

ADDRESSING AUTOIMMUNITY:

America's \$100 Billion Ticking Time Bomb

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According to the CDC - Autoimmune disease is a category that affects 50 million Americans. It is one of the top ten causes of death in women under the age of 65, is the second highest cause of chronic illness, and is the top cause of morbidity in women in the United States. Additionally, autoimmune diseases have been reported to be on the rise in the U.S. and around the world, making this poorly understood category of disease a public health crisis at levels comparable to heart disease and cancer.

What is Autoimmunity?

There are 100+ known autoimmune diseases, all caused by the common thread that is autoimmunity. The process of autoimmunity is initiated when one's immune system becomes overactive, and rather than destroy foreign invaders, such as bacteria and viruses, it targets one's own healthy cells and tissues causing various autoimmune diseases. Autoimmune diseases can affect any system in the body. Symptoms vary widely among the diseases, making the diseases difficult to diagnosis. Exactly what triggers an autoimmune response is unknown; however, researchers do know that autoimmune diseases occur where there is a genetic predisposition in the family towards autoimmunity and the presence of an environmental trigger, such as, viruses, bacteria, medications, pollutants, hormones, or stress.



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The Immune System

Our immune system protects us from foreign invaders. It is our body's military system to identify and destroy organisms that may harm us such as bacteria, parasites, and viruses. It does this like any military service, with weapons. The problem that people with autoimmune disease encounter is that their military no longer has a general, it can attack whoever, whenever, wherever, leading to the destruction of healthy tissue.

The immune system coordinates its attacks by use of things called inflammatory cytokines. Think of them as messengers that give orders to your cells on how to respond to molecules and microbes they come in contact with. Some of these messengers can tell the cells to cause more damage than others. One of the worst inflammatory cytokines is called NF- κ B. Most inflammatory cytokines use a firecracker to try and destroy foreign invaders, although NF- κ B uses a stick of dynamite. Unfortunately, NF- κ B can produce a perpetual cycle of destruction; even when the trigger that set off the initial response is removed.

Your body has a system in place to help keep your cells from being damaged by these inflammatory cytokines when they are on the attack. One of the main protectants is something called glutathione. The research demonstrates that supporting this glutathione system is a key step in potentially dampening an immune response. It mainly does this by quenching NF- κ B, by supporting a part of your immune system called TH-3, and helping restore your bodies natural barriers, such as your gastrointestinal (GI) lining.



It's All About Balance

Think of your immune system like a seesaw. One side is called TH-1, and the other side is called TH-2. In the middle of that seesaw is a fulcrum. This fulcrum is called TH-3, and this part helps regulate the immune system and the responses it has against foreign invaders. As with all things in the body, the immune system is all about being in balance. With autoimmune patients, there is usually an imbalance in the immune system. In these scenarios, one side is more dominant than the other. The higher the imbalance, the greater the severity of the immune response. This severity is determined by another branch of the immune system called TH-17. Therefore, if the immune system is brought closer to balance, this lowers the amount of healthy tissue being destroyed.

Food for Thought

Certain foods are known to stimulate either one side of the immune system or the other. An example of a TH-2 stimulator coffee. It is not uncommon to hear some people comment on how they feel like they are going to "fall apart" after drinking a cup of coffee whereas other people may say that they feel so much better after drinking a cup of coffee. There are several known TH1 and TH2 stimulants in the average person's diet which may need to be evaluated. Other non-food triggers that can stimulate the immune system can be the common cold. This can cause more collateral damage to your healthy tissues as your body is doing what it is designed to do and kill a foreign invader. Other things like inflammation and stress can also activate the immune system, which we will discuss later.



The Three-Legged Stool of Autoimmunity

The most accepted theory of how a person can acquire an autoimmune condition is called the 'triad theory'. This theory states that three factors have to be in place to trigger a reaction. The first is the right genetics. As most people are aware, these types of diseases run in the family. The second is that there has to be exposure to a trigger to cause a reaction. Thirdly, a person must have what is called intestinal hyper-permeability, or what is commonly called a "leaky gut." Over the past few decades, research has shown there is a high correlation between developing autoimmunity and inflammatory conditions in the GI tract. This makes sense because the majority of your immune system is in your GI tract.

1. The Role of Genetics

As most people are aware; autoimmune conditions tend to run in the family. There are certain genetic predispositions; called genotypes and phenotypes, and these types of diseases are usually more common in women. For the most part, women are usually the carriers of these genes. There are certain autoimmune diseases, however, that favor men. The list is short, but the most common ones are Ankylosing Spondylitis and Type 1 Diabetes.

