Assessing and managing the heart health of your patients can be enhanced through the use of diagnostic tools. Information from these tools helps you make confident decisions and recommendations for patients at risk of heart disease or heart failure. The Cardiopet® proBNP Test provides you with additional information about your patients’ heart health, and improvements to the test now make it even easier for you to add it to your current cardiac protocols:

- No special tube required.
- Reduction in sample volume when requesting as either a Stand Alone test or in a Profile.
- Extension of the Canine Results Range. Expanded dynamic range from 3,000 to 10,000 pmol/l.
- Clear recommendations provided with each result.

How Can the Cardiopet® proBNP Test Help?
The Cardiopet® proBNP Test is an additional diagnostic tool for assessing the presence of increased stretch and stress on the myocardium and provides another objective measure for monitoring cardiac disease severity and progression. The determination of ultra-sensitive Troponin I at the same time helps to assess the presence and extent of an existing myocardial cell damage.

Background Information: Cardiopet® proBNP Test
B-type or brain natriuretic peptide (BNP) is a neuroendocrine hormone that is produced as a prohormone (proBNP) in atrial myocytes. Normal physiologic stretch of the atria causes the proBNP peptide to be cleaved and released as two smaller peptides: an inactive N-terminal peptide (Nt-proBNP) and a biologically active C-terminal peptide (BNP). With the development of cardiac disease, the hormone is also produced and released by ventricular myocytes in an amount that is proportional to the severity of the disease. The physiologic properties of BNP cause it to counteract the stretch which triggered its release from the myocardium. The hormone acts on receptors in blood vessels and the kidney to induce vasodilation and diuresis. The active BNP hormone is tightly regulated by a process of rapid intracellular degradation. The half-life of BNP in the dog is only about 90 seconds, making it particularly challenging to measure.1 The Nt-proBNP peptide, as the inactive portion of the prohormone, has a much longer half-life relative to BNP; making it more suitable for laboratory measurement.2 The Cardiopet® proBNP Test measures the concentration of Nt-proBNP in circulation, which is a surrogate marker for increases in atrial and ventricular size as well as wall stress.3 In general, the Nt-proBNP is released in proportion to the degree of stretch and stress on the myocardium, and concentrations increase with increasing severity of cardiac disease.

Other Reasons Nt-proBNP May Be Increased
Plasma Nt-proBNP concentrations should be evaluated in the context of other diagnostic tests including renal parameters and blood pressure. Concurrent disease, such as pulmonary hypertension or renal disease, could result in increased Nt-proBNP concentrations that are secondary to the effects that these conditions have on the cardiovascular system.
Heart Disease in Dogs
The most common cause of heart disease in dogs is chronic degenerative valve disease (CVD). This disease involves myxomatous degeneration of the atrioventricular (AV) valves, with the mitral valve more commonly affected than the tricuspid valve. Older (>5 yrs) small-breed (<20 kg) dogs are generally at greatest risk of CVD, although large-breed dogs can also develop this disease. A systolic murmur heard best at the left apex in an adult small-breed dog is consistent with a diagnosis of myxomatous mitral valve disease (MMVD). Often, murmurs associated with CVD are incidental findings on otherwise healthy patients. It is recommended that dogs with CVD be staged according to a thorough history, physical examination, thoracic radiographs with vertebral heart score (VHS) and systemic blood pressure. Echocardiography is recommended for a definitive diagnosis, especially in large-breed dogs.

Myocardial disease is also recognised in dogs with idiopathic dilated cardiomyopathy (DCM) being one of the most common forms. Idiopathic DCM is associated with a systolic dysfunction of the ventricles and is often accompanied by dilation in all four chambers. It is typically a disease of large- and giant breed dogs, and the incidence of disease increases with age. One of the most commonly affected breeds is the Doberman pinscher; the overall incidence of disease in dogs over 5 years of age is 25% – 30%. Dogs with preclinical or occult DCM may have slowly progressive disease in the absence of any clinical signs. Echocardiography, Holter monitoring (or ECG) and measurement of systemic blood pressure are recommended for diagnosis and staging.

