Research to learn more about two canine health conditions, degenerative mitral valve disease (DMVD) in small-breed dogs and immune-mediated hemolytic anemia (IMHA), is producing better understanding that may one day lead to better care for affected dogs.

Recognizing Signs of DMVD

Chris and Renee Coney are Chihuahua lovers. "Dexter," who turns 14 in July, is their second pet Chihuahua. When the smooth coat Chihuahua was diagnosed with a heart murmur three years ago, the couple, who live in Turner Falls, Mass., did not know what to expect. Their spunky Dexter couldn’t have heart disease, they thought.

As it turned out, learning about Dexter’s heart murmur meant the Cones could help monitor the dog’s health and look for signs of the slow, progressive degenerative mitral valve disease, also known as chronic valvular disease. If necessary, medications could be given to help manage the fluid in the lungs and the arrhythmia, or irregular heartbeats, which often accompany the disease. The best part was learning that Dexter’s heart murmur meant the Cones could help monitor the dog’s health and look for signs of the slow, progressive degenerative mitral valve disease, also known as chronic valvular disease. If necessary, medications could be given to help manage the fluid in the lungs and the arrhythmia, or irregular heartbeats, which often accompany the disease. The best part was learning that Dexter might never develop the severe form of the disease that requires medications.

DMVD affects 30 percent of small breeds over the age of 10. Most owners do not learn their dogs have DMVD until they reach the advanced stage. Coughing, tiring after exercise and a rapid respiratory rate clue them in that something could be wrong. The reasons small breeds are prone to the disorder are a mystery. Because the affected breeds have other diseases associated with connective tissue problems, such as luxating patella and collapsing trachea, and because the mitral valve has a lot of connective tissue, it is possible these conditions are somehow related.

Believed to be a polygenic disorder involving many genes, DMVD is transmitted by carrier dogs to their offspring. Besides Chihuahua, other affected breeds are Cavalier King Charles Spaniel, Cocker Spaniel, Japanese Chin, Lhasa Apso, Miniature and Toy Poodle, and Norfolk Terrier. Cavaliers, which have the greatest risk, develop an early-onset form that progresses rapidly. Located between the left atrium and left ventricle of the heart, the mitral valve helps regulate the flow of blood in and out of the heart and prevents a back flow from going into the atrium. The mitral valve is made of thin flaps of tissue, or valve leaflets, attached by long, tendon-like structures, the chordae tendineae, to the muscles of the left ventricle. These valve leaflets open and close to regulate the flow of blood, but as the disease progresses, they begin to thicken, contract and lose flexibility.

When the mitral valve functions correctly, blood in the left ventricle is pumped to the body as the heart contracts. As the mitral valve degrades, it cannot close properly and small amounts of blood leak back into the left atrium. Over time, the valve degrades until the heart can no longer compensate. Stress from the leak causes the heart to enlarge, eventually resulting in congestive heart failure. In severe cases, the chordae tendineae may rupture, damaging or causing the complete collapse of the mitral valve.

Deciphering the Disease Process

Mark Oyama, D.V.M., DACVIM—Cardiology, professor of clinical studies and chief of cardiology at the University of Pennsylvania, has been investigating in dogs with DMVD the role of a neurotransmitter called serotonin that is important in maintaining normal cardiovascular functions throughout the body. Oyama and his colleagues have reported that dogs with DMVD had more serotonin in their blood than dogs without disease. The research, which was published in 2009 and 2013 in the Journal of Veterinary Internal Medicine, suggests that serotonin signaling may play a role in the progression of early stages of DMVD.

"Higher levels of serotonin are associated with higher levels of glycosaminoglycan, one of the pathological molecules that is common in DMVD valves," Oyama says. "Serotonin is found not only in the brain and nerves but also in blood platelets and the heart. It is interesting that high serotonin levels are found in the heart and platelets of dogs with DMVD because other studies have shown that high serotonin can damage the valves."

Similar comparative research at Cornell University College of Veterinary Medicine involves studying the mechanical differences of the heart and mitral valve of normal dogs and those with DMVD. N. Sydney Moise, D.V.M., DACVIM, professor of medicine and cardiology section chief, Cornell University College of Veterinary Medicine, has shown that high serotonin can damage the valves.

