

# Diagnosis and treatment of pulmonary hypertension in the dog and the cat

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## INTRODUCTION

Pulmonary hypertension (PH) is a well-recognised condition in human patients associated with primary or secondary pulmonary vasculature disease. In veterinary medicine, the condition remains under-diagnosed. Primary pulmonary hypertension is extremely rare, but the secondary form has been described with a variety of congenital and acquired cardiorespiratory conditions (Table 1 in previous article - (Vol 8 No 4 p 44)). It has been defined in human medicine by systolic and mean pulmonary artery pressures exceeding 30 and 20 mm Hg at cardiac catheterisation in the absence of pulmonic stenosis.



Fig. 1: A Keeshond presented with cyanosis secondary to interstitial pulmonary fibrosis and pulmonary hypertension.

A good understanding of the underlying pathophysiology is required to enable a sensible approach to the diagnosis and treatment of pulmonary hypertension. This was explained in a previous article (Vol 8 No 4).

## DIAGNOSIS

Primary pulmonary hypertension is a diagnosis of exclusion. In secondary PH diagnosis of the underlying disease might raise the suspicion of the presence of concurrent PH.

## Clinical signs

PH may be diagnosed in any age or breed of animal. Animals can be asymptomatic or can present with a variety of signs relating to cardiopulmonary disease. The majority

of animals show exercise intolerance, cough, dyspnoea and/or syncope.

## Physical examination

With PH, abnormalities on physical examination reflect the underlying disease process (often cardiorespiratory). Abnormal lung sounds (wheezes, crackles) and cardiac murmurs are a common finding. The latter can be mitral, tricuspid or rarely aortic and pulmonic in origin. A prominent second heart sound may be heard as the pulmonic valve closes against elevated pressure. Additional abnormalities on clinical examination include ascites, cyanosis (Fig. 1) and jugular venous distension.

## Laboratory data

### Haematology and biochemistry

Absolute polycythaemia and the presence of nucleated red cells are an indicator of sustained hypoxia. Additional biochemistry should focus on identifying specific underlying diseases and diagnosing conditions that favour pulmonary thrombo-embolism (hyperadrenocorticism, auto-immune disease, pancreatitis, diffuse intravascular coagulation, neoplasia) (Fig. 2).

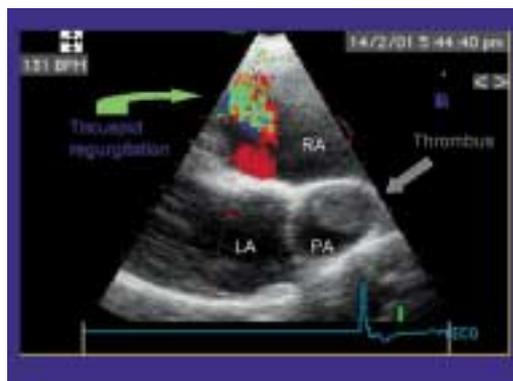


Fig. 2: An echocardiographic image of a canine heart showing a thrombus in the pulmonary artery causing pulmonary hypertension and severe tricuspid regurgitation (LA: left atrium, RA: right atrium, PA: pulmonary artery).

## Clotting profile

D-dimers are a specific blood test for fibrin degradation (more specific than FDP) that have been used in people to

rule-out pulmonary thrombo-embolism (PTE). Close to 100 % of people with PTE have elevated D-dimer levels in their blood, while almost no patient with a clinically significant PTE has a negative result. Pilot-data suggest that D-dimers might be a useful test in dogs with PTE. An in-house latex-agglutination test is already available in the USA and many veterinary laboratories will assay D-dimer (whole blood, serum or plasma but check with your commercial laboratory).

### **Blood gases**

Arterial blood gas analysis would support hypoxaemia ( $\text{PaO}_2 < 90$  mm Hg) or acidosis ( $\text{pH} < 7.35$ ,  $\text{pCO}_2 > 40$  mm Hg) as factors contributing to PH.

### **Heartworm testing**

Heartworm testing is strongly recommended for animals living or having travelled to endemic areas (Mediterranean countries, USA). ELISA, immunochromatographic and haemagglutination based tests are available worldwide for adult heartworm antigen detection.