Managing Patients with Chronic Valve Disease (CVD)
The amount of time between when a murmur is first detected in a dog with CVD to the onset of congestive heart failure (CHF) can be highly variable. Some dogs may never develop CHF while others, like cocker spaniels, Cavalier King Charles spaniels and large-breed dogs, may experience more rapid disease progression. Nt-proBNP is one tool that can help gauge the progression of CVD. For instance, in small-breed dogs (<20 kg) with MMVD and Nt-proBNP >1500 pmol/l, there is an increased risk of heart failure within the next 12 months.4,5 When used in combination with other diagnostic tools, Nt-proBNP can help to improve the cardiac management plan for patients with CVD. Heart size by VHS and Nt-proBNP concentration can be used together to help predict the first onset of CHF with greater accuracy than either diagnostic test alone.6 This additional information can be used to help establish the timing of follow-up exams, frequency of home resting respiratory rates and when to consider initiating therapy. When trending Nt-proBNP concentrations, a marked change would be another indication for recommending additional diagnostics.

Expanding Your Cardiac Protocols: New Recommendations for the Use of the Canine Cardiopet® proBNP Test

<table>
<thead>
<tr>
<th>Name</th>
<th>Sample requirements</th>
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<tbody>
<tr>
<td>Cardiopet® proBNP (dog)</td>
<td>0.3 ml EDTA plasma</td>
</tr>
<tr>
<td>Cardiopet® proBNP (cat)</td>
<td>0.3 ml serum</td>
</tr>
<tr>
<td>Cardiopet® proBNP (dog)</td>
<td>0.3 ml EDTA Plasma + 0.5 ml serum cooled</td>
</tr>
<tr>
<td>Cardiopet® proBNP (cat)</td>
<td>1 ml serum cooled</td>
</tr>
<tr>
<td>Cardiopet® proBNP , Troponin ultra-sensitive</td>
<td>1.5 ml serum cooled</td>
</tr>
<tr>
<td>Cardiopet® proBNP , SpeciPL®, Protein/Creatinine Ratio, Endoparasites</td>
<td>0.5 ml serum + 1 ml urine + 5 g faeces</td>
</tr>
</tbody>
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*NOTE: The parameter Nt-proBNP is stable for 24 hours at room temperature. Should this duration be exceeded, we recommend that cooled samples are submitted. Please indicate on the tube if the sample contains serum or EDTA plasma.*
Screening Doberman Pinschers for Occult Dilated Cardiomyopathy (ODCM)\(^7,8\)

In Doberman pinschers with preclinical DCM, early treatment with pimobendan has been shown to extend the preclinical phase of the disease and improve overall survival rates.\(^9\)

Cost-effective tools are needed to identify those dogs at greatest risk for the onset of this disease at 4 years of age and older. A recent report indicated that Nt-proBNP concentrations > 735 pmol/l were 92% sensitive and 92% specific for identifying those Doberman pinschers at greatest risk of ODCM and for signaling the need for additional, more costly diagnostics at that time (echocardiogram, Holter monitoring, etc.).\(^10\) Note that this medical decision point is lower than the limit used for dogs with CVD and may reflect both a breed and pathophysiologic difference in the production and/or release of the proBNP hormone.

Differentiating CHF from Other Disease-producing Respiratory Clinical Signs

A number of published studies have shown that Nt-proBNP can be used to evaluate patients with respiratory signs and help to differentiate the underlying cause as either cardiac or respiratory in origin.\(^11,12\) The Cardiopet\textsuperscript{®} proBNP Test can be particularly helpful in those dogs with active clinical signs where the results of other diagnostic tests (auscultation, radiographs, etc.) are ambiguous. If the concentration of Nt-proBNP is < 900 pmol/l, the likelihood that clinical signs are due to CHF is very low, and other differential diagnoses should be considered. Plasma Nt-proBNP concentrations exceeding 1,800 pmol/l increase the likelihood that the underlying cause of respiratory signs is CHF. In general, the concentration of Nt-proBNP increases with increasing severity of cardiac disease.

Evaluating Heart Health

Just Got Easier with the new Feline Cardiopet\textsuperscript{®} proBNP Test

Heart Disease in Cats

Cardiomyopathies are the most common cardiac diseases in cats, and hypertrophic cardiomyopathy (HCM) is the most commonly diagnosed form of the disease. HCM is typically recognised in young to middle-aged male cats, but any cat can be affected. Certain breeds of cats, like the Bengal, Forest cats, Himalayan, Maine coon, Persian, Ragdoll, Rex, American and British Shorthairs are at increased risk of the disease. European Shorthairs are also often affected by an idiopathic hypertrophic cardiomyopathie and is one of the most common case in the practices. HCM is characterised by concentric hypertrophy of the left ventricle and associated diastolic dysfunction (impaired ventricular relaxation). As the disease progresses, enlargement of the left atrium (LA) leads to an increased LA pressure and risk of developing congestive heart failure. Cats with an enlarged LA are also at increased risk of developing thromboembolic disease (saddle thrombus).

