

Functional Medicine University's Functional Diagnostic Medicine Training Program

Module 3 * FDMT 521A

Dysfunctions of the Immune System

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Additional Reading (Articles located on FMU website library):

Th1/Th2 Balance: The Hypothesis, its Limitations, and Implications for Health and Disease

Food Allergies and Other Food Sensitivities

Thymulin and zinc contents of the thymus glands of malnourished children

IMMUNE SYSTEM DYSFUNCTION

When describing optimal immune function, the concept of balance or equilibrium should be employed. If the immune system is 'in balance' the body is able to manage invading organisms with little to no negative side-effects. If an 'imbalance or dysfunction' of the immune system exists, the susceptibility to infection, cancer, allergies and autoimmune diseases increases.

In the first lesson of this module we learned that the controller of the immune system response was the T-helper cell. As you may recall, the antigen presenting cell stimulates the T-helper cell to bind to it. The T-helper cell (Th0) then determines how the immune systems will respond. The activated T-helper cell (Th0) then differentiates into either T-helper cell 1(Th1) or T-helper cell 2 (Th2). This differentiation is dependent upon the environment the Th0 is in. Molecules released by the antigen presenting cell effect different transcription factors of the Th0 cells which then determines whether the Th0 cell is differentiated to a Th1 or Th2 cell. This differentiation allows for the appropriate immune response to a specific invader.

Th1 cells produce the following cytokines:

1. IL-2
2. IL-12
3. Interferon –gamma
4. Tumor necrosis factor- beta

Th1 cells mediate activation of macrophages and neutrophils and are involved cell-mediated immune responses and organ-specific diseases. They also stimulate the production of IgG antibodies. Some of the diseases associated with Th1 dominant immune response are: rheumatoid arthritis, Crohn's disease, Thyroiditis, multiple sclerosis and insulin dependent diabetes mellitus.

Th2 cells produce the following cytokines:

1. IL-4
2. IL-5
3. IL-6
4. IL-10
5. IL-13

Th 2 cells stimulate the activation of mast cells, eosinophils, basophils, IgE antibodies and IgG4 antibodies and are also involved in humoral responses, systemic autoimmune diseases and chronic diseases. Some of the diseases associated with Th2 dominant immune response are: asthma, contact dermatitis and allergic diseases.

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The Th1/Th2 hypothesis has its basis on the different cytokines released by the cells. The cytokines influence the immune response and tolerance. The key to an optimal functioning immune system is to have balance between the two responses. Under expression and over expression of cytokines and signaling proteins have been associated with the cause of autoimmune disease and malignancy. Some examples are: IBD, SLE, Type 1 diabetes, vasculitis, rheumatoid arthritis and lymphoma.

One consideration with this hypothesis is that cytokine activities rarely fall into exclusive Th1 or Th2 patterns. I believe it is more important to appreciate that an imbalance exists and to look for the root cause(s) of the imbalance and learn how to use nutrients and hormones to restore balance.

Nutrients and other orthomolecular substances that modify (balance) the immune system:

1. Melatonin
2. DHEA (dehydroepiandrosterone)
3. Progesterone
4. Selenium (also needed for the peripheral conversion of T4 to T3)
5. Zinc
6. Probiotics (esp. *L. rhamnosus* GG)
7. Phytochemical: Phytosterols and Sterolins
8. Essential Fatty Acids (omega 3)

*Please read the following article found on FMU website library:
Th1/Th2 Balance: The Hypothesis, its Limitations, and Implications for Health and Disease*

CATEGORIES OF IMMUNE DYSFUNCTION

Two categories of immune dysfunction have been described: *underactive* and *overactive*. An underactive or weakened immune system response has been attributed to toxic exposure and other external influences. The cause of a weakened immune system in a small percentage of people is genetic abnormalities that usually manifest during the first few years of life. This type of weakened immune system is called "primary immune deficiency".

