The Immune System

by Debra M. Eldredge, DVM

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The **Immune** System Part 1

Your dog's immune system can save her life or kill her. It is one of the most complex systems in the body and vitally important. This series will run from the normal immune system to what can happen when an immune system "goes bad."

The immune system consists primarily of free-ranging cells, as opposed to most body systems such as the respiratory system that has a primary organ (the lungs). The larger issues associated with the immune system are the spleen and bone marrow, where immune-related cells are made and stored; the lymph nodes which provide "local" supplies of cells; and the thymus. The immune system also works along with the lymphatic system and the circulatory system to transport cells.

The bone marrow's main function is to produce cells - both cells involved with immune function and red blood cells. Bone marrow is located inside large bones such as the femur. One type of immune cell is called the B lymphocyte, with the B standing for bone marrow. Bone marrow is active and functioning throughout your dog's life.

The spleen helps to produce lymphocytes and red blood cells and acts as a major storage site for these cell types. The spleen also works to remove any damaged cells. Dogs can survive without their spleens, which may be damaged by trauma, involved in torsions or become cancerous.

The thymus is a gland located near the heart inside the chest. While this gland is obvious in puppies, it shrinks with age so that it may not be obvious in an older dog. The thymus is important for immunity in puppies and is their first line of defense. The lymphocytes made here are call T lymphocytes.

Lymph nodes work to filter out wastes transported in the lymph, a fluid with proteins and fats that circulates throughout the blood stream and in lymphatic channels. Lymph nodes can also trap infectious agents such as viruses and the provide a place for immune cells to destroy those agents. Lymphocytes travel in the circulation, rotating from blood to lymph nodes to lymph fluid to blood. Lymph nodes themselves are located at strategic drainage points throughout the body. You may feel them, especially if the draining an infection, under the jaw, in the armpit and behind the stifle. There are many others, located both near the body surface and internally.

Another area with aggregations of lymphoid tissue is in the gastrointestinal tract. You may see mention of GALT - gut associated lymphoid tissue - in discussions of immunity. The immune cells in this area must distinguish food antigens and helpful bacteria, which while foreign are not harmful, from toxins and harmful bacteria, viruses and parasites.

The basic job of the immune system is to recognize "self" versus "nonself" or normal tissues and cells versus foreign invaders of the body. The first lines of defense in these battles are the physical barriers. These include the skin, ciliated epithelium in the respiratory tract that shoves foreign particles and agents back out of the body, mucus coatings in the respiratory and gastrointestinal tracts, tears to wash infectious agents and foreign material out of the eyes, and the acidic pH of the stomach that destroys many foreign agents that get swallowed.

The physical barriers are very nonspecific - the respiratory cilia move any virus and bacterial particles back out, as well as dust, etc. Some cellular responses to invasion are also nonspecific. When your dog mounts a fever, she may be killing off viruses that have a very small range of temperatures at which they can replicate. Macrophages are cells that literally eat damaged cells and any foreign cells and materials. Neutrophils are other nonspecific warriors of the immune system that attack anything that is not "self." Some of these nonspecific cells produce interferons. There are glycoproteins that interfere with viral replication.

The immune system also adapts to individual threats to the body, with lines of cells developed to fight a specific invader. An example would be immune cells that only fight parvo virus but might be of no help against streptococcus bacteria.

For specific immunity to be effective, cells must be exposed to the foreign molecules - often called the antigen. Many antigens are proteins. A macrophage may attack and bind an invader such as a virus. The abnormal proteins are then presented to lymphocytes to stimulate production of specific infection-fighting proteins. The B cell lymphocytes develop very specific antibodies that bind with just those antigens and render them incapable of causing an illness. Your may hear B cells referred to as plasma cells and antibodies as immunoglobulins. The antibody system may also be called humoral immunity. About 30 percent of all lymphocytes are B cells.

The T cell lymphocytes that are presented with antigen react a bit differently. They stimulate cell-mediated immunity. Instead of using proteins such as antibodies, they actively destroy the foreigners and send out chemical messages to tell other cells, such as macrophages, to join the battle. T cells compose approximately 70 percent of all lymphocytes.

A major component of specific immunity is that some cells go on to become "memory cells." These cells literally remember what an antigen is like. The memory cells are present in the peripheral circulation where they can easily detect antigens. If that antigen tries to invade your dog's body again, the memory cells can get battle forces up and running rapidly as they don't need the extra steps of identifying an unknown opponent. Memory cells are very long-lived and immunity after disease exposure may last for years, or even the lifetime of your dog. The goal of an immune stimulus such as a vaccine is to develop memory cells that will immediately go into action if you dog is exposed to that antigen, such as the rabies virus, again and prevent any illness from developing.

Recommended resources: www.peteducation.com and www.petplace.com

The **Immune** System Part 4

There are gastrointestinal diseases that are marked as immune problems by their very names, including inflammatory bowel disease, a designations that covers a variety of intestinal problems. In general these diseases are marked by a massive infiltration of immune or inflammatory cells into the lining of the intestines, cells which literally take over, pushing out normal cells and interfering with normal functions, which can lead to increased permeability so that more antigens sneak through the intestinal safeguards. Scarring or fibrosis may eventually occur. The influx of cells may be tied to a deregulation of the immune system, with abnormal reactions to normal antigens such as food proteins.

