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One Reader at a Time...

# PUBLIC HEALTH ALERT

## Lyme Disease Management: Immune Health Part 2

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Lyme disease management requires a healthy immune system. A healthy immune system requires a healthy gastro-intestinal (GI) tract. To summarize the first article on this topic, the GI tract significantly affects the immunological system. The gastrointestinal tract is full of potential immune triggers. For the most part, the body is able to recognize and tolerate most non-harmful triggers. It is when an immunological response occurs and the inflammatory response is uncontrolled then the next level of inflammation is stepped-up. This next level of inflammation includes:

- ❖ Continued deregulation of the immune system
- ❖ Leaky gut syndrome
- ❖ Continued imbalance in the TH1/TH2/TH 17 lymphocyte profile
- ❖ Depletion of the natural killer cells

- ❖ Disruption of the hormonal system
- ❖ Increased sensitivity or allergic response to a wider spectrum of agents

This Part Two of a three-part series will discuss evaluation and testing of the immune dysfunction caused by the GI tract.

### What's Living in You

Throughout all the information on Lyme disease, antibiotics are used without the appreciation of the bacterial flora except for the administration of probiotics. Yet, analysis of the GI flora is rarely examined to determine the extent of the dysbiosis that is occurring within the intestine. Although the short-term use of antibiotics with the use of probiotics might not require such an examination, the long-term use of antibiotics could have detrimental effects which would affect the innate immune system

generating a profile of chronic inflammation. This chronic inflammation profile could complicate the symptoms and compromise improvement, resulting in a confused issue in health management.

There are two methods to evaluate the small intestine for harmful bacteria overgrowth; one method that is specific to leaky gut syndrome, which occurs in the small intestines; and secondly, a test for the evaluation of the large intestine. All of these tests have their benefits and drawbacks. In essence, what is being evaluated is the total antigenic burden in the intestine, resulting in altered GI permeability and over-activation of the immune system.

### Small Intestine

One method that is available to evaluate internal ecology of the small intestine is with a urine analysis for organic acids, Clostridia species, D-Lactate and D-arabinitol. These

measurements could indicate if the patient has small intestinal bacterial overgrowth (SIBO) and/or yeast overgrowth. This test gives specific quantitative results of the type of bacteria. The urine analysis can usually be expanded to include additional metabolic products which would provide clues on deficiencies which would affect detoxification, neurotransmitters, energy production cycles and oxidative stress. The drawback of these tests is the expense.

The second method of measuring bacterial overgrowth is an abnormal hydrogen breath test. Abnormal bacterial overgrowth is usually the result of low stomach acid, maldigestion or stasis. In some cases *Helicobacter pylori* may be the causative bacteria. The main destruction is done by the enzymatic action of the bacteria destroying the integrity of the protective coating of the small bowel, permitting digestive enzymes to further breakdown the lining

# PUBLIC HEALTH ALERT

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cells of the intestines. The drawback with this test is the lack of identifying a quantifiable result of other bacteria that may be present.

The measurement of leaky gut syndrome is, at first, pretty straightforward. Two sugars, lactulose and mannitol, which are minimally metabolized, are given at the same time. Mannitol is passively transported through the intestinal wall while lactulose is impermeable in a healthy gut. The ratios of the two sugars are measured in a urine analysis. The ratio in a healthy gut is less than 0.03. If the lactulose level is high then there is an increase intestinal permeability, whereas, if the mannitol level is low then there is an absorption problem. The lactulose/mannitol challenge test is done fasting and with a meal. The complicated part comes with trying to determine the exact causative agent through an elimination rotational diet. Allergy testing will not always identify the causative agent. The underlying bacterial dysbiosis also needs to be considered in this evaluation.

## Large Intestine

Evaluation of the internal ecology of the large intestine can be done in one or two methods. The first method, which has been more established, is done with cultures and

microscopic evaluation. The advantages are the standardized care-culture technique and the microscopy and enzyme-linked immuno-assay technology and techniques which are well established and validated. This method also has many shortcomings. One of the most obvious is the difficulty in collecting and growing an anaerobic strain of bacteria, which happens to be the predominant organism of the GI tract. Of the bacteria that can be grown, it requires 1,000 to 5,000 cells to culture. The second drawback is the microscopic detection for parasites which require 25,000 cells per gram.

The other method to detect and measure what bacteria is in the large intestine is by DNA strand identification, PCR, and chemical analysis. This has a higher sensitivity for discovering the organisms present in the GI tract and identification. There is an ease of collection and transport. It only requires 1 to 5 cells for identification of bacteria and only 5 cells per gram for parasites. This method has its shortcomings in that PCR techniques and reference ranges are not clinically validated. Correlation between quantification of pathogen or resistance genes based on PCR is not fully known. Ability to determine bacterial strains and specific species depends on limited avail-

ability and cost of commercial probes (especially for anaerobes). There are a few human studies on clinical significance of using PCR evidence of a protozoan pathogen.

