Understanding Autoimmune Diseases

Randy C. Lynn, D.V.M.

Have you ever had poison ivy? It usually involves a small patch of skin that is inflamed with little blisters that itch intensely. After a few days, the blisters break open and the skin heals. But what if your entire body were covered with blisters that itched and never healed? That is what it is like to have an autoimmune skin disorder. It is like being allergic to your own skin. The sores never heal because the skin itself is the source of the allergic reaction.

Autoimmune disease results when the immune system mistakes normal cells for invading bacteria or viruses. When this happens, all of the powerful forces that repel infectious disease and control tumorous cells begin to fight the normal cells in the body. This results in serious, often life-threatening disease as normal cells are killed and their functions are lost. The signs of disease are directly related to the type of cells under attack—and the type of attack the immune system launches.

Immune System Basics

The complex immune system is responsible for protecting the body from invading organisms. When it functions normally, it kills invaders of all types, including viruses, bacteria and parasites. It also detects abnormal tumor cells and clears them from the body.

It starts in the bone marrow and thymus where stem cells produce many different types of white blood cells. B lymphocytes, one type of white blood cell, patrol the bloodstream and lymph nodes, seeking invaders and producing antibodies that bind only to invading cells. Once the antibody binds, it serves as a giant bull's eye, telling other cells to kill the invader. T lymphocytes perform several functions. They secrete signals that alert the immune system, and also secrete poisons that kill tumor cells and infected body cells. In addition, they regulate the function of the immune system so it doesn’t attack healthy cells. Therefore, these suppressor T cells are very important in preventing autoimmune disease.

The macrophages are the heavy artillery of the immune system. After the lymphocytes have targeted the bad guys and the antibodies have mounted the defenses, the macrophages come into the area and engulf the invaders. If the parasite is too large, then several macrophages bind to the outside of the invader and pump chemical poisons all around it to try to kill it. When it is destroyed and starts to break up, the macrophages gobble up the pieces and clean up the area.
Recognition of Self

The question that scientists have pondered for decades is, how do these powerful cells know which cells to kill and which to leave alone? In other words, how does the body recognize itself? Once we answer this question, we can help the body overcome infectious disease such as acquired immune deficiency syndrome and noninfectious diseases such as cancer, and prevent the body from rejecting transplanted organs.

We are just now beginning to unravel this mystery. Apparently each body cell has a set of proteins unique to that individual. These proteins, or histocompatibility complexes, serve as identity cards for cells circulating throughout the body. When immune cells bump into other cells, they compare histocompatibility proteins. If these ID cards match, the immune cells leave the other cells alone. If they don’t match, the lymphocyte begins the attack and sends out chemical signals as a call for reinforcements. Soon hundreds of immune cells come to attack the invader.

What is Autoimmunity?

When the immune system works as it should, it repels the thousands of infectious diseases to which the body is exposed in a normal day. When it doesn’t work, the invaders get through and the body becomes sick. Autoimmunity results when the immune system begins to attack normal cells. It is almost as though they fail to recognize ID proteins that should identify the cells as normal. This is the immunological equivalent of "friendly fire."

Nobody knows exactly what goes wrong when autoimmunity occurs. Some scientists believe that autoimmunity occurs in normal animals and humans to control the growth and activity of normal cells, but that it is tightly controlled by suppressor cells so it does no real harm to the body. When the suppressor cells fail to control the process, the immune system runs wild, attacking many normal cells and causing real harm to the body.

Other scientists suspect that autoimmunity occurs when viral or bacterial invaders have histocompatibility proteins resembling the body’s normal cells, so the immune system begins to attack both invader and normal cells.

The whole picture probably involves both processes—as well as other processes that have not yet been discovered. It seems that the more we learn, the less we really know.

