



Study Guide with Test Questions

Immune System Fundamentals and Autoimmune Disease by Sharlene Peterson (2021)

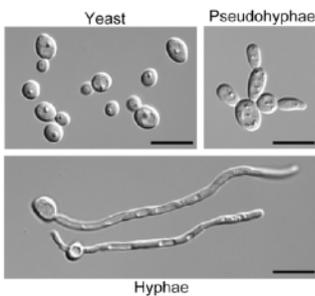
M230 Immune/Autoimmune

The body cells, organs and systems that are actively involved in fighting an infection include white blood cells, antibodies, the complement system, lymphatic system, spleen, thymus, and the bone marrow. Fever helps your body fight infections by speeding up the function of cells so they can respond to pathogens faster. A fever also makes it more difficult for bacteria and viruses to thrive in the body. Organs and systems that physically defend the body from getting an infection to start with include:

- **Skin** - a waterproof barrier that secretes oil with bacteria-killing properties
- **Lungs** - mucous in the lungs (phlegm) traps foreign particles, and small hairs (cilia) wave the mucous upwards so it can be coughed out
- **Digestive tract** - the mucous lining contains antibodies, and the acid in the stomach can kill most microbes
- **Other defenses** - body fluids like skin oil, saliva and tears contain anti-bacterial enzymes that help reduce the risk of infection. Continuous movement of urine and feces also aids in flushing out possible infectious agents.

1. _____ The human body has three layers of protection: physical, biochemical and cellular. Which substances produced by the body are examples of biochemical protection
 - A. T cells (T lymphocytes), red blood cells (erythrocytes), and neutrophils (a type of white blood cell)
 - B. Stomach acid, tears, mucus, and sweat
 - C. Body hair, skin, cilia, cells that line the respiratory tract
2. _____ True or False? Red bone marrow contains the hematopoietic stem cells that continuously produce all of the blood cells (white blood cells, red blood cells, and platelets).
3. _____ After T cells are produced in the red bone marrow they travel to the thymus to develop into mature but naive cells. The thymus is part of which body system?
 - A. Lymphatic system
 - B. Respiratory system
 - C. Gastrointestinal system
4. _____ True or False? The liver plays a role in both the innate and the adaptive immune responses. Kupffer cells, T cells, B cells, natural killer cells, and neutrophils (phagocytes) eliminate pathogens within the liver.

5. _____ True or False? The gut-associated lymphoid tissue (GALT) has the smallest concentration of lymphoid tissue in the body. There are no known drugs or other chemicals that can disrupt gut homeostasis (balance).
6. _____ Bacterial translocation is defined as the migration of bacteria or bacterial products from the intestinal lumen to mesenteric lymph nodes or other extraintestinal organs and sites. Based on this information, which sentence below is most likely:
- Bacteria living in our lymph nodes or other body organs can move into our intestines and cause intestinal disease.
 - Bacteria (or other small organisms or substances) in our intestine can escape and travel to organs or tissues if there is increased intestinal permeability (leaky gut).
 - Bacteria or bacterial products are insoluble in water and far too large to escape the intestines.



The human body is colonized both internally and externally by thousands of different microbes (bacteria, fungi, parasites, and viruses). When balance between the organisms are disrupted, some of the organisms are able to become pathogenic and cause disease or infection. *Candida albicans* is considered a normal inhabitant of the intestines and genital tract but disruption of microbial balance, immune suppression, and medical equipment such as catheters, can lead to both “superficial” and life-threatening bloodstream infections.

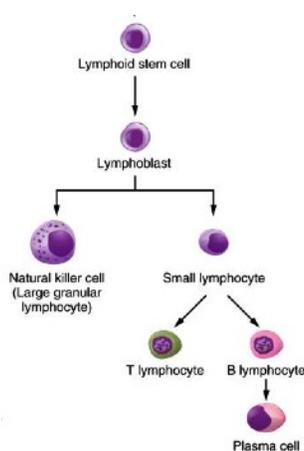
Candida species have the ability to change morphology (yeast, pseudohyphae, and hyphae), create biofilms, and produce toxins (candidalysin, a toxin that is secreted by *Candida* hyphae). Biofilms in general are complex structures that include a community of one or more species of microbes that are able to adhere and invade host tissue or surfaces. This community of microbes are imbedded in/surrounded by extracellular polymeric substances (EpS), mainly polysaccharides and proteins that protect the microbes.