"By observing how the valves move, we hope to detect differences in their motion and thus recognize stress levels of dogs at high risk versus those at low risk for this disease."

N. SYDNEY MOISE, D.V.M., DACVIM, PROFESSOR OF MEDICINE AND CARDIOLOGY SECTION CHIEF, CORNELL UNIVERSITY COLLEGE OF VETERINARY MEDICINE

Understanding Mitral Valve Heart Disease & Immune-Mediated Hemolytic Anemia

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"The stress on the leaflets of the mitral valve may be different in dogs that have a higher rather than lower prevalence of severe valvular degeneration," Moise says. "The altered stress could trigger other factors that accelerate degeneration. The disease is likely multifactorial involving genetics, mechanics and aging."

The Moise laboratory found altered function in mitral valve cell cultures. This research was published in 2012 in the Journal of Veterinary Cardiology. Moise and her research team are now evaluating echocardiograms, or ultrasounds, of the hearts of high-risk small-breed dogs between 1 and 2 years of age and a group of low-risk large-breed dogs. "By observing how the valves move, we hope to detect differences in their motion, and thus recognize stress levels of dogs at high risk versus those at low risk for this disease," she says.
DMVD & IMHA continued from page 1

There is no cure and limited treatment options are available for dogs with DMVD. To help manage the disease, veterinarians prescribe medications on an individual basis to help slow its progression. Dogs may be given 
- diuretics, such as furosemide and spironolactone, to help remove excess fluid from the lungs
- an ACE (angiotensin-converting enzyme) inhibitor to help prevent enlargement of the heart and congestive heart failure by relieving strain on the heart and lowering blood pressure
- pimobendan to dilate blood vessels and improve the strength of the heart muscle

Oyama and his research team are looking at pharmaceuticals that could potentially block the effect of soro- tonin on the mitral valve. They also are evaluating the effect of a new diuretic in helping to manage dogs with the disease.

“This new diuretic has the potential to be more effective at treating and then preventing the recurrence of heart failure and fluid accumulation in the lungs or abdomen than existing diuretics,” Oyama says. “This diuretic is less likely to build up resistance by the patient, and thus may be more effective and safe. We are interested in learning whether this diuretic can improve a dog’s quality of life and longevity.

“Many dogs will never develop the severe form of the disease that causes the clinical signs requiring medications. A relatively small percentage will have progressive heart enlargement and be at risk for heart failure.”

After being diagnosed with DMVD in 2011, Dexter remained asymptomatic for a year and then was given medica- tions to help manage the condition. The almost 14-year-old Chihuahua continues to live a spunky, fulfilling life. “I think Dexter is an example of how this disease can be managed successfully,” says owner Renee Coney.

IMHA: An Attack on Red Blood Cells

Immune-mediated hemolytic anemia, also known as autoimmune hemolytic anemia, is a disease in which a dog’s immune system attacks the oxygen-carrying red blood cells, often resulting in severe, life-threatening anemia.

IMHA was the furthest thing from Diane Richardson’s mind when her 2 ½-year-old Rottweiler bitch, Frontier Life Eternal, OCG, seemed uncharacter- istically bothered by the 100-degree temperatures in July 2010.

Having owned Rotties for 30 years and bred them for 20 years, Richardson, of Claremont, N.H., sensed something different about her dog’s reaction to the heat that summer. Richardson was about to start competing in rally with the female she called “Bonnie,” a usually healthy, energetic dog.

As Bonnie’s condition worsened and she became very weak, veterinary test- ing showed that she had secondary IMHA, which occurs along with another disease. Two things may have con- tributed to her disease: a hornet sting and Mycoplasma haemominutum, a blood pathogen transmitted by fleas and ticks.

The most common sign of IMHA is lameness, which results from the anemia and oxygen starvation that results from the destruction of red blood cells. Blood in the urine also indicates a breakdown of red blood cells. Decreased appetite, diarrhea and vomiting may occur. Jaundice from bilirubin, a byproduct of red blood cell destruction, accumu-lates and can cause yellowing of the skin and the whites of the eyes. If the heart is affected and the disease contin- ues, a lack of oxygen may cause a dog to collapse.

