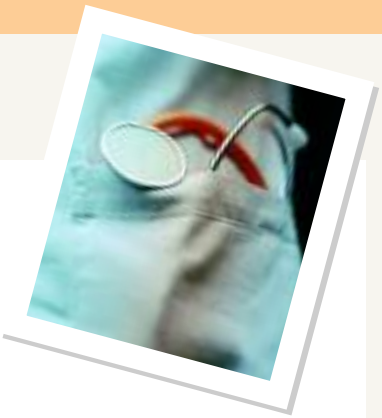

Idiopathic Pulmonary Fibrosis

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Profile

DEFINITION

Pulmonary fibrosis is a form of interstitial lung disease. Idiopathic pulmonary fibrosis is a noninflammatory, progressive, fibrotic lung disease that has no identifiable cause and eventually results in hypoxemia.

SIGNALMENT

- Described more commonly in dogs than cats.
- West Highland white terriers, Staffordshire terriers, other terrier breeds, and poodles most commonly affected dog breeds.
- No breed predisposition described for cats.
- Older animals (typical age of onset is about 9 years).
- Males and females equally represented.

CAUSES

- Any cause of lung injury (infection, inflammation, neoplasia, drug or particulate exposure) can lead to fibrosis, but the cause of idiopathic fibrosis remains undetermined.
- Pulmonary deposition of fibrous tissue gradually replaces functional lung tissue. Idiopathic pulmonary fibrosis is not associated with prior lung injury or inflammation.

SIGNS

Dogs

- Onset is insidious but worsens with disease severity.
- Common historical signs include exercise intolerance, tachypnea, and cough.
- Later, dyspnea and collapse may be seen.
- Physical examination in dogs commonly reveals tachypnea, loud inspiratory crackles, and heart murmur (often tricuspid). Less common findings include wheezes, inspiratory respiratory distress without stridor, or cyanosis.

Cats

- Signs may seem acute since cats seldom display exercise intolerance.
- Typically present with respiratory distress with or without a history of cough.
- Tachypnea, respiratory distress, plus crackles and/or wheezes are often identified.

PAIN INDEX

While not painful, hypoxemia in later stages of disease may cause severe distress.

Diagnosis

- Definitive diagnosis is achieved only via histologic examination of lung tissue from biopsy or necropsy. No other diagnostic tests are able to identify the characteristic histologic changes.
- Differential diagnosis for cough, respiratory distress, and exercise intolerance is vast but can be narrowed with attention to history, physical examination, and radiographs.
- Differential diagnoses in dogs include but are not limited to valvular heart disease with or without congestive heart failure, chronic bronchitis, pulmonary neoplasia, and pneumonia.
- Differential diagnoses in cats include but are not limited to feline asthma, pulmonary neoplasia, congestive heart failure, or pleural effusion.
- Following are nonidiopathic causes of pulmonary fibrosis:
  - Infection (eg, feline immunodeficiency virus, calicivirus, herpesvirus, distemper virus, *Toxoplasma, Histoplasma*).
  - Toxic or environmental insults (eg, paraquat, asbestos, silica, diesel exhaust, oxygen toxicity, bleomycin, radiation).
  - Immune-mediated connective tissue disease (eg, systemic lupus erythematosus, Sjogren's syndrome).
  - Pulmonary neoplasia.
- Routine laboratory testing (ie, CBC, serum biochemistry profile, urinalysis, fecal flotation) is useful to rule out differential diagnoses or concurrent disease.
- Serologic testing may be appropriate to rule out infectious differential diagnoses.
- Radiographic findings in dogs commonly include a widespread and diffuse interstitial lung pattern with varying bronchial involvement and right-sided cardiomegaly. In cats, severe diffuse or

continues

patchy alveolar, interstitial, and bronchial patterns are seen alone or in combination. In humans, CT is preferred to thoracic radiographs for identification of pulmonary fibrosis but CT has rarely been described in pet animals with pulmonary fibrosis.

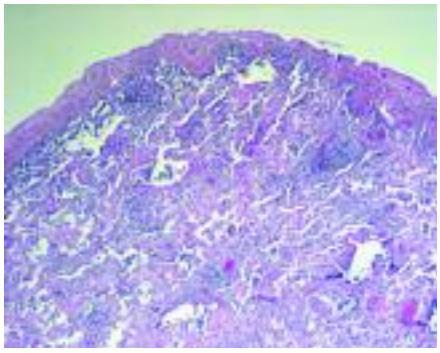
- Echocardiography indicated when differentiation of primary cardiac from primary pulmonary disease is not straightforward. In addition, when tricuspid jet is present, echocardiography allows approximate assessment of pulmonary hypertension, impacting prognosis.
- Invasive respiratory diagnostics, such as tracheal lavage, bronchoalveolar lavage, or pulmonary fine-needle aspiration, are useful to rule out other causes of lung disease. However, such testing should be done with caution, and owners of animals with moderate to severe respiratory distress should provide informed consent.
- Postmortem findings in dogs include right-sided cardiomegaly and fibrotic lungs with thickened alveolar septa, interstitial fibrosis, and pneumocyte hyperplasia. In cats, patchy remodeling of the pulmonary parenchyma, epithelial metaplasia, and honeycomb-lung formation with areas of ongoing fibrosis as well as smooth muscle hyperplasia/metaplasia are seen. Concurrent pulmonary neoplasia is reported in cats.