Types of Autoimmune Disease

All animals are susceptible to autoimmune disease. The easiest way to understand autoimmune disease is to break it into several manageable chunks and look at them individually. One whole family of autoimmune diseases affect only one organ or body system. Another group of autoimmune diseases seem to affect a whole range of different body systems.
Organ-specific autoimmune diseases are the easiest to understand because the damage to the body is limited to one organ system. Therefore, the clinical signs are easily explained by the amount of organ damage that is done. These diseases are even better defined by the specific part of the organ that is attacked. When the immune system attacks, it picks one specific part of the cell. Like a smart bomb that is targeted at one specific part of a building, the immune cells target one specific chemical binding site on the cell (epitope). This epitope then is attacked by specific antibodies designed to bind there. In autoimmune skin disease, for example, the target epitope is the intercellular cement that holds the skin cells together.

**Skin Diseases**

Several autoimmune skin diseases that affect animals are identified with the term pemphigus or pemphigoid, from the Greek word *pemphix*, which means blister.

In all types of pemphigus, the intercellular cement that holds cells together is attacked by the immune system. This disrupts the normal layers of the skin and large patches of skin cells are stripped away. This exposes the lower layers of the skin, resulting in secondary bacterial infections, severe pain and permanent scarring.

*Pemphigus foliaceous* occurs when the most superficial layers of the skin are attacked and very thin blisters form. In most cases, the blisters or pustules (usually smaller than half an inch) are never seen because the animal rubs or scratches them away. Noticeable signs of the disease include extensive crusting, scaling, hair loss and dark pigmentation of the skin. It commonly affects the head and nose, but it may spread to other areas of the body. Some affected animals scratch intensely, as though they had poison ivy, while other animals aren’t bothered by itching at all.

The disease can be diagnosed only through a skin biopsy. The veterinarian uses a circular biopsy punch to cut out a small piece of skin then sends the sample to the pathologist for microscopic analysis. The disease is confirmed by the disruption of the superficial cell layers and by the presence of large numbers of immune cells. Once the diagnosis is made, the veterinarian can begin treatment with high doses of cortisone and other drugs that are known to inhibit the immune system. Because pemphigus foliaceous is the mildest form of autoimmune skin disease it has the best prognosis.

*Pemphigus vulgaris* affects the middle layers of the skin, resulting in larger and deeper blisters around the mucocutaneous junctions—the eyes, nose, lips, prepuce and rectum—as well as on the inner surface of the ear or on the tongue. Because they arise from deeper layers of the skin, the open patches are very raw and sore. The treatment is the same as for pemphigus foliaceous, but these cases are much more serious and the prognosis is very poor.

**Blood Diseases**

Autoimmune blood diseases are defined by the type of blood cells attacked by autoimmune processes. The most common of these is autoimmune hemolytic anemia, in which red blood cells are destroyed. With autoimmune thrombocytopenia or immune mediated thrombocytopenia, platelets are attacked.

*Autoimmune hemolytic anemia* can have a sudden or gradual onset. In this disease, the immune system produces antibodies that become attached to the red blood cells. Once the antibodies are attached, these cells are destroyed in the bloodstream or the spleen. When the rate of red cell destruction exceeds the rate of new cell creation, the cat becomes anemic.

Anemic cats have pale membranes around the eyes and in the mouth. They also are weak and lethargic. Their blood is barely able to carry enough oxygen to keep them alive. Severely affected animals need blood transfusions if they are to survive, and then they are given high doses of immunosuppressive drugs to stop the destruction of red cells.
therapy is successful, the animal’s red cell count will increase slowly until the cells can resume normal activity.

**Autoimmune thrombocytopenia** is caused by the presence of anti-platelet autoantibodies, and it may occur at the same time as autoimmune hemolytic anemia. Because the immune system attacks the platelets, which are necessary for blood to clot normally, affected animals bleed profusely for no apparent reason. Tiny bruises appear in the skin and in the membranes around the mouth and eyes. In severe cases, obvious signs include nose bleeds, large bruises and blood in the stool and urine. Again, transfusions with platelet-rich blood may save the animal’s life. Long-term therapy with high doses of immunosuppressive drugs give the body a chance to replenish platelets to normal levels.

**Multisystem Diseases**

The most severe, most life-threatening and most perplexing autoimmune diseases are those that affect several organ systems at the same time.