2. Autoimmune Triggers

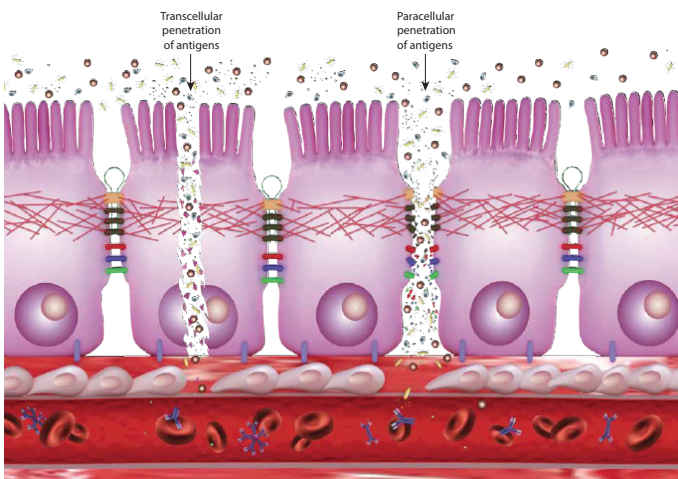
Here are a few common categories of the different varieties of things that can trigger an immune response that may develop into autoimmunity. The correlation between autoimmunity and these triggers vary; but they are worth noting.

- **Diet**- there are certain foods that are either known triggers, or are highly correlated with certain autoimmune diseases.
 - Gluten – Celiac's disease and type 1 diabetes
 - Milk – type 1 diabetes
- **Estrogen** – a common trigger for autoimmune thyroid issues.
 - Start of puberty
 - Pregnancies
 - Hormone replacement therapy
 - Birth control
- **Viruses and Parasites**- the incidence is low, but it is still present.
 - Coxsackie B virus and Type 1 diabetes
 - Hep. C and autoimmune hepatitis
 - Epstein-barr virus and Rheumatoid Arthritis
 - Ochoerca volvulus nematode and lupus (SLE)
- **Chemicals**- this is just a short list; as only 1% of chemicals are tested for safety.
 - Scleroderma and metals: the risk of scleroderma to miners is high, particularly silica; other possible metals involved are mercury, copper, and iron.
 - Iodine and autoimmune thyroid.
 - Silicone in breast implants and lupus (SLE)
- **Medications** - the incidence of these triggering and autoimmune response is low, but the risk is still there. Luckily a lot of these medications are either off the market, or utilized less by prescribing physicians.
 - Older blood pressure medications
 - Certain antibiotics
 - Certain anesthetics



3. The Role of the GI Tract in Autoimmunity?

Your GI tract is made up of cells that are tightly packed together. The cells are connected and held together by tight junctions. Similar to when you pull your shoelaces, both sides come together and tighten up. When the digestive tract becomes inflamed, these tight junctions become widened and allow substances like undigested food particles, toxins, and bacteria to enter the bloodstream. Once these undigested foreign substances are absorbed, the immune system reacts and starts to attack them, since they are viewed as invaders, and therefore, a threat. This creates a vicious cycle of further inflammation, which then promotes more permeability.



It is not uncommon for this to take years to progress. As the GI tract gets damaged, the cells become unable to fully digest food. This can lead to malnutrition, more inflammation, bacterial/yeast overgrowth, more food sensitivities and an immune system constantly on the attack. These vicious cycles can be difficult to unwind unless strategic dietary and nutritional strategies are employed.

What can cause leaky gut?

There are several things that can contribute to a leaky gut. A diet high in sugars, processed foods, fast food, dairy, gluten, and alcohol. Certain medications like corticosteroids, antibiotics, and antacids can contribute as well. Dysbiosis – or an overgrowth of bad bacteria, parasites, yeast, or a virus can also contribute to a leaky gut. A high stress lifestyle can also contribute due to high cortisol levels.

What do you do for a leaky gut?

The honest answer is, it depends. If you have an overgrowth of harmful organisms then bringing the microbes in your GI tract back into balance will help. Balancing blood sugar, thyroid hormones and sex hormones will also help in repairing a leaky gut.

Reducing stress will also help. Eating a healthy diet full of raw and organic food instead of “food” made with sugar and chemicals can be beneficial as well. Eliminating certain foods that your immune system attacks can be hugely beneficial.

