Integrative medicine and leaky gut syndrome

Brom B, MBChB, CEDH (Homeopathy, France), Dip Acup (Singapore)
Private Practitioner
Correspondence to: Dr Bernard Brom, email: drbbrom@mweb.co.za
Keywords: leaky gut; functional disturbances

Abstract

Leaky gut syndrome, also called increased intestinal permeability, is not a well-established diagnosis in general practice and yet is a well-recognised and common diagnosis within the community of integrative doctors. Perhaps this is because the integrative medical focus is not on the disease, but more on the functional dysregulation behind the disease. While the diagnosis of ulcerative colitis, for example, may satisfy most doctors, integrative doctors would also consider the underlying dysfunction, of which leaky gut may be an important consideration.

Leaky gut is regarded as the harbinger of a great deal of ill health and the later development of many chronic diseases, such as food intolerance, inflammatory bowel disease, rheumatoid arthritis and other autoimmune diseases. The mucosa lining of the intestinal tract is a protective layer between the contents of the intestine and the inside of the body. When dysfunctional, it becomes the entry point of pathogens and micro-toxins. As indicated in previous articles, any area of dysfunction in the body becomes the source and origin of ill health. The gastrointestinal mucosa is the largest interface between the internal body and the external environment and covers more than 400 square metres, hence its importance as a possible source of ill health.

Ⓟ **Peer reviewed. (Submitted: 2009-11-25, Accepted: 2010-03-10). © SAAFP** **SA Fam Pract 2010;52(4):314-316**

Structural and functional considerations

The gastrointestinal layer consists of a single layer of cells covering the villi and extends down into the crypts. There are some mucous (neck) cells that secrete a mucous gel which, in the stomach, is comprised of phospholipids protecting the surface epithelium from the gastric secretions.

The epithelial cells are joined at their apices by the zona occulodens, also called the 'tight junctions', and are supported at the deeper level by a thin vascular layer of connective tissue called the lamina propia. This pathway between the cells consists of two components, namely the tight junctions and the subjunctional space. The tight junctions form a circumferential seal at the luminal pole of adjacent epithelial cells and are the rate-limiting factor that regulates paracellular permeability.[1]

The tight junction can be seen as a netlike meshwork of strands and grooves that determine the resistance of this paracellular pathway. These strands have channels or pores that can open or close, and this may be influenced by intracellular events such as cAMP, calcium and protein kinases.[2]

The gastrointestinal mucosal layer has the specific function of allowing in only health-promoting nutrients and phytonutrients, while keeping out toxins, pathogenic organisms and other possible damaging molecules.

There are two pathways for transport across the epithelium. Firstly, there is the transcellular pathway. This is the pathway through the cell, which is controlled by the cell membrane. The second pathway is the paracellular pathway, which is the pathway between the cells that is controlled by the permeability of the tight junctions. In a normal healthy membrane there is very limited transport through the tight junction, forcing most substances to go through the cell in order to get into the circulation. This requires specific uptake systems for most substances to enable easy regulation of these substances. There is, however, some passive movement of some substances, such as fat-soluble substances, across the cell.

The lamina propia contains structural mesenchymal cells as well as the full complement of our immune system. The larger part of the immune system is located in the gut. About 60% of the immune system and more than 80% of the immunoglobulin-producing blasts and plasma cells are located within the mucosa of the gastrointestinal tract, which

collectively is referred to as the gut-associated lyphoid tissue (GALT) and indicates the importance of the defence system between the external environment of the bowel and what is allowed through.[3] The autonomic nervous system sends some fibres into this area and has an important role to play in the control of intestinal transport.[4]

In addition to all the above, the microflora within the lumen of the intestinal tract and the liver, towards which all absorbed intestinal contents must flow for further processing, also play very important roles.

From function to dysfunction

The above short review of the functional integrity of the mucosa lining suggests a very complex and integrated system, such that a very clear barrier is created between the intraluminal space of the bowel and the blood towards which all nutrients are directed. Any increased permeability at the level of the tight junctions could lead to pathogens entering or allowing unprocessed proteins or large amino acids that have intact antigenic sites on them entering. In the healthy intestinal tract the tight junctions limit the transport of large molecules (0.500 Da) across the epithelium, but in the unhealthy bowel the tight junctions become leaky. 'Leaky gut' is the name given for this increase in intestinal permeability and is commonly seen in patients presenting with inflammatory bowel disease,[5] food allergies and intolerances[6] and celiac sprue.[7]

Intestinal permeability may be the main cause of sensitivity to particular types of food. In a study authored by Ventura, a statistically significant difference was found in intestinal permeability in subjects with food allergy or hypersensitivity compared to controls, and the results indicated that the worse the permeability, the more serious the clinical symptoms.[8]

In a more recent study, scientists evaluated the function of the gut in patients with chronic heart failure and found that these patients, compared to controls, had a 35% increase in small intestine permeability and a 210% increase in large intestine permeability. They suggested that chronic heart failure may be a multisystem disorder.[9]

Having passed through the leaky gut and past the immune barrier, gut-derived chemical substrates must still be dealt with by the liver's detoxification mechanism. The cost of this, however, is high, as free radicals are generated and anti-oxidants consumed. There may be an increased production of oxygen radicals and there is some evidence that multiple organ dysfunctional syndrome may have its roots in increasing intestinal permeability.[10,11]

Increased gut permeability can also cause immunological disturbances. These may be classic hypersensitivity responses to foods and components of normal gut flora, bacterial endotoxins, cell-wall polymers and dietary gluten, which may cause 'non-specific' activation of inflammatory pathways mediated by cytokines.[12] McKay et al[13] indicate in their article that cytokines have an important role to play in the regulation of homeostasis in the intestine.