CAUSES OF IMMUNE DYSFUNCTION

The cause of immune dysfunction is usually multi-factorial. The concept of 'toxic load' or 'toxic overload' on the body systems is described as the sum of the total amount of deleterious external influences on the body. If the body has an adequate supply of internal reserves, that is, optimal gastrointestinal function, optimal nutrition status, optimal liver function, hormonal balance, good genetics and low stress levels, it is usually able to cope with most external influences. Our challenge as functional medicine practitioners is to identify and treat all deleterious influences on the immune system

Deleterious external influences on the immune system

1. Nutritional deficiencies (malnutrition, poor diet)
2. Pharmaceuticals (e.g. Antibiotic overuse)
3. Gastrointestinal dysbiosis (bacteria, fungus, virus and/or parasitic)
4. Environmental toxins (chemicals [xenobiotics], toxic metals, radiation)
5. Food sensitivity, food allergy, food intolerance
6. Liver dysfunction (poor detoxification and excretion)
7. Systemic infections (virus, bacterial)- herpes simplex I, herpes simplex II, Epstein-Barr virus, cytomegalovirus, human herpes virus 6, HIV/AIDS, hepatitis
8. Elevated stress levels
9. Lack of exercise
10. Free radical damage
11. Hormonal imbalances (adrenal/thyroid/male/female)

It is generally easier to identify patients with an overactive immune system based on the overt signs and symptoms. Some examples are food allergies and rheumatoid arthritis.

Signs And Symptoms Of Immune Dysfunction

- Chronic Runny Nose (indications)
 - chronic sinusitis
 - dysbiosis of the small intestine and/or sinuses
- Frequent colds
 - hypothyroidism
 - intestinal dysbiosis
 - need for immune support
- Chronic lung congestion
 - need for immune support
 - need to detoxify
- Itchy skin/dermatitis/cysts/boils/rashes
 - immune system support
 - need to detoxify
 - gastrointestinal dysfunction
- Chronic infections
 - intestinal dysbiosis
 - need for immune support
- History of:
 - autoimmune disease
 - chronic fatigue syndrome
 - fibromyalgia
 - chronic fatigue and immune deficiency syndrome (CFIDS)

Adverse Food Reactions

Food allergies have the potential for *contributing* to immune dysfunction and well as *being the result* of a dysfunctional immune system. Food allergies cause immune dysfunction by the following mechanisms:

- Stimulation of cytokine release
- Immune complex formation and deposition
- Damage to the intestinal lining
- Molecular mimicry (structures similar to human molecules cause a cross-reacting immune response)

*Please read the following article found on the FMU website library:
Food Allergies and Other Food Sensitivities*

Types of Food Reactions

Although there is some disagreement on underlying mechanisms, most experts agree that adverse reactions to food should be classified as food allergy, food sensitivity, or food intolerance.

Food allergy

- This term will be used to designate a response mediated by food-triggered basophil or mast cell histamine release. This can be caused by either IgG or IgE food-specific antibodies. These reactions are immediate in nature and can be severe. This is the type Type I allergic reaction.

Food sensitivity

- This term relates to a purely immune system-mediated response involving various classes of food-specific immunoglobulin molecules that can form food immune complexes. These complexes can stimulate the complement cascade and localized inflammation. These reactions tend to be delayed –hours and up to 7 days after food consumption – in some cases. This is a Type III allergic reaction.

Food intolerance

- This term refers to a non-immunological mechanism of adverse food response. Examples would include lactose intolerance and MSG sensitivity.

Dysbiosis

Dysbiosis has been defined as a non-acute host-microorganism that adversely affects the host. Aside from *intestinal dysbiosis*, dysbiosis can also occur in other parts of the body such as: the skin, the mouth and teeth, the respiratory system, the genitourinary system, and the parenchyma of the liver; all of which can be caused by environmental dysbiosis/toxins (dust, mold and chemicals).