Although **systemic lupus erythematosus** is greatly feared, it is a rare disorder of cats. The underlying defect in affected patients is the production of large amounts of antibodies against DNA molecules that circulate throughout the body. The antibodies cause damage through several mechanisms. First, they combine in the blood stream with free DNA molecules and form globs that impair the kidneys, culminating in kidney failure. These globs also are deposited in the joints, causing arthritis similar to rheumatoid arthritis. The damage doesn’t stop there, however. Antibodies attack the red cells, causing hemolytic anemia, and bind to the platelets, causing an immune-mediated thrombocytopenia. They also damage muscle and skin. It is as though the immune system attacks everything at once.

The only way to treat this disease is to administer large quantities of immunosuppressive drugs to shut down the runaway immune system. Of course, none of these drugs can cure the disease, it is a lifelong condition. The best hope is to control the disease and reduce the severity of the symptoms.

**The Only Prevention**

Scientists do not have adequate information about autoimmune diseases, and our understanding about such diseases in animals lags behind our knowledge of such disease in humans. They take many forms, attacking different organ systems, but they all seem to be related to an immune system that has gone out of control. In most instances, a genetic factor appears to set the stage for illness. None of the autoimmune diseases can be cured, but many of the symptoms can be controlled.

The only way we can hope to prevent autoimmune diseases in pets is to cull all affected animals from breeding populations.

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**Regional Cat Health Seminars**

If you live in the Southwestern or Eastern United States you may want to register for one of the following "Short Courses for Breeders." The program is designed for breeders, serious cat owners, and veterinary practice staff. Instructors are from the College of Veterinary Medicine at Cornell University.

**Houston, Texas—May 8 at Doubletree Hotel**

Topics will include nutrition, feline infectious diseases and reproduction. The seminar is being sponsored by The Iams Company.

**Towson, Maryland—June 5 at Quality Inn**

Topics will include feline infectious diseases and reproduction and is being cosponsored with the Chesapeake Cat Club.

For a registration form call (607) 253-3414.
Q. After rescuing an abandoned kitten with a severe upper respiratory infection he continues to have bouts of “kitty colds.” Could you address this problem, and possible alternative treatments to antibiotics. Any preventive measures I can take, such as vitamin supplements?—L.S., Pennsylvania

A. “Colds” in cats are usually caused by feline herpesvirus type 1 (FHV-1) or feline calicivirus (FCV), or by both. Neither of these viruses can infect people, nor will the viruses that cause colds in people affect cats. Two other organisms—mycoplasma and chlamydia—can cause similar signs in cats although they primarily affect the conjunctiva (the pink lining of the eyelids and the tissue partially surrounding the eye). Variable degrees of sneezing, runny eyes with occasional squinting, and a runny nose are the typical signs. However some cats—particularly kittens—become very ill from viral infections.

Vaccinations are available for FHV-1, FCV and chlamydia, but they do not provide 100% protection against infection. However, the vaccines do help by preventing severe illness. Although antibiotics are helpful in ridding a cat of mycoplasmal and chlamydial infections, no antiviral medication has proved to be helpful in viral infections. Fortunately, most cats regain their health, but many cats will remain as “carriers” of the viruses. Carriers do not necessarily show any signs of illness, but are shedding the organism and serving as a source of infection to other cats. Intermittent recurrence of upper respiratory infection (URI) signs or conjunctivitis is very common in cats with herpesvirus infections and is oftentimes associated with an event that the cat’s system perceives as stressful.

Often accompanying viral URI in cats are acute or chronic bacterial upper respiratory tract infections. In the acute form, bacteria that are normally present in the respiratory tract infect the tissues that have been damaged by the viruses. Antibiotics are commonly used by veterinarians at this stage to destroy the “secondary invaders” to speed the patient’s recovery. Chronic bacterial infections usually result from serious viral infections that have changed the delicate structure of the nasal passages. A normal architecture of these structures is necessary to provide a strong defense against bacterial infections, but if damaged, the secondary invaders can cause persistent infections. These cats typically do very well when taking antibiotics but may develop signs of URI shortly after being off medication.

Prevention of serious disease due to upper respiratory tract infections depends mostly on proper vaccination. Even though vitamin supplements have not been shown to be helpful in those cats that have already been infected and are having recurrent signs, good nutrition and general health care and reducing stress can minimize, but not necessarily prevent, the incidence of recurring “colds.”