(Reader Caveat: The following section is detailed and technical. If you find this a bit overwhelming, advance to the summary paragraph to obtain the pertinent concepts)

## Identification of GI inflammation

Both lactoferrin and calprotectin are proven markers of intestinal inflammation. They distinguish inflammatory bowel disease from irritable bowel syndrome.

Fecal lactoferrin is an iron-binding glycoprotein which is expressed by a white blood cell seen in acute inflammation or infection, the neutrophil. Elevated levels of lactoferrin indicate neutrophil infiltration of the inner layer of the intestines, the mucosa. Lactoferrin is 90% specific for active inflammatory bowel disease versus irritable bowel syndrome, thereby lactoferrin uniquely discriminates an inflammation from infection.

Fecal calprotectin plays a regulatory role in inflammatory process. It is a reliable marker for the presence of infectious, inflammatory or malignant disease. It is released by mobilized and activated

neutrophils in the gut in response to cell or tissue damage, increased permeability of the mucosa, or infectious processes.

## What About Your Immune System

An over-expression of the immune system caused by gut inflammation normally responds as a systemic inflammatory response of the cytokines. This results in inflammation messaging throughout the whole body. These over-expressions of an inflammatory response through cytokine chemical messengers are imitated by the dendritic cells. Upon a dendritic cell encountering a pathogen, cytokines or specific tissues, it will process that information and either engulf it; facilitate antibody production through another lymphocyte, the B cells; cause an oxidative burst of the substance; deliver cytokines to the foreign substance; or lead to further cytokine production by means of activating T- lymphocytes. T lymphocytes belong to a group of white blood cells known as lymphocytes, and play a central role in cell-mediated immunity.

The immature T lymphocyte is activated and the T lymphocyte activation begins at an immature T lymphocyte or Th-naive cells (Th0 cells). The Th0 cells are transformed into Th1, Th2 or Th17 lymphocytes, which have different

levels of interaction. For those without an immunology background, mainly get the idea that Th1, Th2, and Th17 will respond to a stimulus differently, as outlined below. Please refer to the first article to clarify cellular versus humoral immunity.

The dendritic cells can also signal the Th0 cells to produce T-regulatory cells. The T-regulatory cells' net effect in the gut is to maintain tolerance by dampening immune responses to ingested antigens. The T-regulatory cells also modulate and balance TH1, TH2 and TH17 lymphocyte subsets. It is the modulation lymphocyte subsets which maintain balance throughout the whole body.

- ❖ Th1 produces mostly cellular immunity and is measured by IFN gamma, IL-6, and TNF-alpha.
- ❖ TH2 produces mostly humoral immunity and is measured by IL-4, IL-5, IL-6, IL-10
- ❖ Th17 produces chronic inflammatory immunity and is measured by IL-17

❖ Tregulatory for example CD4+CD25+ and is measured by IL-10 and TGF-beta

Th17 is the primary driver of chronic inflammation by producing interleukin 17 cytokines, IL-17. IL-17 further stimulates NFkB (COX-2) and MAP kinases production, which initiate inflammation in Lyme arthritis. NFkB is a measurable unit and can be used to determine the degree of inflammatory response the body is undergoing.

Another inflammatory marker of the innate immune system are complements, c3a and c4a. These will guide to determine whether the inflammation is an autoimmune versus infectious process. The Inflammatory markers of the erythrocyte sedimentation rate, anti-nuclear antibody, C reactive protein and the immunoglobulin subclasses may also be of assistance.

A measure of a healthy and responsive innate immune system is the level of the functional natural killer cell activity.

These cells are depleted in response to chronic inflammation and the imbalance of excessive Th1 expression. The NK cells can be monitored to reflect the improvement of the immune system.

## Summary

The foundational testing associated with both Lyme disease and gastrointestinal inflammation are many. If the situation occurs when the use of antibiotics are not giving the symptomatic relief expected and it appears that the Lyme is still prevailing, look at other regions which can interfere with a healthy immune response. Of importance is the possible inflammation harbored in the GI tract. This can be investigated by exploring the function and possible bacterial overgrowth of the small intestine. The intestinal permeability or leaky gut syndrome should be reviewed. There could be a possible harmful bacteria or parasites in the large intestine. All of these interactions

should be compared to the current presentation of possible decline in immune status as fatigue, skin rashes, diarrhea, toxic feelings, shortness of breath, joint and muscle pain, fevers of unknown origin, food intolerance, abdominal discomforts and cognitive changes. To determine the immune directed pathway for the symptoms, utilize laboratory measurements of immune activation and immune tolerance, as described above.

Next article will present a case study and treatment.

For any further information please visit our website page on Lyme disease: <http://www.alternativemedicinehealthcare.com/immune-health/lyme-disease>.

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