

LRA by ELISA/ACT® CLINICAL UPDATE # 4

Gut Immunology

Intestinal Immunoregulation of Gut-Associated Antigens

The risk of developing food allergies leading to systemic disease is increased in individuals with transient or permanent immune deficiency disorders. This is also true of children who are formula-fed instead of breast-fed and/or have had whole foods introduced prematurely (within the first 3-6 months of life). The primary reason for this is that the local (gut-associated) and systemic immune systems make up a major part of the intestinal mucosal barrier. In newborns these systems are still immature and inexperienced, while in adults with immune deficiency problems, they are dysfunctional. In both cases, the systems are inadequate, therefore unable to optimally process the myriad of gut-associated antigenic substances from food as well as microbial organisms. When these substances are not processed adequately, systemic exposure occurs. This often results in immediate or delayed type hypersensitization and local and systemic inflammation.

Below is an overview of the immunologic components of the gut mucosal barrier. The immunologic component of the gut mucosal barrier is made up of a number of elements of the immune system that work closely together to regulate and process dietary and microbial antigens from the gut.[1,2] These elements include:

- 1 The gut associated lymphoid tissues (GALT)**
 - Peyer's patches (lymph nodes of the intestine) located mainly in the mucosa and submucosa of the ileum
 - Diffuse lymphoid tissue of the lamina propria (a deep layer of the intestinal mucosa)
 - Intra-epithelial lymphocytes (IEL)
- 2 The Peyer's patch-activated, systemically recirculating T lymphocytes, and the local immune-active cells**
- 3 T and B lymphocytes (the majority of B cells commit to sIgA synthesis and the T cells play a major immunoregulatory role)**
- 4 Plasma cells**
- 5 Macrophages**
- 6 Eosinophils**
- 7 Basophils.**

There are three basic, closely interrelated mechanisms involved in the immune response to food antigens.[2] These include:

- 1 Immune exclusion** - involves mucosal protection mediated by secretory immunoglobulins (sIgA) in conjunction with nonspecific mechanisms.

- 2 Immune elimination** - involves the clearing foreign substances/antigens from the circulation that have penetrated the mucosal barrier.
- 3 Immune regulation** - involves T cell-mediated (possibly along with other mechanisms) immune regulation for the establishment of oral tolerance.

The clinical consequences of breakdown of these intestinal immunoregulation mechanisms include:

- 1 Food sensitive enteropathies** (intestinal mucosal damage) due to immunologic damage and increased uptake of large protein molecules,
- 2 Increased intestinal permeability of "leaky gut",**
- 3 Immune complex formation** with gut-associated (dietary and microbial) antigens,
- 4 Immune complex deposition** in tissues with resultant inflammation,

INDEX

Immunoregulation . . . 1
Depressed Immunity . . . 2
References 2
Contact. 2

- 5 **IgE mediated systemic pathology** (anaphylaxis, asthma), and
- 6 **Further intestinal mucosal damage** from T cell mediated (Type IV) local inflammation.

Upon reviewing the immunologic components of the gut mucosal barrier, the importance of the immune system is apparent. It regulates and processes gut associated antigens to prevent their entrance into systemic circulation with subsequent sensitization and pathology. This is why we, at EAB, stress the importance of optimizing immune function. It is a key therapeutic intervention for preventing gut hyperpermeability, food allergies, and their resulting problems. Whenever there is an immunocompromised state in an individual, (genetically or developmentally induced or caused by other exogenous factors such as infections, environmental toxicities, or distress) it should be corrected. When immunity is compromised, the gut mucosal barrier is compromised.

Gut-Associated Antigens and Depressed Immunity

It is now becoming well known that the gut mucosal barrier is not impermeable to large, antigenic molecules and that it is, therefore, a major portal of entry for foreign antigens from a number of sources (foods, bacteria, parasites, drugs, and environmental chemicals).[3-8]

It is also becoming well known that these gut-associated antigens can initiate and/or promote local and systemic immune responses resulting in inflammation and tissue/organ pathology.[3-13] What is not yet well known, however, is that these gut-associated antigens can also impair systemic immunity and put the host at great risk for infectious disorders.[13]

Dr. E.A. Deitch and colleagues from the Department of Surgery and Microbiology at the Louisiana Medical Center

recently published results of their study demonstrating an association between bacterial translocation from the gut and impaired systemic immunity.[12] According to their results, translocation of gut-associated bacterial antigens can suppress systemic immune responsiveness through the induction of oral tolerance. This down-regulation of the systemic immune response may "increase survival of the translocating bacteria" and "predispose a patient to subsequent infectious complications". It may also be interesting to note that the basic mechanisms that induce and promote gut-associated bacterial translocation include:

- 1) disruption of the balanced population of host-friendly, indigenous microflora (dysbiosis) resulting in overgrowth of gram-negative, enteric bacilli
- 2) impairment of host immunity
- 3) disruption of the gut mucosal barrier.[3,13-15] Sound familiar?

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Contact

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