Food Sensitivity Testing

In virtually every case, testing for food sensitivities can help dramatically. By objectively identifying which foods cause an immune response, we can take a personalized diet to the next level. This test cannot be overstated, especially since people with a gluten sensitivity are ten times more likely to develop an autoimmune disease! Foods such as dairy also have a high correlation with type 1 diabetes.

By removing certain foods, we can calm down the immune system allowing the GI lining to heal. It is important to remember that usually the food itself is not the problem, it is your body's reaction to that food that is the problem. Foods that are considered healthy such as avocados and bananas can also be on the list of foods to remove.

The reason these foods can start an inflammatory cascade by your immune system is because of a certain component of your immune system in your GI tract called your Gut Associated Lymphatic Tissue, or GALT. What the GALT does is sample the environment in your GI lumen. Once it detects molecules of food that your immune system has flagged as bad, it sounds the alarm to alert your immune system that there is an intruder. The inflammatory cytokines that are released by your immune system don't stay in the GI tract, they have been shown to cause inflammation throughout your entire body. This can help explain why food sensitivities can manifest their symptoms in areas other than the GI tracts such as the joints, heart, or brain.



Daily Grind

The word stress is ubiquitous in our society. In fact, people don't even realize how stressed they are these days. The three sources of stress are chemical, physical, and emotional. An example of chemical stress would be preservatives in food, as your body has to deal with these foreign chemicals. A physical source of stress would be like running a marathon or a chronic injury. The most common form of stress that people recognize is emotional, such as the loss of a loved one. Regardless of where the stress comes from, your body reacts the same way: by releasing stress hormones such as catecholamines and cortisol.



How does stress affect autoimmune disease?

Remember how we talked about your immune system being balanced? Well the higher the imbalance, the more the immune system gets ramped up. Stress can also activate TH-17 causing an immune flare-up. Not only that, but cortisol also thins the lining of the gut and can contribute to leaky gut as we discussed earlier. There are many ways to reduce stress or to learn to live with it. Exercise, meditation, and doing things you find enjoyable are a few examples. Stabilizing your blood sugars through diet and meal timing can also be a big help.


Constant Exposure

Another thing ubiquitous to our society is toxins. We come in contact with 84,000 chemicals a year, and only 1% of those have been tested for safety. Only 5 chemicals have been banned in the last 34 years!

Toxins are found in:

- Lotions
- Creams
- Plastics
- Make-up
- Toothpaste
- Fast foods
- Air fresheners
- Cleaning products
- Deodorants
- Water
- And many more

Many of these items you come in contact with daily and don't even think about. When we hear a patient talk about how they can no longer stand the perfume section in a store, or that pumping gas or other chemicals make them sick, it sets off a red flag.



“When a person starts to lose tolerance of the chemicals in their environment, they are usually also starting to lose tolerance to their own tissues as well.”

The chemical stress can cause the immune system to go into attack mode, and your own healthy tissue can be tagged as an enemy. Once a tissue is tagged, how fast the tissue gets destroyed is based on a few factors:

- the amount of antibodies
- the forcefulness of the attack
- the amount of tissue
- the antibodies accessibility to the tissue
- the amount of exposure to a particular trigger

Be mindful of what you put on your skin, the water you drink, the food you eat, and the air you breathe because they all play a critical role in your autoimmune condition.

Your Action Plan

Autoimmune diseases are diseases of inflammation and loss of tolerance to your own tissues. Research is showing that curcumin, a dietary spice from turmeric, can help dampen the inflammation that ultimately destroys your own cells. Also, another potent anti-inflammatory that has been shown to dampen the TH-17 response is called resveratrol. Research has also shown that to balance your immune system, TH-3 is heavily dependent on vitamin D, essential fats, and supporting glutathione levels.

It has been shown that exercising regularly is a natural anti-inflammatory. Also, learn to cope with stress with things like meditation or yoga, as stress heightens the immune response. Maintaining steady blood sugars can be of vital importance when trying to dampen an autoimmune response as well.

Getting tested to see if you have a leaky gut and food sensitivities is of primary concern when dealing with an overzealous immune system, as this can be a constant source of inflammation that you may be unaware of.

Checking your immune status is important as well. As we mentioned earlier, there is often an imbalance in the different parts of your immune system. Avoiding supplements and foods that can provoke your immune system to attack is a good tactic.

Another step is to get tested for any hidden infections. These are usually present in the GI tract. Most Americans are under the impression that parasites and other common over-growths are only in third world countries. Sadly, this is not the case. The majority of people that have an overgrowth are unaware of it, and you can't see a dysbiosis on a scope. The testing we recommend uses DNA technology to detect microbes, which is 5,000 times more sensitive than using a culture like traditional stool testing.