## **Cardiopulmonary evaluation**

### **Thoracic radiography**

Chest radiographs can show a variety of abnormalities, but none are pathognomonic. Right-sided cardiomegaly associated with respiratory abnormalities (upper and lower airways) are dominant features in PH. Enlargement of the main pulmonary artery segment, poorly perfused peripheral lung fields, and large but rapidly tapering main pulmonary arteries can be seen. Non-cardiogenic pulmonary oedema (with its typical caudodorsal distribution, Fig. 3) is sometimes evident. Common radiographic abnormalities with pulmonary thrombo-embolism include pulmonary vessel abnormalities, pleural effusion and peripheral consolidation but PTE cannot be excluded on the basis of normal chest radiographs. Severe vessel tortuosity is a feature of heartworm disease.



**Fig. 3:** A thoracic radiograph of a dog with right-sided cardiomegaly, non-cardiogenic pulmonary oedema and pulmonary hypertension.

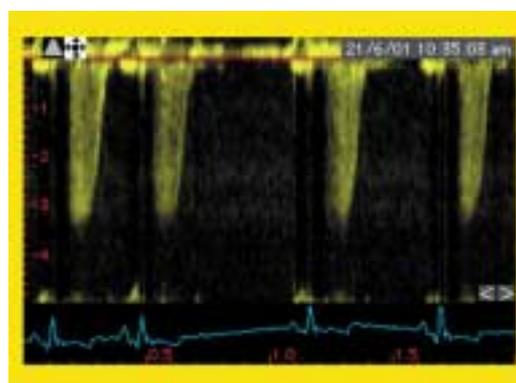
### **ECG**

Tall P-waves in lead II (P-pulmonale) and right-axis deviation are occasionally seen with PH but remember that an ECG does not accurately predict changes in chamber dimension.

### **Doppler echocardiography**

On 2-D echocardiography right ventricular hypertrophy and a dilated pulmonary artery can be observed. This is often associated with decreased LV chamber size. M-Mode echocardiography can show paradoxical septal movement suggestive of increased right-sided pressures. Uncommonly, prolapse of the pulmonic and/or tricuspid valves might be noticed by experienced eyes.

On Doppler echocardiography a tricuspid regurgitant velocity of more than 2.8 m/s (Fig. 4) or a pulmonary insufficiency jet of more than 2.2 m/s in the absence of pulmonic stenosis will indicate the presence of PH. Dogs are categorised in mild ( $< 50$  mm Hg), moderate (51-75 mm Hg) and severe ( $> 75$  mm Hg) PH. The pulmonary artery velocity profile can be divided in 3 types (I-II-III).



**Fig. 4:** A continuous wave Doppler pattern across the tricuspid valve showing high velocity regurgitation consistent with pulmonary hypertension.

### **Cardiac catheterisation**

Use of a Swan-Ganz balloon-flotation catheter allows measurement of right ventricular pressure and pulmonary capillary wedge pressure. Catheterisation remains the gold standard in experimental studies but is very invasive and pulmonary artery pressure varies with sedation and general anaesthesia. It is still very useful for the evaluation of therapeutic response.

### **Other more advanced techniques**

In human medicine and in more specialised veterinary institutions scintigraphy (ventilation/perfusion scan) (London RVC), spiral computed tomography (Glasgow University and others) and magnetic resonance angiography (Animal Health Trust Newmarket) are available to contribute to the challenging diagnosis of PH.

## THERAPEUTIC STRATEGY

Treatment of PH involves management of the primary disorder. There is little data on the treatment of PH in veterinary medicine and most recommendations are extrapolated from human medicine or from animal models for human disease.

Physical activity can be associated with elevated pulmonary artery pressure and therefore graded exercise activities are recommended. In the acute setting **cage rest** will be indicated. Maintaining **body warmth** is very important since hypothermia alone can induce PH; exposure to cold reduces vascular capacity through vasoconstriction.

**Oxygen** is a very potent pulmonary vasodilator alleviating arterial hypoxaemia and attenuating PH. Oxygen administered through a nasal catheter, or via an oxygen-enriched environment (oxygen cage, Elizabethan collar with cling film: Fig. 5) can be extremely useful in the acute setting. Acidosis should be corrected immediately since it increases the likelihood of pulmonary vasoconstriction (by correcting the hypoxaemia).