There is a question whether IBD is primarily genetic or environmental: in reality the syndrome is probably a combination of factors.

Dogs with IBD tend to present with diarrhea, sometimes vomiting, and often weight loss. They may have a ravenous appetite or not act hungry at all. True IBD must be distinguished from parasite infestations, bacterial overgrowth syndromes, pancreatic problems, and cancers such as intestinal lymphomas. The best way to get a clear diagnosis is with biopsy, which can often be accomplished via endoscopy, a tube passed down the dog's throat so that no surgical incision is required. Laboratory tests may be helpful as well: dogs with bacterial overgrowth tend to have high levels of folate in their blood, and dogs with pancreatic problems can usually be identified by the levels of tyrpsin-like immunoreactivity in their blood work - also called the TLI test. Still, a biopsy is the best way to confirm a diagnosis. It is very important with a dog suspected of having IBD to rule out sites, as treatments are quite different; thus the expense of a biopsy is well worth it.

IBD may be characterized by the types of cells that invade the cell walls of the intestine. The most common form is lymphocytic/plasmacytic enteritis (LPE) with lots of lymphocytes. The second most common is eosinophilic. Eosinophils are immune cells that are often present with parasites and/or allergic reactions.

Simple IBD is seen in German Shepherd Dogs, Cocker Spaniels and Yorkies. In GSDs the presence of IBD may be associated with an increased risk of bloat, with chronic diarrhea and occasional vomiting generally the presenting signs. I'll emphasize again how important a biopsy is to diagnosing IBD; GSDs are also prone to bacterial overgrowth and pancreatic problems and the treatments vary. Steroids may be used but are often not strong enough to control clinical signs of IBD on their own. Budesonide is a new drug being used successfully by many practitioners. Sulfasalazine is often used for treatment, but this drug may predispose a dog to "dry eye: or keratoconjunctivitis sicca (KCS), and dogs that develop KCS require lifelong treatment with drops to keep the eyes moist and prevent damage to the corneas.

The first case of true IBD I ever encountered was in a wonderful Basenji that had been donated to Cornell with LPE.

Another form of IBD seen in Basenjis is IPSID - immunoproliferative small intestinal disease, a genetic anomaly. With IPSID the immune regulation is defective so the intestines react against antigens they should recognize as normal. Extensive protein loss serves to further weaken the immune system, and stress may be a factor in the progression of the disease. This disease is generally first noted by 3 to 4 years of age and most dogs die, despite therapy, in two to three years.

Affected Basenjis may have diarrhea that is difficult to control. vomiting, a decrease in appetite and/or weight loss. Protein loss can be quite severe. Symptoms can be controlled for awhile with immunosuppressive drugs such as the steroids prednisone and dexamethasone; Azathioprine and metronidazole are used to try to control inflammation and bacterial overgrowth side effects. Chemotherapy drugs such as cyclosporine can be tried as well. Dogs with severe protein loss may benefit from IV treatments to help replace lost plasma proteins.

Diet manipulations may also help with IBD cases, and highly digestible, low-residue diets with low fiber, a single, novel protein source and a single carbohydrate source work best. Omega 6 and omega 3 fatty acids may be added to help decrease inflammation. While high levels of fiber have been used in the past, Dr. Debra Zoran, DVM, Ph.D., DACMIM of Texas A & M University feels they reduce the availability and digestion of proteins and carbohydrates that these dogs need.

Chinese Shar-Pei also have a type of chronic enteropathy, with symptoms of diarrhea, vomiting and weight loss despite increased appetite. Along with protein loss is a decrease in cobalamin (vitamin B 12) on blood testing. Treatment may include prednisone, metronidazole and antibiotics such as amoxicillin or tylosin. Dr. Zoran recommends cyanocobalamin injections for dogs with low cobalamin levels.

Histiocytic or ulcerative colitis has been associated with French Bulldogs and Boxers and is considered to be an immune reaction against normal bacteria of the intestinal tract. Usually at less than a year of age the dogs will show chronic diarrhea. Diet changes may help, along with immunosuppressives like azathioprine and anti-inflammatory drugs like metronidazole and sulfasalazine. This reflects the possibility that affected dogs have a genetic defect causing an overreaction to normal bacteria in the intestines.

In all cases, it should be noted that the goal is to control the disease. Actually curing IBD is extremely rare and a "cure" may be a case of misdiagnosis - perhaps a dog with a severe case of whipworms that was cured with deworming.

Resources:

Immune Mediated Intestinal Disease by Edward Hallm MA, VetMB, Ph.D., ECVIM-CA, MRCVS in Proceedings of the WSAVA Congress in 2007
Inflammatory Bowel Disease in Dogs by Todd Tams. DVM, DACVIM in ACVC Proceedings in 2001
Nutrition Mainstay to Success by Johnny Hoskins, DVM, DACVIM, in DVM magazine on Nov., 1, 2007