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Some of the mechanisms of disease induced by microorganisms are:

- Molecular mimicry – structures similar to human molecules cause a cross-reacting immune response.
- Endotoxins from bacteria – lipopolysaccharides (LPS) can cause inflammation, leaky gut and liver dysfunction.
- Immune-complex formation and deposition – these complexes are difficult for the body to clear and are known to deposit in the skin and joints, causing tissue destruction.
- Damage to the intestinal lining

Some conditions that suggest dysbiosis are:

- Food allergies
- Ankylosing Spondylitis – Klebsiella overgrowth
- Crohn's disease
- IBS
- Rheumatoid arthritis – Yersinia, Salmonella overgrowth
- Eczema
- Psoriasis
- Colon cancer

External toxins

External toxins can cause immune dysregulation. On average, in industrialized countries, humans consume several pounds of toxins per year, which include:

- Food additives
- Pesticides
- Prescription drugs
- Herbicides
- Toxic metals
- Petrochemicals
- Out gassing from plastics
- Chemotherapy
- GMO (genetically modified foods)

THE IMPORTANT ROLE OF ZINC

The average adult male body contains between 1.5-2.5 grams of zinc, most of which is found in the bones and muscles. There are no reserves of zinc in the body that are readily mobilizable; therefore, a steady intake is important to prevent deficiency. Zinc is required for the functionality of over 300 enzymes and plays a role in the metabolism of lipids, carbohydrates, proteins and nucleic acids. Zinc is necessary for normal T lymphocyte and macrophage activity. Zinc deficiency, even if borderline can cause an imbalance between T-helper cell subpopulation.

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Some important zinc metalloenzymes are:

- Alkaline phosphatase
- Carboxypeptidase
- DNA polymerase
- RNA polymerase
- Carbonic anhydrase
- Zinc-copper superoxide dismutase

Note: The functions of metal ions include:

- *Electron transport/transfer*
- *Small molecule/atom transport and transfer*
- *Bind and activate substrate*
- *Stabilize protein structures*

Zinc functions

- Stabilizes DNA-binding protein which regulate gene expression
- Needed for synthesis of collagen
- Needed for thymic hormone (thymulin). Thymulin is involved in T-cell differentiation and enhancement of T-cell and NK-cell activity. Thymulin may also prevent overproduction of pro-inflammatory cytokines
- Reproduction, taste, vision and vitamin A metabolism
- Needed for serotonin, sex hormone and insulin production
- Needed for some digestive enzymes

*Please read the following article found on the FMU website library:
Thymulin and Zinc Contents of the Thymus Glands of Malnourished Children*

Deficiency of zinc –clinical indication

- Depressed growth
- Poor immune function (susceptible to colds, infections and flu)
- Alopecia
- Eye and skin lesions (acne)
- Diarrhea
- Reduced smell and taste
- Benign prostatic hypertrophy
- White spots on nails

Assessing zinc status

To date, there is no generally accepted standard index for zinc status. *RBC-zinc* may be useful due to high concentration of zinc enzymes and *Alkaline phosphatase* can serve as a supportive measure. *Urinary zinc* is a poor indicator of early zinc depletion. A measure of 24- hour urine can be clinically useful. *Hair analysis* remains controversial.

Zinc Taste Test

- Use aqueous zinc
- Procedure:
 - Do not eat, drink or smoke less than one hour before testing. Hold and swish about 10 ml of zinc solution in mouth for 10 to 30 seconds.

Finding	Grade	Interpretation
No taste (tastes like water)	1	Marked zinc deficiency
No immediate taste though a vague taste develops over time	2	Moderate zinc deficiency
Slight initial taste that becomes stronger over time: may be unpleasant	3	Mild zinc deficiency
Very strong, unpleasant and immediate taste	4	Zinc sufficient

- Optimal forms of zinc:
 - gluconate, amino acid chelates
 - Food sources: red meat, oysters, whole grains
- Zinc repletion:
 - Zinc gluconate has been used at zinc equivalent doses of 5 mg/day, 10mg/day and 50 mg/day. (25mg/day is a good repletion dose for 1 to 2 months)
- Zinc can interfere with copper absorption. Do not take large doses of zinc over a long period of time without assessing copper and iron levels.
- Retest zinc taste test and or RBC-zinc in 6 to 8 weeks.

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5. Functional Medicine University has obtained permission to reprint the articles provided for this lesson and are available with the Insiders Guide download.