Simplified, a biofilm is often described as a slime layer that develops on almost every surface in contact with water and microorganisms and is capable of protecting the microbes from external threats like drugs and disinfectants.

Macrophages of the innate immune system provide the first line of defense against *Candida*. However, the fungus has developed strategies to counteract macrophage activity. The toxin candidalysin, produced by *Candida*, has the ability to damage immune cell membranes. Thankfully, candidalysin also triggers a pro-inflammatory response which protects phagocytes.

Recent studies have demonstrated that *C. albicans* is capable of promoting cancer by producing carcinogenic by products, triggering inflammation and a Th17 response, and by molecular mimicry. Very few studies have focused on a link between *Candida* overgrowth and autoimmune diseases however, individuals with a chronic *Candida* infection of skin, nails, **and** mucous membranes (i.e. throat, intestines, vaginal area) are more susceptible to autoimmune endocrinopathies. Autoimmune endocrinopathies is the term used to describe autoimmune reactions in the pituitary, thyroid, parathyroids, pancreatic islet cells, adrenals, and gonads.

7. _____ Cells need energy to function (i.e., muscle cells need to work together to contract) and the energy is in the form of adenosine triphosphate (ATP). ATP is produced inside the cell itself by little organelles called mitochondria. It is like needing gas for your car and you have a gas maker in the trunk! Which supplements may reduce the fatigue caused by chronic illness by supporting the function of mitochondria?
- A. L-carnitine, alpha-lipoic acid, CoQ10, nicotinamide adenine dinucleotide (NADH), and phospholipids
 - B. Alpha-carnitine, P90-X, nicotine, and caffeine
 - C. There are no known vitamins or minerals needed by human cells
8. _____ True or False? A phagocyte describes white cells (immune cells) that have the ability to wrap around a pathogen, engulf it, and kill it with toxic substances. Phagocytes include macrophages, dendritic cells, neutrophils, and eosinophils.
9. _____ True or False? An antigen is a specific part of a foreign substance or organism that is identical to the substances found on human cells (self-cells).



Lymphoid stem cells that are created in the bone marrow are able to differentiate (change/develop) into lymphoblasts which differentiate into natural killer cells and small lymphocytes. The small lymphocytes differentiate into T cells (also called T lymphocytes) and B cells (also called B lymphocytes).

B cells, after they receive or detect an antigen, will change into plasma cells. It is the plasma cells that produce the antibodies to fight infections. In addition, B cells will use the antigen information to create memory B cells. Memory cells often last indefinitely in the body to fight the substance or pathogen if it returns. B cells, like T cells, have many subtypes (i.e., T cell independent B cells, memory B cells, etc.).

T cells differentiate into several types and subtypes. The type of T cell called a helper T cell (Th cell) has many subtypes and researchers continue to find additional ones. What typically makes one helper T cell different from the others are the molecules and/or receptors found on the T cell membrane surface. The molecules and receptors found on T cell surfaces determine what it is able to do, how it interacts with other cells (i.e. CD8+ T cells and CD4+ T cells). Like B cells, T cells are also able to create memory T cells after an infection has been eliminated.

10. _____ True or False? Th17 helper cells protect surfaces (e.g., skin, intestinal lining) from bacteria.
11. _____ True or False? Cytokines are dangerous and should always be suppressed with drugs or supplements because the human immune system is unable to make correct decisions.

12. Which immune cells are part of the **innate** immune response and are created to kill the cells infected with viruses (or other pathogens) and cancerous cells?
- A. T lymphocytes (T cells)
 - B. Cytokines
 - C. Natural Killer Cells
13. Which immune cells are part of the **adaptive** immune response and are created to kill the cells infected with viruses (or other pathogens) and cancerous cells?
- A. Cytotoxic T cells
 - B. Natural Killer Cells
 - C. B lymphocytes (B cells)
14. _____ True or False? Cytotoxic T cells (specifically effector cytotoxic CD8+T cells) circulate through the blood and lymphatic systems “looking” for any body/self cell that has placed an antigen complex on its surface. The antigen complex is an antigen attached to a molecule called MHC 1 and it is a signal, a red flag, that tells the cytotoxic CD8+T cells that it is infected and needs to be destroyed.