The amount of jaundice and the level of albumin, or plasma protein, contribute to the likelihood of a dog’s long-term survival. The mortality rate ranges from 30 to 70 percent that many dogs dying within the first two weeks of diagnosis. The condition can be expensive to treat due to the cost of diagnosis and medications. Dogs that survive the initial crisis face the risk of relapse and complications related to having a chronically depressed immune system.

Anthony Carr, D.Med.vet., DACVIM, professor of small animal clinical sci- ences at the University of Saskatchewan Western College of Veterinary Medicine in Canada, has studied IMHA for 20 years. “It is a broad term that includes an array of diseases in which the immune system destroys red blood cells,” he says.

Primary & Secondary IMHA

Although Bonnie had secondary IMHA, the disease also can be primary, or idiopathic, when there is no known cause. Primary IMHA occurs when a dog’s own immune system is the cause of the disease. It is thought to be a genetic, or inherited, condition that typically affects middle-aged females and occurs more commonly in some breeds. Affected breeds include the American Cocker Spaniel, Clumber Spaniel, Collie, Dachshund, English Setter, English Springer Spaniel, Irish Setter, and Old English Sheepdog, though it can occur in any breed and at any age.

Secondary IMHA is caused by a reaction to another illness, medications or toxins. It may occur in dogs battl- ing cancer, such as lymphosarcoma, leukemia and hemagiosarcoma, or when a dog has a blood parasite, such as M. haemominutum and Babesia, which causes an abnormal immune reaction.

In both primary and secondary IMHA, destruction can be extravas- cular (outside the blood vessels) or intravascular (in the bloodstream). Extravascular destruction, which may affect the spleen, liver or bone marrow, has a more favorable prog- nosis because the hemoglobin released by the destroyed cells is engulfed by macrophages, or white blood cells, rather than being released into the bloodstream.

When the destruction is intravascular, the released hemoglobin endangers a dog’s kidney function. Regardless of the site of destruction, massive inflam- mation results and can affect multi- ple organ systems. Stroke can result from blood clotting.

In necropsy studies, Carr has found that 80 percent of dogs with IMHA had blood clots in various organs. “Inflammation and hemostasis, the process of clotting to stop bleeding, are definitely linked,” he says. “IMHA is a condition of massive inflammation that promotes hemostasis and the formation of clots.”

Prompt veterinary treatment is the key to stop the destruction of red blood cells, stabilize a dog and allow the red blood cells to regenerate.

Blood transfusions may be needed to buy time until medications can work. Laura West, D.V.M., DACVIM, of the Veterinary Specialty Hospital in San Diego, received an AKC Canine Health Foundation grant in 2011 to study new treatments for IMHA.

“You have to think of IMHA as being like a snowball rolling downhill,” she says. “By the time the disease is diagnosed, it has already picked up momentum and speed.”

A series of tests are used to diag- nose IMHA. These include complete blood count, blood chemistry analysis, blood smear evaluation to assess the clumping of red blood cells, and a Coombs test to detect antibodies attached to red blood cells. An abdominal ultrasound or radiograph can be used to check for other causes of anemia, such as a tumor. Veterinarians usually use a three- pronged approach to medications that involves suppressing the immune system, preventing stroke and treating clinical signs of anemia. Prednisone is the first line drug used,” West says. “It is very effective but has side effects that can affect a dog’s quality of life, such as excessive thirst and urination, panting, gastrointestinal ulcers, and increased susceptibility to infections.”

Prednisone therapy may be com- bined with a second immunosuppres- sant for better control. Prednisone is a fast-acting medication that success- fully suppresses the immune system. By giving a second, slower-acting drug, such as azathioprine or cyclosporine, a dog can be tapered off prednisone sooner. Dogs also may receive low doses of anticoagulants such as heparin or Plavix to help prevent blood clots.

Although the ideal treatment for IMHA has yet to be discovered, and is likely to vary on an individual basis, more research is warranted. “Hopefully, we will come to understand the efficacy and the pros and cons of any course of treatment,” West says. 2
Creating a lasting impression with his easy, graceful gait and thick, curly black coat, GCH Claircreek Impression De Matisse is leading the pack in the Pro Plan Champions Cup standings with 234 points earned through April 30.