Q. Could lacrimal duct obstruction/scarring cause an increase in “kitty colds?”—L.S., Pennsylvania

A. A potential result of severe conjunctivitis, particularly due to either herpesvirus or chlamydia, is called symblepharon. This refers to adhesions of the conjunctiva to itself, to the third eyelid, or to the surface of the eye. These adhesions or scars can constrict the opening of the tear ducts and cause chronic tearing, similar to the way a clogged downspout on a house can cause the roof gutters to overflow during a rainstorm. A thorough examination by a veterinarian should be able to distinguish between chronic tearing as a result of symblepharon or some other cause. Unfortunately, if the problem is caused
by adhesions scarring down the openings of the tear ducts, the prognosis is poor for recovery of normal tear duct function. However, it would not make the cat more prone to "colds."

Q. One of my cats has had urinary tract problems for 6 of her 7 years of life. I am concerned about the long-term effect of Urigard, a type of urinary acidifier, which the veterinarian prescribed. Can you recommend other means to acidify her urine? Are there foods that could help accomplish this? I currently feed my cats Hill’s Prescription Diet w/d.—B.O., Illinois

A. Not all lower urinary tract (i.e. urinary bladder and urethra) disorders have the same cause. However, if the disease is caused or complicated by the formation or entrapment of a mineral called struvite (magnesium ammonium phosphate hexahydrate) in the bladder or urethra, a diet designed to minimize its production should be helpful in prevention.

Basically two forms of struvite precipitates are associated with lower urinary tract disease in cats—uroliths and urethral plugs. Uroliths are hard, stone-like substances of variable size, and can be found anywhere in the urinary tract. According to a recent survey, 72 percent were found in the urinary bladder and 5 percent were found in the urethra. Urethral plugs are softer with a toothpaste-like consistency and are a major cause of urethral obstructions in males and neutered male cats.

Diet plays a major role in struvite formation in cats. Specifically, the pH of the urine that is produced by the diet, and to a lesser extent, the amount of magnesium in the diet, determine whether or not struvite will precipitate in the urine. Most experts feel that if the diet can maintain a mean urine pH of about 6.0 to 6.4 then struvite will not form. Even if the urine pH is as high as 6.8, it is unlikely that struvite will form unless dietary magnesium levels exceed 20 mg/100kCal of metabolizable energy. If your cat has a urinary tract disease that is associated with the formation of struvite precipitates, it should benefit from the feeding of a diet that meets those criteria.

Prescription Diet Feline w/d is designed to allow production of urine in the recommended pH range and contains no more than 20 mg/kCal of magnesium. If urine pH remains high even when fed this type of diet, perhaps either a urinary tract infection is present or the cat is eating something in addition to w/d. Also, urine pH will normally be higher for several hours after eating. If the cat is eating only one or two meals per day, it would be better to check the pH about 4 to 6 hours after eating to more accurately assess mean urine pH. In most instances, using urinary acidifiers like ammonium chloride or D-L methionine is not recommended when cats are being fed this particular type of diet for fear of excessive dietary acidification. Overzealous acidification can cause harmful effects on mineral balance and bone metabolism and may also allow the formation of other kinds of urinary stones.

Many veterinary nutritionists agree that the feeding of a diet that results in the formation of an acidic urine and does not contain excess dietary magnesium is the best way to prevent urinary struvite in those cats that are predisposed to the disorder. ■
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The Chesapeake Cat Club made a very generous donation of $18,000 to the Cornell Feline Health Center in January. A special fund has been created and will be used to continue and expand our current research efforts on feline diseases, particularly feline infectious peritonitis and feline immunodeficiency virus, and also to expand our educational efforts.

The Chesapeake Cat Club is affiliated with the Cat Fanciers' Association (CFA) and annually holds one of the largest cat shows in the country. Although they are a small club—about 20 members—they have had members serve on various positions with the CFA. The club donates to several local groups—humane societies, scouting troops and WBAL Kids Campaign for disadvantaged children in Baltimore.