Disruption in the development, function, or control of immune cells is considered a primary cause of autoimmune and inflammatory diseases. The development of immune cells requires all the proper nutrients for healthy bone marrow - where all of the blood cells are first produced. The health of the thymus is critical for the continued development of the T cells, including getting rid of the overly self-reactive/autoreactive T cells. After passing the thymus test, T cells travel to the lymph nodes. A non-congested lymphatic highway is crucial for all the immune cells traveling. Regulatory T cells are crucial for controlling immune responses. The B cells will stay and mature in the bone marrow before they travel to the spleen and lymph nodes to monitor the blood for antigens (foreign substances/pathogens).

The function of all immune cells, from both the innate and adaptive systems, are dependent upon having sufficient nutrients and healthy body organs/systems to function and travel. Organs that are central to health, determine which nutrients are absorbed and metabolized, are the intestines and the liver. Diet is crucial and all possible food sensitivities, allergies, and intestinal pathogens need to be addressed to lower inflammation and heal “leaky guts”. Even a small amount of intestinal inflammation interferes with the absorption of nutrients.

15. Regulatory T cells (Tregs) are specialized for _____?
- A. Activating the immune system cells
 - B. Suppressing the cells involved in the immune response
 - C. Engulfing dead cells and creating antigens
16. _____ True or False? All autoimmune diseases are caused by viruses (like EBV) or bacteria (like *Borrelia* which causes Lyme disease).

17. The most widely-accepted autoimmune triggers through epigenetic mechanisms include:
- A. Breastfeeding, mineral supplements, adaptogens, and homeopathics
 - B. Oral-contraceptives, heavy metals, pathogens, and radiation
 - C. Epigenetics is a theory that has rejected as having a role in autoimmune disease.

There are three common names for the immune response that results in the production of memory T cells and memory B cells: Adaptive Immunity, Humoral Immunity, Antibody Immunity. All three are used in various research papers and text books.

Without the ability to form memory T cells and memory B cells humans would never have immunity to various viruses, bacteria, and parasites. When we speak of immunity it is very specific - if you get measles your body will create memory cells that will activate and immediately start the process of creating antibodies if the measles virus returns. The memory cells are specifically created to fight the measles virus and will not activate if you get infected with a different virus. Humans have thousands of different and specific memory cells because we are constantly exposed to pathogens.

18. _____ True or False? Dendritic cells, when actively presenting antigen information, will release cytokines to alert other immune cells that their assistance is required.

19. When a B cell has an antigen attached to its surface it will attract a helper T cell (specifically a CD+4 helper T cell) which will bind to the B cell and release cytokines. The cytokines released by the helper T cell will prompt the B cell to change into a/an:
- A. Antigen presenting cell
 - B. Natural killer cell
 - C. Plasma cell

20. The immune system contains three types of antigen presenting cells (APCs): macrophages, dendritic cells, and B cells. B cells act as APCs when they detect a soluble antigen while traveling through the lymphatic and blood systems. Which statement is true?
- A. When a B cell is activated by a soluble antigen, the B cell will differentiate (develop) into plasma cells which produce antibodies. T cells are not required to help the B cell via cytokines to produce antibodies and the response does not result in memory B cells.
 - B. When a B cell is activated by a soluble antigen it will require a helper T cell to produce antibodies. The end result is the production of memory B cells.
 - C. When a B cell is activated by a soluble antigen it creates uncontrolled cytokine production which results in excessive inflammation. T cell-independent activation is not a natural immune response.

21. _____ True or False? Antibodies protect humans from infection by three main actions: Neutralization, Opsonization, and Complement Activation. Neutralization describes how antibodies bind to a pathogen or toxin which interferes with its ability to enter and damage our cells.

Antibodies produced by B cells form the backbone of the adaptive immunity. Are we born sterile? Are we born with no immunity?