Diagnosing Heart Disease in Apparently Healthy Cats

Cats with cardiomyopathies can appear healthy even though they may have moderate to severe structural and functional heart disease as assessed by echocardiography.\(^4\) When diagnosing heart disease, all cats should have a thorough history and physical examination. On auscultation, a systolic heart murmur at the sternal or parasternal border may be present with or without a gallop sound or arrhythmia. Keep in mind that not all cats with cardiomyopathy will have a murmur, and innocent murmurs in healthy older cats can be quite common. Auscultation cannot distinguish between an innocent murmur and one caused by heart disease. Both thoracic radiographs and electrocardiograms (in the absence of an arrhythmia) have low sensitivity when screening apparently healthy cats for heart disease, as abnormalities may be absent in occult cardiac disease. Thoracic radiographs, however, are an important part of the minimum database for a patient with heart disease because cardiomegaly, early vascular or pulmonary changes could be detected. Measuring systemic blood pressure in a cat with a murmur is important for determining that the cat is normotensive, as hypertension, along with hyperthyroidism and anaemia, can be underlying causes of a murmur. The only way to correctly identify and diagnose an underlying cardiomyopathy in an apparently healthy cat is with an echocardiogram.

How Can the Cardiopet\textsuperscript{®} proBNP Test Help?

The Cardiopet\textsuperscript{®} proBNP Test can be used to help encourage client compliance with an echocardiogram on those asymptomatic cats at greatest risk of underlying cardiac disease. An apparently healthy cat with a murmur is at increased risk of having an underlying cardiomyopathy, and an echocardiogram should be recommended. Approximately 16% – 44% of apparently healthy cats have a murmur, and 20% – 30% of those will have evidence of cardiomyopathy by echocardiogram.\(^5,7\) The Cardiopet proBNP Test can be used to help encourage compliance with an echocardiogram on those asymptomatic cats at greatest risk.
of underlying cardiac disease. Concentrations of Nt-proBNP >100 pmol/l suggest that there is increased stretch and stress on the myocardium. The patient has an increased likelihood of cardiac disease and should undergo echocardiography for diagnosis and staging.8,9 If echocardiography is declined, thoracic radiographs with a vertebral heart score (VHS) should be considered. Moderate to severe left atrial enlargement is usually evident on the dorsocentral view, while the VHS may help to identify mild to moderate increases in heart size.

Because cardiac disease can develop at any time, a single normal Nt-proBNP concentration (<100 pmol/l) may not reflect disease status in the future.

The Cardiopet® proBNP Test can also be used to help differentiate congestive heart failure from other respiratory diseases causing dyspnea.9,10 In cats with respiratory signs, the results of the Cardiopet® proBNP Test should be interpreted in combination with history, physical examination and thoracic radiographs and are particularly helpful when other diagnostic findings are inconclusive. A concentration of Nt-proBNP ≥ 270 pmol/l is supportive of congestive heart failure (CHF) with a sensitivity and specificity of 90% and 87%, respectively.10 In cats with respiratory signs, Nt-proBNP values <270 pmol/l suggest that clinical signs are not likely secondary to heart failure. Furthermore, values <100 pmol/l have very good negative predictive value for ruling out CHF in dyspneic cats.

The Cardiopet® proBNP Test can serve as an additional tool for identifying cats at risk of cardiomyopathy when included as part of a comprehensive profile for adult and senior patients.

Feline cardiomyopathy may be present in cats that may not have a murmur. In one study, the sensitivity of auscultation for detecting occult cardiomyopathy in cats was 31% relative to echocardiography.7 The Cardiopet® proBNP Test can serve as an additional tool for identifying cats at risk of cardiomyopathy when included as part of a comprehensive profile for adult and senior patients. Concentrations of Nt-proBNP ≥ 100 pmol/l suggest that there is increased stretch and stress on the myocardium, and additional diagnostics are recommended to determine the clinical significance of cardiac disease. Because cardiac disease can develop at any time, a single normal Nt-proBNP concentration may not reflect disease status in the future. When trending Nt-proBNP concentrations, a marked change in Nt-proBNP concentration would be another indication for recommending additional diagnostics.

References

Expert Feedback When You Need It
If you have any questions on when to use the Cardiopet® proBNP Test or how to interpret test results, or if you would like treatment advice, please call for a consultation at:

Toll-free hotline 00800 1234 3399

Address for sample submission

Vet Med Lab GmbH
Division of IDEXX Laboratories
Mörkestra. 28/3
D-71636 Luchwigsburg
www.idexx.eu