Diagnosing intestinal permeability

The diagnosis of intestinal permeability is best achieved by the intestinal permeability test,[14] which is a non-invasive test using two innocuous sugars, namely mannitol, a monosaccharide, and lactulose, a disaccharide, with different absorption criteria. Both are water-soluble molecules that the body cannot use. Mannitol is easily absorbed by people with healthy intestinal linings. Lactulose is a larger molecule and is only slightly absorbed. If high levels of both are found in the urine after a specific time period, this suggests leaky gut. This test is currently not available in South Africa.

A good history can also offer some indication of a possible leaky gut. Intestinal symptoms of bloating, indigestion and irregular bowel actions are already suggestive, especially if associated with food intolerance and intestinal inflammation.

Why is the diagnosis important?

Many diseases are associated with leaky gut and it is possible that leaky gut itself is the forerunner of these conditions rather than merely the consequence of the disease. Once the gut's mucosal integrity is disturbed, this can lead to GALT activation mediated by food proteins and microbial agents. This in turn initiates a Th2 allergic response or a Th1 autoimmune response. Systemic inflammation then ensues, along with a wide host of common and often difficult-to-treat ailments.[15]

A number of precipitating factors are associated with leaky gut, such as anti-inflammatory drugs and cortisone.[16] Other factors include alcohol consumption,[17] radiation therapy for cancer, stress, excessive simple sugar consumption, food allergies, nutrient insufficiencies, premature birth and whole-food exposure before the age of four months.

Treating the disease with drugs without considering the possible underlying dysfunction that could have led to the disease should be regarded as incomplete and even poor medical practice. Leaky gut is often only one of the underlying dysfunctional problems within the system. Integrative doctors would also consider other possible problems such as insulin resistance, bacterial flora disturbances, especially in someone who has been prescribed antibiotics repeatedly, stomach acid hyposecretion, nutritional deficiencies and metal and other toxicities that are commonly present today.

Management of leaky gut

One of the classical approaches used by integrative doctors is to use the 4 R approach of Remove, Replace, Reinoculate and Repair.[18]

Remove applies to the removal of aggravating or precipitating factors. This may include foods to which the system is intolerant – often wheat or dairy products. Refined

sugars and carbohydrates should be avoided, as should be alcohol and certain drugs that are known to cause leaky gut such as non-steroidal anti-inflammatory drugs (NSAIDs). Dysbiosis due to micro-organism overgrowth, especially fungal problems, may require a broad-spectrum antifungal. A general elimination diet is a good way to start the process.

Replace refers to the replacement of digestive factors. Hydrochloric acid from the stomach keeps the upper bowel sterile; enzymes may be deficient and should be replaced if there is any evidence of maldigestion.

Reinoculate refers to the reintroduction of friendly bacteria. Fructo-oligosaccharides support the growth of probiotics and can be added to the programme.

Repair refers to nutritional and other medications that support healing. The emphasis can be seen as supporting health, and a great deal can be done without the use of drugs, which may only aggravate the problem. Nevertheless, depending on the whole picture, well-placed drugs may still be essential in the management. Healing nutrients include l-glutamine, an amino acid considered to be a principal carrier of nitrogen. The enterocytes and many of the components of GALT (Gut Associated Lymphoid Tissue) use glutamine as a preferred respiratory fuel.

Discussion

Physiological functions within the body are exceedingly complex, with multiple feedback loops such that any attempt to trace a disease backwards is almost impossible. The result has been that most doctors do not go further than the conventional medical diagnosis and treat the disease as if it is the problem. This would be equivalent to treating the crack in the wall that can be easily identified and not bothering with the structural problem of the building, which would be impossible to identify with exact precision.

Leaky gut syndrome or increased intestinal permeability is one of the background causes and/or aggravating factors in many diseases. Many diseases are associated with leaky gut and the treatment used can often aggravate the problem. Substances that damage the integrity of the intestinal mucosa, disrupting the desmosomes that bind epithelial cells and increase the passive, paracellular absorption, include infectious agents (viral, bacterial and protozoa), ethanol and NSAIDs. Other factors identified include hypoxia of the bowel (occurring as a consequence of open-heart surgery and shock), elevated levels of reactive oxygen metabolites and cytotoxic drugs.

Conclusion

Leaky gut may be the primary cause of a whole range of different medical disorders. It may also be one of the underlying contributing factors, as the human biological system is exceedingly complex and it is unlikely that the background problem of disease has only one underlying cause. There will often be associated nutritional deficiencies and metal toxicity – especially mercury and aluminium and other toxins from the environment – all of which contribute to a state of dysfunction, which in turn causes the whole system to become stressed. This stress will eventually translate into a 'disease'.

The integrative approach is to assess the underlying dysfunctional integrity of the system and to treat this together with the diagnosed disease. The medical practitioner must also discuss with the patient lifestyle changes that are required to prevent further pressure on the system.

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