“The newborn's immune system grows fast from a small size at birth by exposure primarily to the intestinal microflora normally obtained from the mother at and after birth. While building up its immune system, the infant is supported by the transplacental IgG antibodies, which also contain anti-idiotypic antibodies, possibly also actively priming the offspring. The second mode of transfer of immunity occurs via the milk. Numerous major protective components, including secretory IgA (SIgA) antibodies and lactoferrin, are present. The breastfed infant is better protected against numerous common infections than the non-breastfed. Breastfeeding also seems to actively stimulate the infant's immune system by anti-idiotypes, uptake of milk lymphocytes, cytokines, etc. Therefore, the breastfed child continues to be better protected against various infections for some years”. (<https://pubmed.ncbi.nlm.nih.gov/12727640/>)

“IgM is the first immunoglobulin developed during human fetal development at 20 weeks. Unlike IgG antibody which provides passive immunity to the fetus, IgM antibody is restricted from crossing the placenta due to its size. It is also the first antibody to respond during infection. IgM antibody earned the title of the "natural antibody" as it can bind to specific antigens without prior immunization. This ability to react, despite naïve immune status, is likely due its avidity and polyreactivity”. (<https://www.genscript.com/IgM-antibody.html>)

During the fourth week of pregnancy some of the cells that are busy dividing and specializing will eventually become immune system cells. “These early immune system cells, called hematopoietic progenitor cells, have proteins on their surface that allow scientists to identify them as precursors of immune system cells...The early progenitor cells travel through the blood into organs associated with the immune system, such as the liver, spleen and thymus. By the second or third month of pregnancy, some are already becoming T cells. Although these T cells are functional by the third or fourth month of pregnancy, **the sterile environment of the womb does not require the fetal immune system to fend off potential pathogens...** Macrophages can be found in the fetal intestine by 11 or 12 weeks of gestation, and quantities increase rapidly during the fourth and fifth months of pregnancy. Likewise, B and T cells can be found in the intestine by about 16 weeks of gestation; and by about 19 weeks of gestation, they are organized into specialized lymph nodes in the intestine, called Peyer's patches”. (<https://www.chop.edu/centers-programs/vaccine-education-center/human-immune-system/development-immune-system>)

22. _____ True or False? The complement system is a secondary system, optional to the health of the individual. While complement protein C3 plays a role in a healthy immune response their function is not associated with autoimmune diseases.
23. Cytokines that regulate _____ immunity are produced primarily by phagocytes such as macrophages and dendritic cells but can also be produced by T-cells, natural killer cells, endothelial cells and mucosal epithelial cells.
- A. Adaptive
 - B. Innate
 - C. Holistic

24. Chemokines are a group of cytokines with many different immune functions. Which statement best describes the role chemokines?
- A. Chemokines enhance the migration ability of white blood cells, increase adhesion factors, “tell” immune cells to release cell killing toxins, regulate the movement of B cells and T cells, and damage healthy tissues if produced in excess.
 - B. Chemokines enhance the migration ability of white blood cells, increase adhesion factors, “tell” immune cells to release cell killing toxins, regulate the movement of B cells and T cells, and when produced in excess they heal damaged tissues.
 - C. Chemokines, while able to enhance the migration ability of white blood cells and increase adhesion factors used by leukocytes, are always damaging to healthy cells and should be controlled with immune inhibiting drugs.

“The tumor necrosis factor (TNF) inhibitors that have been approved by the FDA include infliximab, adalimumab, etanercept, golimumab, and certrolizumab. To decrease side effects and costs, most patients with mild or moderate disease are treated with methotrexate before adding or switching to a TNF inhibitor. These agents can be used by themselves or in combination with other medications such as prednisone, methotrexate, hydroxychloroquine, leflunomide or sulfasalazine”. (<https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Treatments/TNF-Inhibitors>)

“Is exposure to tumor necrosis factor inhibitors associated with risk of inflammatory demyelinating and nondemyelinating central nervous system events in patients with an autoimmune disease?...In this case-control study of 212 patients with or without inflammatory CNS events, exposure to tumor necrosis factor inhibitors was associated with an increased risk of inflammatory central nervous system events. The association was similar for both inflammatory demyelinating and nondemyelinating central nervous system events...This study found that exposure to TNF inhibitors in patients with autoimmune diseases appeared to be associated with increased risk for inflammatory CNS events. Whether this association represents de novo or exacerbated inflammatory pathways requires further research”.(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7235930/>)

25. _____ True or False? Cytokines as a group, includes chemokines, tumor necrosis factor, interleukins, and interferons.
26. Cytokines are critical to fight infections but, the immune response, which includes inflammation, must stop as soon as the infection is cleared. Which T cells play a critical role in the prevention of autoimmune disease by controlling several proinflammatory cytokines?
- A. helper T cells (Th cells)
 - B. effector T cells (T cells that have been activated by receiving an antigen)
 - C. regulatory T cells (Tregs)
27. _____ True or False? Rheumatoid arthritis and other autoimmune diseases are not caused by factors such as bacteria, mycoplasmas, viruses, low nutrient status, toxicity (heavy metals, pesticides, etc.) and increased intestinal permeability (leaky gut).