As you can see, there are many factors to consider when trying to manage an unruly immune system. Unfortunately, the current standard of care is severely lacking in addressing the dietary and lifestyle components of managing autoimmune diseases.

Working with a practitioner that is aware of this research is critical to the management of your case. There are many action steps that you can take to ensure your autoimmune disease is handled using the latest research and best functional medicine and lifestyle medicine strategies.



References

1. Ruland J. Return to homeostasis: downregulation of NF- κ B responses. *Nat Immunol*. 2011 Jun 19;12(8):709-14
2. Yan J Greer JM. NF- κ B, a potential therapeutic target for the treatment of multiple sclerosis. *CNS Neurol Disord Drug Targets*. 2008 Dec; 7(6): 536-57.
3. Zhao Y, Krishnamurthy B, Mollah ZU, Kay TW, Thomas HE. NF- κ B in type 1 diabetes. *Inflamm Allergy Drug Targets*. 2011 Jun; 10(3):208-17.
4. Hushmenday S, Jayakumar L, Hahn AB, Bhoiwala D, Bhoiwala DL, Crawford DR. Select phytochemicals suppress human T-lymphocytes and mouse splenocytes suggesting their use in autoimmunity and transplantation. *Nutr Res*. 2009 Aug; 29(8):568-78.
5. Shindler KS, Ventrua E, Dutt M, Elliott P, Fitzgerald DC, Rostami A. Oral resveratrol reduces neuronal damage in a model of multiple sclerosis. *J Neuroophthalmol*. 2010 Dec;30(4): 328-39.
6. Petro TM. Regulatory role of resveratrol on Th17 in autoimmune disease. *Int Immunopharmacol*. 2011 Mar; 11(3): 310-8. Epub 2010 Aug 12.
7. Anekonda TS, Adamus G. Resveratrol prevents antibody-induced apoptotic death of retinal cells through upregulation of Sirt1 and Ku70. *BMC Res Notes*. 2008 Dec 1; 1: 22.
8. Yoshida Y, Shioi T, Izumi T. Resveratrol ameliorates experimental autoimmune myocarditis. *Circ J*. 2007 Mar; 71(3):397-404.
9. Mito S, Watanabe K, Harima M, Thandavarayan RA, Veeraveedu PT, Sukumaran V, Suzuki K, Kodama M, Aizawa Y. Curcumin ameliorates cardiac inflammation in rats with autoimmune myocarditis. *Biol Pharm Bull*. 2011; 34(7): 974-9.
10. Xie L, Li XK, Takahar S. Curcumin has bright prospects for the treatment of multiple sclerosis. *Int Immunopharmacol*. 2011 Mar; 11(3): 323-30. Epub 2010 Sep 8.
11. Kurien BT, D'Souza A, Scofield RH. Heat-solubilized curry spice curcumin inhibits antibody-antigen interaction in in vitro studies: a possible therapy to alleviate autoimmune disorders. *Mol Nutr Food Res*. 2010 Aug; 54(8): 1202-9.
12. Xie L, Li XK, Funeshima-Fuji N, Kimura H, Matsumoto Y, Isaka Y, Takahara S. Amelioration of experimental autoimmune encephalomyelitis by curcumin treatment through inhibition of IL-17 production. *Int Immunopharmacol*. 2009 May; 9(5): 575-81.
13. Tewthanom K Janwityanuchit S, Totemchockchyakarn K, Panamvana D. Correlation of lipid peroxidation and glutathione levels with severity of systemic lupus erythematosus: a pilot study from single center. *J Pharm Pharm Sci*. 2008; 11(3): 30-4.
14. Yan Z, Garg SK, Kipnis J, Banerjee R. Extracellular redox modulation by regulatory T cells. *Nat Chem Biol*. 2009 Oct; 5(10): 721-3.
15. Yan Z, Banerjee R. Redox remodeling as an immunoregulatory strategy. *Biochemistry*. 2010 Feb 16; 49(6): 1059-66.
16. Vaarala O. Gut and the induction of immune tolerance in type 1 diabetes. *Diabetes Metab Res Rev*. 1999 Sep-Oct; 15(5): 353-61.
17. Fasano A, Shea-Donohue T. Mechanisms of disease: the role of intestinal barrier function in the pathogenesis of gastrointestinal autoimmune diseases. *Nat Clin Pract Gastroenterol Hepatol*. 2005 Sep; 2(9): 416-22.
18. Karper WB. Intestinal permeability, moderate exercise, and older adult health. *Holist Nurs Pract*. 2011 Jan-Feb; 25(1): 45-8.