Treatment

- There is no curative treatment—fibrotic change is irreversible. Therapeutic goals include controlling complications and clinical signs of disease.
- Corticosteroids are often used for idiopathic pulmonary fibrosis; however, there is no proof that these drugs slow progression of this noninflammatory disease. Improvement in some animals may be related to concurrent chronic bronchitis.
- Oxygen supplementation is indicated for respiratory distress pending diagnosis and stabilization, if possible; however, oxygen supplementation is not practical on an ongoing, outpatient basis.
- Bronchodilators (eg, theophylline) and/or cough suppressants (eg, hydrocodone, butorphanol) may improve quality of life for some pets but have no proven efficacy.
- Pulmonary hypertension is documented in most dogs with pulmonary fibrosis. Although not proven effective, angiotensin-converting enzyme inhibitors, calcium-channel blockers, and sildenafil have been used to reduce pulmonary hypertension.
- Animals should be allowed to self-limit activity, as exercise intolerance is part of the condition.
- Clients should understand that this condition is not curable and eventually results in death.

Medications

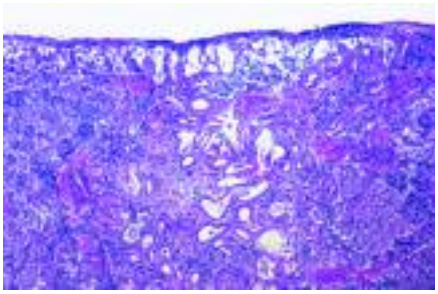
- Prednisone 0.5–1 mg/kg/day PO.
- For dogs with documented pulmonary hypertension (tricuspid regurgitant velocity ≥ 2.8 m/s or pulmonary insufficiency velocity ≥ 2.2 m/s), treatment of hypertension may be attempted. Systemic pressures as well as pulmonary pressures are affected, so systemic blood pressure should be monitored when these drugs are used. Options include angiotensin-converting enzyme inhibitors (eg, enalapril 0.5 mg/kg PO Q 12–24 H); calcium-channel blockers (eg, amlodipine 0.1 mg/kg titrated up to maximum of 0.4 mg/kg PO Q 12 H); sildenafil (0.5–2 mg/kg/day PO)
- Bronchodilator therapy may be useful for some dogs. Pharmacokinetics of different brands of theophylline vary greatly in dogs. For Inwood Labs brand extended-release theophylline, a dose of 10 mg/kg PO Q 12 H is suggested.
- Cough suppressants (eg, hydrocodone 0.22 mg/kg PO Q 6–12 H; butorphanol 0.05–1 mg/kg PO Q 6–12 H) improve the quality of life for some dogs.
- Sedatives may be appropriate for animals with respiratory distress and severe anxiety (eg, acepromazine 0.05 mg/kg SC or IM)
- Diuretic therapy is not indicated for treatment of pulmonary fibrosis.



Canine pulmonary fibrosis: The alveolar interstitium is markedly expanded by abundant fibrous connective tissue, and there is little inflammation present (hematoxylin & eosin; original magnification, 4×).

Follow-up

- If drug therapy is used to treat pulmonary hypertension, systemic blood pressure should be monitored to prevent hypotension. Ideally, pulmonary pressures should also be monitored to assess efficacy of therapy.
- Assessment of oxygenation via arterial blood gas or pulse oximetry may provide information relevant to progression of disease severity.



Feline pulmonary fibrosis: Alveoli are replaced by dilated air spaces lined by cuboidal to columnar epithelium (ie, honeycomb lung). Smooth muscle proliferation and fibrosis are present (hematoxylin & eosin; original magnification, 4×).

- Because the cause of idiopathic pulmonary fibrosis is unknown, there are as yet no preventive strategies.
- Pulmonary fibrosis eventually leads to pulmonary hypertension, worsening hypoxemia, and death.
- Idiopathic pulmonary fibrosis progresses slowly. Because clinical signs may not manifest in cats until late in the process, progression may appear fulminant in this species.
- At-home treatment consists primarily of administration of corticosteroids, bronchodilators, and cough suppressants.

In General

- The cost of medical therapy with bronchodilators, cough suppressants, angiotensin-converting enzyme inhibitors or calcium-channel blockers, and immunosuppression is modest ($$), but the use of sildenafil adds to costs ($$$).
- Idiopathic pulmonary fibrosis is associated with a guarded to grave prognosis.

Cost Key

$ = < $100	$$$$ = $500-1000
$$ = $100-250	$$$$$ = > $1000
$$$ = $250-500	

Most dogs die within 18 months of initial clinical signs, while the course in cats is often only days to weeks.

- Various medications and cytokine modulators aimed at slowing the progression of fibrosis have been tried in humans with idiopathic pulmonary fibrosis, but none has yet proven effective.

Tx at a glance

- **There is no cure for this fatal disease**
- **Typical treatment includes:**
  Corticosteroids (0.5–1 mg/kg/day PO prednisone)
  +/–
  Bronchodilators (eg, 10 mg/kg/day PO Q 12 H theophylline [Inwwod Labs extended release])
  +/–
  Antitussive medications
- **Pulmonary hypertension is treated as a complication of fibrosis. For animals in severe respiratory distress:**
  Oxygen supplementation
  +/–
  Sedatives

Acknowledgment

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See Aids & Resources, back page, for references, contacts, and appendices.