28. _____ True or False? The brain-gut axis encompasses the gut microbiome, intestinal barrier and the immune system. Individuals with multiple sclerosis have been shown to have an altered microbiome, increased intestinal permeability and changes in bile acid metabolism.
29. Examples of gram-negative bacteria that have been linked to autoimmune disease include *Salmonella*, *Escherichia coli*, *Klebsiella*, *Proteus*, *Enterobacter*, *Citrobacter*, *Yersinia*, *Shigella*, *Neisseria*, *Haemophilus spp.*, *Helicobacter pylori*, and *Chlamydia trachomatis*. When antibiotic use disrupts the microbiome balance, _____ can colonize in the intestines and activate Th1 cells and weaken tolerance for the oral bacteria reaching the intestine.
- A. *Klebsiella pneumoniae*
 - B. *Cleaver-bacterial particles*
 - C. *Klubellia intestina*

“*Proteus mirabilis* is often isolated from the gastrointestinal tract, although whether it is a commensal, a pathogen, or a transient organism, is somewhat controversial. It is thought that the majority of *P. mirabilis* urinary tract infections (UTI) result from ascension of bacteria from the gastrointestinal tract while others are due to person-to-person transmission, particularly in healthcare settings. This is supported by evidence that some patients with *P. mirabilis* UTI have the same strain of *P. mirabilis* in their stool, while others have no *P. mirabilis* in their stools. In addition to urinary tract infection, this species can also cause infection in the respiratory tract, eye, ear, nose, skin, throat, burns, and wounds and has been implicated in neonatal meningoencephalitis, empyema, and osteomyelitis”. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4638163/>)

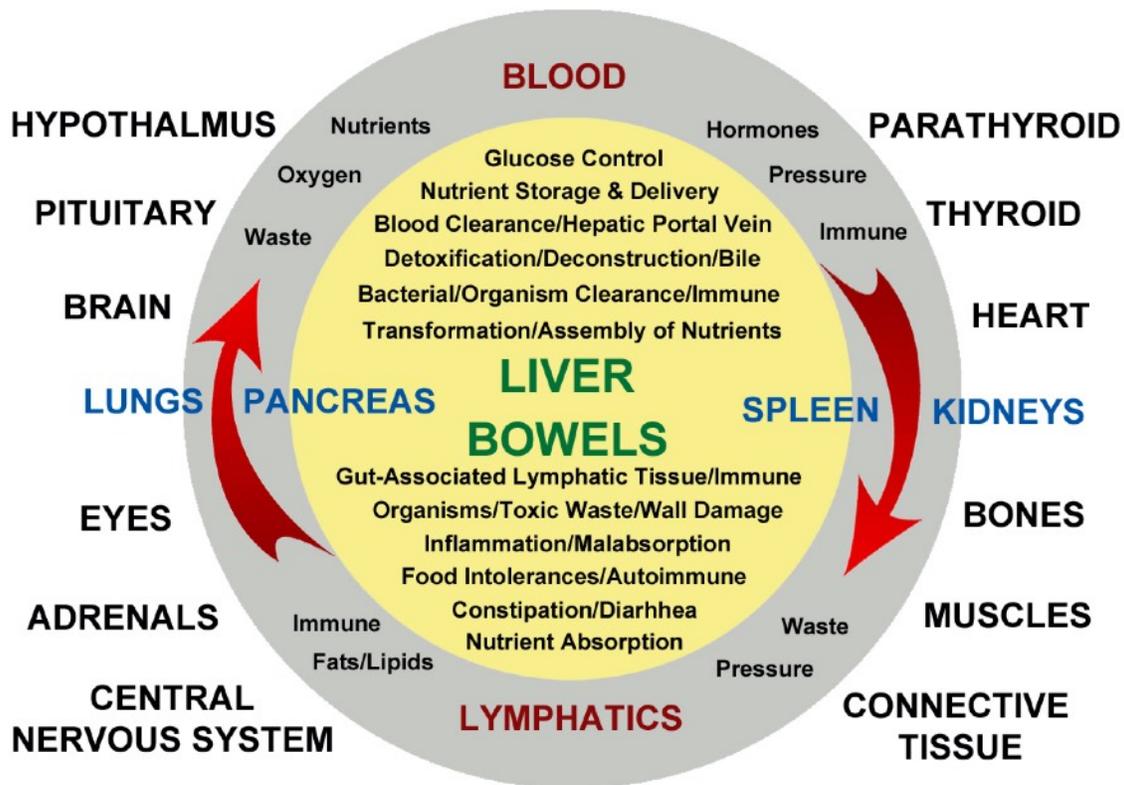
30. A wide variety of bacterial infections have been associated with rheumatoid arthritis (RA). However, *Porphyromonas gingivalis*, *Proteus mirabilis*, *Prevotella copri*, *Escherichia coli*, *Mycoplasma arthritidis*, *M. pneumoniae*, *M. salivarum*, and *M. fermentans*, has been _____ associated with RA. *Proteus mirabilis*
- A. Rarely
 - B. Strongly
 - C. Meagerly