19. Terjung B, Spengler U. Atypical p-ANCA in PSC and AIH: a hint toward a "leaky gut"? *Clin Rev Allergy Immunol*. 2009 Feb; 36(1): 40-51.
20. Hollander D. Intestinal permeability, leaky gut, and intestinal disorders. *Curr Gastroenterol Rep*. 1999 Oct; 1(5): 410-6.
21. Bock G, Prietl B, Mader JK, Holler E, Wolf M, Pilz S, Graninger WB, Obermayer-Pietsch BM, Pieber TR. The effect of vitamin D supplementation on peripheral regulatory T cells and B cell function in healthy humans: a randomized controlled trial. *Diabetes Metab Res Rev*. 2011 Nov; 27(8): 942-5.
22. Kleijwegt FS, Laban S, Duinkerken G, Joosten AM, Koeleman BP, Nikolic T, Roep BO. Transfer of regulatory properties from tolerogenic to proinflammatory dendritic cells via induced autoreactive regulatory T cells. *J Immunol*. 2011 Dec 15; 187(12):6357-64.
23. Hewison M. Vitamin D and immune function: an overview. *Proc Nutr Soc*. 2012 Feb; 71(1): 50-61. Epub 2011 Aug 1
24. Yan Z, Garg SK, Banerjee R. Regulatory T cells interfere with glutathione metabolism in dendritic cells and T cells. *J Biol Chem*. 2010 Dec 31; 285(53):41525-32.
25. Tada-Oikawa S, Murata M, Kato T. [Preferential induction of apoptosis in regulatory T cells by tributyltin: possible involvement in the exacerbation of allergic diseases]. *Nihon Eiseigaku Zasshi*. 2010 Sep; 65(4): 530-5.
26. Waite JC, Skokos D. Th17 response and inflammatory autoimmune diseases. *Int J Inflamm*. 2012; 2012:819467.
27. Yamada H. Current perspectives on the role of IL-17 in autoimmune disease. *J Inflamm Res*. 2010; 3:33-44.
28. Lubberts E. IL-17/Th17 targeting: on the road to prevent chronic destructive arthritis? *Cytokine*. 2008 Feb; 41(2):84-91.
29. Xuzhe G, Komai-Koma M, Leung BP, Howe HS, McSharry C, McInnes IB, Xu D. Resveratrol modulates murine collagen-induced arthritis by inhibiting Th17 and B-cell function. *Ann Rheum Dis*. 2012 Jan; 71(1): 129-35.
30. Petro TM. Regulatory role of resveratrol on Th17 in autoimmune disease. *Int Immunopharmacol*. 2011 Mar; 11(3): 310-8. Epub 2010 Aug 12.
31. Vojdani A, Lambert J. The Role of Th17 in Neuroimmune Disorders: Target for CAM Therapy. Part II. *Evid Based Complement Alternat Med*. 2009 Jul 21.
32. Culotta E, Koshland DE Jr. NO news is good news. *Science*. 1992; 258:1862-5.
33. Southan GJ, Szabo C. Selective pharmacological inhibition of distinct nitric oxide synthase isoforms. *Biochem Pharmacol*. 1996; 51(4): 383-94.
34. Reid MB. Role of nitric oxide in skeletal muscle: synthesis, distribution and functional importance. *ACTA Physiol Scand*. 1998; 162:401-409.
35. Kronke KD, Fehsel K, Kolb-Bachofen V. Inducible nitric oxide synthase and its product nitric oxide, a small molecule with complex biological activities. *Biol Chem Hoppe Seyler*. 1995; 376:32-343.
36. Buck M, Chojkier M. Muscle wasting and dedifferentiation induced by oxidative stress in murine model of cachexia is prevented by inhibitors of nitric oxide synthesis and antioxidants. *EMBO J*. 1996; 15:1753-1765.
37. Gius D, Botero A, Shah S, Curry HA. Intracellular oxidation/reduction status in the regulation of transcription factors NF- κ B and AP-1. *Toxicol Lett*. 1999; 106:93-106.
38. Turner JR. Molecular basis of epithelial barrier regulation: from basic mechanisms to clinical application. *Am J Pathol*. 2006 Dec; 169(6): 1901-9.