**Fig. 5:** Oxygenotherapy by the means of an Elizabethan collar partially closed with Clingfilm in a dog with pulmonary hypertension.

**Diuretics** are of marked benefit in symptom relief in humans with primary PH. Their traditional role has been limited to patients manifesting right ventricular failure and systemic venous congestion. Patients with advanced PH can have increased left ventricular filling pressures that contribute to the development of dyspnoea and which can be relieved by diuretics. However, in dogs with chronic lung disease, diuretics can dehydrate bronchial mucus and worsen gas exchange by causing mucus plugging of the airways.

For chronic therapy several vasodilators are used in human medicine. **Prostacyclin** infusion and or inhalation therapy appears very promising but will probably not be available for dogs and cats in the near future. High

dosages of **Ca-channel blockers** (amlodipine) with vascular selectivity are often second choice in human medicine but only 15-25% of humans respond. **Tissue ACE-inhibitors** (enalapril, benazepril, ramipril) appear to be beneficial in PH not only because of their vasodilatory properties, but also mainly because of their beneficial effects on pulmonary vascular remodelling.

**Anti-coagulation** is always indicated if no contra-indication is present. Heparin and warfarin are used most frequently. **Aspirin** at a standard dose of 100 mg twice weekly did not reduce pulmonary hypertension in feline heartworm disease. However, it is now believed that a lower dosage of aspirin (5 mg/cat q 72 hrs and 5 mg/kg BW q 24 hrs in dogs) has platelet anti-aggregatory function without inhibiting endothelial prostacyclin production (which has a vasodilatory action), and might thus be a more appropriate dosage.

Bronchodilators, like **theophylline** will cause sustained pulmonary vasodilation and improvement in right ventricular function on a long-term basis in humans with chronic obstructive pulmonary disease and PH.  $\beta_2$  agonists, such as **terbutaline** also improve pulmonary haemodynamics but no long-term benefits have been seen with these drugs. **Clenbuterol** has not been proven to be useful in exercise-induced PH in horses.

Studies in cats performed on the utility of **digoxin** in right ventricular systolic overload showed that prior administration helped preventing the reduction in contractility of the right ventricle.

**Phlebotomy** might be indicated in reverse shunting (right to left) intra or extracardiac communications (VSD, ASD, PDA) or to reduce blood viscosity in chronically hypoxic animals with a high PVC (>65 %).

**Endothelin antagonists** (Bosentan), **c-GMP phosphodiesterase inhibitors** (Sildenafil), **L-arginine elastase inhibitors** and many others are currently under investigation and appear to show favourable effects on pulmonary functional capacity and haemodynamics.

## CONCLUSION

With the advancement in technology and the awareness of the condition and its underlying pathophysiology the diagnosis of pulmonary hypertension has become less challenging in veterinary medicine. Unfortunately very little is known about the acute and chronic management of this condition, and hopefully more information will become available in the near future.

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- 1. Which statement is false? Primary pulmonary hypertension is:**
  - a. Very common in the dog and cat
  - b. A primary disease of the pulmonary vasculature
  - c. Well recognised in human medicine
  - d. Defined in human medicine by mean pulmonary artery pressure exceeding 20 mm Hg at cardiac catheterisation
  - e. Can induce cor pulmonale
- 2. Which of the following is not a clinical sign associated with pulmonary hypertension?**
  - a. No clinical signs
  - b. Dyspnoea
  - c. Exercise intolerance
  - d. Syncope
  - e. PU/PD
- 3. Which statement is false? Thoracic radiography in pulmonary hypertension can show:**
  - a. Pathognomonic lesions
  - b. Right-sided cardiomegaly
  - c. Prominent pulmonary artery bulge
  - d. An alveolar pattern with caudodorsal distribution
  - e. Poorly perfused peripheral lung fields
- 4. The gold standard for diagnosis of pulmonary hypertension:**
  - a. Thoracic radiography
  - b. Cardiac catheterisation
  - c. Ventilation perfusion scan
  - d. Doppler echocardiography
  - e. Combination of clinical signs and physical examination
- 5. Which of the following is NOT indicated for pulmonary hypertension:**
  - a. Oxygen
  - b. Calcium-channel blockers
  - c. Exercise
  - d. Anti-coagulation
  - e. Bronchodilators