31. _____ True or False? As with almost all diseases, there are likely numerous pathways to the same disease. Low nutrients, agricultural chemicals, pharmaceutical drugs, heavy metals, bacterial, viral and parasitic infections, intestinal permeability, vaccinations, stress, genetic mutations, improper clearance of cellular debris and epigenetic control have all been implicated in autoimmune diseases.

32. _____ True or False? Polyautoimmunity refers to having one autoimmune disease. Polyautoimmunity affects approximately 25 percent of individuals diagnosed with an autoimmune disease.

33. While the symptoms of each autoimmune disease vary greatly, it appears that they all share the presence of autoreactive B cells and/or autoreactive T cells. Recent studies have found that there are naturally-occurring autoreactive antibodies in healthy individuals. Natural autoantibodies are:
- A. found in the serum of newborns and their polyreactivity provides broad antibacterial activity.
 - B. only found in specifically bred mice but they can enter a baby's body via vaccinations.
 - C. not natural as the name implies. "Natural" antibodies are impossible, the clonal theory is the only correct theory.
34. A key difference between natural autoreactive antibodies and autoantibodies associated with autoimmune disease is that NAbs bind to self-antigens with low affinity whereas cells involved with autoimmune reactions bind with high affinity. Which statement describes antibodies with low affinity?
- A. Antibodies that form a weak bond with another antibody
 - B. Antibodies that form a weak bond with an antigen
 - C. Antibodies that are able form a quick and strong bond with an antigen
35. _____ True or False? Apoptosis refers to the natural death of human cells and is required for balance and health. Necrosis refers to cells that die because of toxins or injury.
36. _____ True or False? Steroids, corticosteroids, are potent anti-inflammatory pharmaceutical drugs which are safe to take during an active infection because they are immunosuppressive.
37. _____ True or False? Zinc levels likely affect both the number and the function of various types of immune cells, including macrophages, neutrophils, dendritic cells, mast cells, T cells and B cells. It has been accepted that dysregulated zinc homeostasis in macrophages causes impaired phagocytosis and an abnormal inflammatory response.
38. Eicosanoids are a large family of lipid signaling molecules derived from omega-6 and omega-3 fatty acids and include prostaglandins, thromboxanes and leukotrienes. Which statement is true?
- A. Prostaglandins are mediators in cell division reactions.
 - B. Leukotrienes are derived from omega-3 fatty acids, the precursor of prostaglandins.
 - C. Prostaglandins are mediators during inflammatory and allergy reactions and leukotrienes cause inflammation and bronchoconstriction during an asthma attack.

39. Mineral balance is important in both health and disease states and this is specifically true for zinc and copper. There is an inverse relationship between zinc and copper in the body, when an individual has elevated copper levels the zinc level is low. Which statement about copper is true?
- A. Copper tends to increase estrogen levels in the body and estrogen tends to cause copper levels to increase.
 - B. Elevated copper levels decrease feelings of agitation or overstimulation, anxiety, panic, racing thoughts and insomnia.
 - C. The best way to identify copper toxicity is with a serum/blood test.
40. _____ True or False? Folate is essential for the survival of regulatory T cells in the small intestine?



~ END OF TEST ~