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PULMONARY HYPERTENSION

The pulmonary circulation serves as a low-pressure system with pulmonary artery systolic pressures of ~25 mmHg and diastolic pressures of ~10 mmHg. Within the systemic circulation, the physiologic reaction to hypoxia generally tends towards vasodilation to allow improved circulation and oxygen delivery to the hypoxic tissue. However, within the pulmonary circulation the physiologic response to hypoxia generally tends towards vasoconstriction. This physiologic adaptation generally helps minimize blood flow to hypoxic areas, which can help improve ventilation-perfusion (V/Q) matching (i.e. help minimize V/Q mismatch). Delivering blood to a relatively hypoxic region of the lung serves little purpose as the blood would not depart the pulmonary circulation well-oxygenated. However, this adaptation can contribute to pulmonary hypertension in disease states.

Respiratory conditions (e.g. chronic bronchitis) in dogs can lead to smooth muscle hypertrophy around the pulmonary vasculature. With the diffuse development of smooth muscle hypertrophy, a patient can develop an increasing risk for the development of pulmonary hypertension. If such a patient experiences more global hypoxia (either acutely, such as a shift to higher altitude, or more chronically with progression of primary respiratory disease), more global vasoconstriction will tend to occur throughout the pulmonary circulation. This vasoconstriction will lead to an increase in pulmonary resistance and potentially the development of pulmonary hypertension.

Pulmonary hypertension does not seem to occur frequently in the veterinary population as a primary disease. Pulmonary hypertension in dogs is rarely primary and is generally considered to be secondary to another pathologic state. Potential causes include true pulmonary artery hypertension (e.g. heartworm disease, shunting as occurs with a patent ductus arteriosus), left heart disease (e.g. mitral valve disease or cardiomyopathy), pulmonary disease or hypoxia (e.g. high altitude, pulmonary fibrosis, chronic obstructive pulmonary disease), or thrombotic/embolic disease. The most common causes appear to be either left-sided heart disease or primary pulmonary disease.

The clinical signs of pulmonary hypertension include exercise intolerance, cough, increased respiratory effort, and potentially syncope. In some instances, it may be difficult to differentiate the clinical signs of pulmonary hypertension from the underlying cause. Similarly, physical examination abnormalities may refer to the underlying disease or the pulmonary hypertension (or a combination). Common abnormalities may include a heart murmur, split second heart sound, tracheal sensitivity, pulmonary crackles or wheezes, or cyanosis.

Chest radiographs may be reflective of the underlying disease and show a change in pulmonary pattern (e.g. development of a bronchial pattern). With more chronic pulmonary hypertension, right-sided heart enlargement may be noted with increased sternal contact recognized on the lateral projection. The ventral-dorsal projection may show a "Reverse D" appearance to the cardiac silhouette.

The gold standard for diagnosis of pulmonary hypertension would be direct measurements via a pulmonary artery catheter; however, pulmonary hypertension is rarely diagnosed in this fashion and is generally confirmed via echocardiogram. Some echocardiographic changes may be consistent with pulmonary hypertension; right ventricular hypertrophy, septal flattening, or pulmonary artery enlargement. In order to properly diagnose pulmonary hypertension via an echocardiogram, a regurgitant jet must be detected: either through the tricuspid valve during systole or the pulmonic valve during diastole. Tricuspid regurgitation may allow estimation of the pulmonary arterial systolic pressure while pulmonic insufficiency may allow estimation of the pulmonary arterial diastolic pressure. Echocardiogram can be used to estimate the velocity (V; in meters/second) of the regurgitant jet and the modified Bernoulli equation (4V2) can be used to convert that velocity to an approximate pressure. A tricuspid regurgitant jet of 4 m/s equates to a pulmonary artery systolic pressure of 64 mmHg, while a pulmonary insufficiency jet of 2 m/s across the pulmonic valve equates to a pulmonary artery diastolic pressure of 16 mmHg.

Pulmonary artery systolic pressure of 25-50 mmHg is generally considered to be mild while pressure ranging from 50-75 mmHg is generally considered to be moderately elevated. Pulmonary artery systolic pressure >75 mmHg is considered markedly

elevated. Treatment of pulmonary hypertension was historically quite challenging. However, the relatively recent availability of affordable sildenafil has markedly improved treatment success. Sildenafil provides the mainstay of treatment for pulmonary hypertension; the drug functions as a highly selective phosphodiesterase-5 (PDE-5) inhibitor. PDE-5 is expressed in the lungs and inhibition seems to induce pulmonary artery vasodilation. Some studies have documented a decrease in pulmonary hypertension with sildenafil treatment while other studies show no significant change in the pulmonary artery pressure, but do show an improved quality of life. Sildenafil is recommended as a three times daily treatment in dogs, and concurrent oxygen therapy may be necessary in more severely affected patients as treatment is initiated. Other PDE-5 inhibitors may have appeal as administration may only be necessary once or twice daily, but definitive studies have not been published to date.

Pimobendan is a calcium-sensitizing drug which also has an effect as a phosphodiesterase-3 (PDE-3) inhibitor. PDE-3 inhibitors function at the level of smaller pulmonary arteries (rather than the large pulmonary arteries). Positive inotropy (through calcium sensitization) combined with PDE-3 inhibition may help in treatment of pulmonary hypertension – especially as a large proportion of pulmonary hypertension cases appear to result from left-sided heart disease.

References

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