The 2 ½-year-old male Portuguese Water Dog, who is called “Matisse,” was bred by Donna Gottdenker, who co-owns him with Milan Lint and Peggy Helming. After finishing second in last year’s Champion Cup program, Matisse continues to dazzle judges and spectators with help from professional handler Michael Scott.

The yearlong Pro Plan Champions Cup award program is based on points tabulated from Bests in Show and Group placements at more than 200 Purina-sponsored all-breed dog shows in 2014. This year’s winner will be determined in early 2015. The Pro Plan Champions Cup winner will receive a $10,000 cash prize, an original oil painting by dog portrait artist Linda Draper and a keepsake Pro Plan Champions Cup trophy. A permanent Pro Plan Champions Cup is displayed at the Purina Event Center in Gray Summit, Mo., along with a plaque engraved with the winners’ names.

Cash prizes also will be awarded to the top-placing dogs as follows:
- Second place, $5,000
- Third place, $2,500
- Fourth place, $1,250

To view a tabulation of individual dog’s points and a listing of qualifying shows, please visit the Purina Pro Club website at purinaproclub.com. The Pro Plan Champions Cup is sponsored by Purina Pro Plan brand dog food.

FortiFlora Now Eligible for Purina Points

Did you know that Purina Veterinary Diets FortiFlora brand canine nutritional supplement has been added to the list of products eligible for Purina Points? Weight circle submissions from FortiFlora, a nutritional supplement available by prescription only that provides dietary management of dogs with diarrhea, are 390 points per box. “We are excited to add FortiFlora to the Pro Club program,” says Lisa Walsh, Purina Pro Club Communications Manager. “This product can have such a great impact on dogs’ digestive health, helping to protect them from the stress of extended trips and changes in routine, which is a common concern with show and sporting dogs.”

Purina-Sponsored Sporting Events* | June to August 2014

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Want to Reach the Editor?

Have comments about the Purina Pro Club Update? Send them to us at: Purina Pro Club Update, c/o Editor, Nestlé Purina PetCare, 2T Checkerboard Square, St. Louis, MO 63164 or via email at today’sbreeder@purina.com.
**Purina Pro Plan SAVOR Additions Boost Meals with Palatability & Nutrition**

When dogs are traveling on the circuit to field trials or conformation shows, it is not uncommon for them to lose their appetite. Purina Pro Plan is introducing SAVOR Additions Natural Purées, a natural, nutritious flavor enhancer, to help stimulate meals. Purina Pro Plan SAVOR Additions are highly palatable and made with nutrients such as antioxidants or prebiotic fiber. They do not contain added artificial colors, flavors or preservatives, and are formulated without corn, wheat or soy. They are made with human-grade ingredients.

Available in four purée blends, Pro Plan SAVOR Additions come in squeezable, resealable 4.5-ounce pouches that are convenient and easy to use. This enables owners to lightly coat a dog’s dry kibble and then mix it in. The featured blends are:
- Beef & Carrot Purée with antioxidants from vitamins A and E
- Berry Blend Purée with antioxidants from vitamins A and E
- Chicken & Pumpkin Purée with prebiotic fiber from inulin
- Oatmeal & Apple Purée with prebiotic fiber from inulin

Pro Plan SAVOR Additions should not exceed 10 percent of a dog’s daily calories. Toy and small breeds up to 30 pounds should be fed one-quarter to one-half pouch per day; medium-sized breeds from 31 to 49 pounds up to one pouch a day; and large and giant breeds more than 50 pounds up to two pouches per day.

The new Purina Pro Plan SAVOR Additions Natural Purées will be sold individually starting in June at pet specialty and farm supply stores. For information, visit proplan.com or to talk with a pet nutrition consultant, call 800-PRO-PLAN (800-776-7526) from 7 a.m. to 7 p.m. Central time Monday through Friday.

### Purina-Sponsored Dog Shows*
**June to August 2014**

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* This table lists some, but not all, upcoming Purina-sponsored dog shows.