39. Nusrat A, Turner JR, Madara JL. Molecular physiology and pathophysiology of tight junctions. IV. Regulation of tight junctions by extracellular stimuli: nutrient, cytokines, and immune cells. *Am J Physiol Gastrointest Liver Physiol*. 2000 Nov; 279(5):G851-7.
40. Cuvelier C, Barbatis C, Mielants H, De Vos M, Roels H, Veys E. Histopathology of intestinal inflammation related to reactive arthritis. *Gut*. 1987 Apr; 28(4):394-401.
41. Rakoff-Nahoum S, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. *Cell*. 2004 Jul 23; 118(2):229-41.
42. Cario E, Gerken G, Podolsky DK. Toll-like receptor 2 enhances ZO-1 associated intestinal epithelial barrier integrity via protein kinase C. *Gastroenterology*. 2004 Jul; 127(1):224-38.
43. Lee J, Mo JH, Katakura K, Alkaly I, Rucker AN, Liu YT, Lee HK, Shen C, Cojocar G, Shenouda S, Kagnoff M, Eckmann L, Ben-Neriah Y, Raz E. Maintenance of colonic homeostasis by distinctive apical TLR9 signalling in intestinal epithelial cells. *Nat Cell Biol*. 2006 Dec; 8(12): 1327-36.
44. van Ampting MT, Schonewille AJ, Vink C, Brummer RJ, van der Meer R, Bovee-Oudenhoven IM. Intestinal barrier function in response to abundant or depleted mucosal glutathione in Salmonella-infected rats. *BMC Physiol*. 2009 Apr 17; 9:6.
45. Lammers KM, Lu R, Brownley J, Lu B, Gerard C, Thomas K, Rallabhandi P, Shea-Donohue T, Tamiz A, Alkan S, Netzel-Arnett S, Antalis T, Vogel SN, Fasano A. Gliadin induces an increase in intestinal permeability and zonulin release by binding to the chemokine receptor CXCR3. *Gastroenterology*. 2008 Jul; 135(1):194-204.e3.
46. Machowska A, Brzozowski T, Sliwowski Z, Pawlik M, Konturek PC, Pajdo R, Szlachcic A, Drozdowicz D, Schwarz M, Stachura J, Kontruk SJ, Palik WW. Gastric secretion, proinflammatory cytokines and epidermal growth factor (EGF) in the delayed healing of lingual and gastric ulcerations by testosterone. *Inflammopharmacology*. 2008 Feb; 16(1):40-7.
47. Money SR, Cheron RG, Jaffe BM, Zinner MJ. The effects of thyroid hormones on the formation of stress ulcers in the rat. *J Surg Res*. 1986 Feb; 40(2):176-80.
48. Braniste V, Leveque M, Buisson-Brenac C, Bueno L, Fioramonti J, Houdeau E. Oestradiol decreases colonic permeability through oestrogen receptor beta-mediated up-regulation of occludin and junctional adhesion molecule-A in epithelial cells. *J Physiol*. 2009 Jul; 587(Pt 13):3317-28.
49. Drago F, Montoneri C, Varga C, Laszlo F. Dual effect of female sex steroids on drug-induced gastroduodenal ulcers in the rat. *Life Sci*. 1999; 64(25):2341-50.
50. Gareau MG, Silva MA, Perdue MH. Pathophysiological mechanisms of stress-induced intestinal damage. *Curr Mol Med*. 2008 Jun; 8(4): 274-81.
51. Zen K, Chen CX, Chen YT, Wilton R, Liu Y. Receptor for advanced glycation endproducts mediates neutrophil migration across intestinal epithelium. *J Immunol*. 2007 Feb 15; 178(4):2483-90.
52. Korenaga K, Micci MA, Tagliatela G, Pasricha PJ. Suppression on nNOS expression in rat enteric neurones by the receptor for advanced glycation end-products. *Neurogastroenterol Motil*. 2006 May; 18(5): 392-400.
53. Purohit V, Bode JC, Bode C, Brenner DA, Choudhry MA, Hamilton F, Kang YJ, Keshavarzian A, Rao R, Sartor RB, Swanson C, Turner JR. Alcohol, intestinal bacterial growth, intestinal permeability to endotoxin, and medical consequences: summary of a symposium. *Alcohol*. 2008 Aug; 42(5):349-61.
54. Bansal V, Costantini T, Ryu SY, Peterson C, Loomis W, Putnam J, Elicieri B, Baird A, Coimbra R. Stimulating the central nervous system to prevent intestinal dysfunction after traumatic brain injury. *J Trauma*. 2010 May; 68(5):1059-64.