, Entamoeba, and other parasites.⁸⁶⁻⁹⁰

Infections with pathogenic microflora result in mucosal damage from swelling, inflammation and infiltration, villus destruction, sIgA depletion, and gutassociated immune activation. The direct result of this pathology is gut hyperpermeability and malabsorption.

4) Present or past medical history of gastrointestinal and/or hepatobiliary disease such as irritable bowel, inflammatory bowel disease, peptic ulcers, colon cancer, diverticulosis/itis, gastritis, hypochlorhydria, hepatitis, cholecystitis, cirrhosis, etc.⁸⁷

All of these diseases promote, as well as are promoted, if not initially caused by, gut hyperpermeability.

5) Immune overload dysfunction from daily exposures to environmental chemicals (formaldehyde, petroleum by-products,

solvents, pesticides, benzene compounds, etc.) toxic metals (lead, cadmium, mercury, arsenic, aluminum), oxidants, and allergens (pollens, dusts, molds, foods, chemicals) or from chronic viral, bacterial, or parasitic infections.⁹¹⁻¹⁰⁵

Daily exposures to these compounds can significantly stress immune defense and repair and intracellular antioxidant mechanisms leading to:

a) chronic deferral of necessary routine repair mechanisms with consequent: breakdown of connective tissue matrix and increased permeability of tissues; impaired tissue ionic selectivity often with loss of trace ions (potassium, magnesium, calcium, etc.); and access to tissue structures which are normally isolated structurally. (This makes them susceptible to immunologic response with possible anti-tissue antibodies autoimmunity.)

b) depletion of buffering reserve with consequent: intracellular acidosis, increase in free (unbound) water in the cell, cell and tissue swelling, and impaired metabolism ("leaky cells").

c) metabolic uncoupling with consequent: decreased production and/or utilization of high energy compounds, and bioelectrical short circuits.¹⁰²

6) Repeated use of or prolonged therapy with nonsteroidal anti-inflammatory drugs; NSAIDs (aspirin, ibuprofen, indomethacin, and others), steroids (prednisone, cortisone), antacids, and/or antibiotics.

a) NSAIDs cause GI inflammation, bleeding, and significant mucosal damage. They have been shown to increase gut permeability even with moderate use.^{42,106}

b) Long-term steroid use can cause stomach and duodenal ulcers and immune suppression (among many other side effects) contributing significantly to gut hyperpermeability and its complications.¹⁰⁶

c) Antacids decrease the acidity of the stomach, reduce the activity of pepsin (a protein-digesting enzyme) and significantly

limit the stomach's ability to adequately digest proteins. $^{106}\,$

This compromise in protein digestion may increase the number of undigested, intact, large protein molecules entering the bowel and, potentially, systemic circulation. By decreasing stomach acidity, antacids can also impair the absorption of minerals such as calcium.

d) Antibiotics disrupt the normal balance of bacterial microflora in the gut, as well as the mouth, vagina, and skin. This often leads to serious overgrowth of C. *difficile*, yeasts, and fungi in these areas resulting in infection and inflammation. Proliferation and overgrowth of Candida and other yeasts in the gastrointestinal tract can result in a complex of symptoms from gas, bloating, and gastrointestinal distress to unexplained chronic fatigue, depression, and various local gut and systemic inflammatory disorders.^{17,73-74,89-90,106}

7) Multiple nutrient deficiencies. These deficiencies particularly include antioxidants (vitamin A and carotenes, ascorbate, vitamin E, zinc, selenium, glutathione, Coenzyme Q10, sulfur amino acids); B complex (especially folate and pyridoxine); choline; inositol; magnesium; calcium; and pure, unoxidized fatty acids, particularly of the omega-3 variety. These nutrients are especially needed to promote optimal hepatic and digestive functions, epithelial growth and repair, and immune defense and repair mechanisms important in supporting an intact mucosal barrier.¹⁰⁷⁻

How can gut hyperpermeability be successfully treated and/or prevented?

Successful treatment and prevention of gut hyperpermeability is primarily dependent on removing and/or successfully treating the major causes.

This includes:

1) Avoid and reduce distress.^{55-60,116-127} This can be accomplished through the use of:

a) Counseling and/or group therapy;

b) Daily physical exercise (combination of passive stretching and aerobic exercise);

- c) Massage;
- d) Therapeutic biofeedback;
- e) Deep Breathing;
- f) Rest and sleep;
- g) Meditation;
- h) Play.

2) Change disease-oriented dietary patterns to health-promoting patterns by consuming a high-fiber, high-complex carbohydrate, low-fat (<20% total daily calories), moderate protein (mostly plant protein and fish) diet of WHOLE, unprocessed, organic (when possible) foods.^{77-80,128-132} Also, supplemental mucilaginous fiber (psyllium, flaxmeal, oatbran, etc.) can be extremely beneficial.²⁵⁻³²

3) Include many cultured/fermented foods in the diet and/or supplement with "host-friendly" microflora, especially of the Lactobacillus variety.¹⁷⁻²³

4) Successfully treat and/or reduce the pathology from any previous or concurrent gastrointestinal disorder, in the most least-invasive and conservative manner possible.⁴⁴

5) Minimize immune overload dysfunction. 34,95-105

This can be accomplished by:

a) identifying and reducing daily exposures to environmental chemicals, toxic metals, oxidants, and allergens as well as eliminating them from tissue stores in the body.

b) effectively treating any chronic viral, bacterial, or parasitic infections in a manner that is least disruptive to the normal physical economy.

6) When possible, minimize/reduce or totally eliminate the use of NSAIDs, steroids, antacids or antibiotics. If they can't be eliminated then concurrently treat with food supplements, nutrients, or medications which counteract their adverse effects.¹⁰⁶

7) Provide essential nutrients (amino acids, fatty acids, vitamins, minerals, and cofactors) in the most bioavailable and bioabsorbable forms and adequate doses to assure OPTIMAL metabolic functioning and restoration of reserves.¹⁰⁷⁻¹¹⁵

If you would take time to review the complete LRA by ELISA/ACT program of behavior, dietary, and nutritional supplement recommendations that come with your patient's results and interpretation, you will notice that we have taken the time to provide you with clear, therapeutic guidelines that address ALL the above therapeutic and preventive aspects of gut hyperpermeability.

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Contact

If you have any questions or would like more information about LRA by ELISA/ ACT testing, please contact ELISA/ACT Biotechnologies' Client Services

Department at 800-553-5472.