Idiopathic Pulmonary Fibrosis – "Westie Lung Disease"

In order to appreciate the effects of pulmonary fibrosis, it first is important to understand the basic anatomy and physiology of the pulmonary system. The pulmonary system is comprised of the airways and the lungs. The airways include the trachea, the bronchi and their divisions into the very small bronchioles. The lungs are comprised of the alveoli (air sacs) and their surrounding capillaries, where exchange of oxygen and carbon dioxide take place, and the tissues and spaces that surround the alveoli. Collectively, these latter components of the lung, which are called the interstitium, are made up of elastin, collagen, smooth muscle cells, mast cells and a few other types of less common cells. The purpose of the interstitium is to provide both structure and strength to the lungs.

Breathing problems can arise from a number of factors including developmental problems, injury, obstruction of airways, circulation problems, viral, bacterial and fungal infections, and interstitial disease. Acute interstitial pneumonia is a disease affecting the interstitium in which the cells and fibers comprising the interstitium are damaged and eventually are replaced with scar tissue (see **Figure 3.1**). The body's response to injury that results in scarring is called fibrosis. Consequently, the disease is called pulmonary fibrosis. Because the underlying cause for the injury remains unknown, the disease also is referred to as idiopathic ("unknown cause") pulmonary fibrosis, This disease, which also is known as "Westie Lung Disease", prevents the lungs from functioning normally, resulting in difficulty breathing and, eventually, death. In a recent study of affected Westies with this disease, the median survival time from onset of clinical signs was 32 months. This condition primarily affects middle-aged to older Westies, and individual survival time varies considerably. A similar chronic and ultimately fatal disease also affects humans.

While it was once thought that idiopathic pulmonary fibrosis was the result of an inflammatory reaction to an individual injury, it is now understood that fibrosis most likely occurs as the result of repeated injuries caused by some unknown agent or agents. It may be that these agents are a combination of allergens in the air, pollution, and infectious organisms. The body's natural response to injury is to replace damaged cells and fibers with fibrous connective (scar) tissue. While the scar tissue fills in the space where damage occurred, it leaves the area less flexible and less functional than normal. Excessive and repeated scarring, as occurs in pulmonary fibrosis, leaves the lungs unable to expand fully or to contract properly. As a result, they lose their ability to bring oxygen into the body or to expel waste gases. There appears to be a genetic component to pulmonary fibrosis and Westies appear, in particular, to be at risk.

The Westie Foundation of America (WFA) sponsored a 1-day meeting in October 2007 at Purdue University. As a result, a paper "An Official American Thoracic Society Workshop Report: Comparative Pathobiology of Fibrosing Lung Disorders in Humans and Domestic Animals" was published and is available online **(http://www.atsjournals.org/doi/full/10.1513/AnnalsATS.201309-321ST).** The purpose as cited in this publication was "to improve awareness and communication regarding spontaneous progressive fibrotic lung disorders in mammals and to stimulate interaction between human and veterinary medical professionals".

As a next step, the WFA fundraised approximately $125,000 to host a second meeting "Fibrosis Across Species Workshop"

Common Clinical Findings
Difficulty Breathing (Dyspnea)
Coughing
Exercise Intolerance
Abnormal Lungs on Radiographs

on April 27-29, 2014 convening almost 70 human and veterinarian pulmonologists, pathologists, geneticists, radiologists, immunologists to discuss the "One Health" concept comparing disease in the Westie breed and humans. Several research studies resulted from this meeting to determine if pulmonary fibrosis in the Westie is comparable to the disease in humans. Continued research using the Westie as a naturally occurring model of pulmonary fibrosis will further treatment options in humans as well as our beloved Westies. A paper of this meeting is forthcoming and planned for both veterinary and human scientific journals.

Clinical Symptoms and Diagnosis

The major symptom of dogs with pulmonary fibrosis is difficulty in breathing – a clinical symptom known as "dyspnea". Some canine patients will also cough frequently and may have a fever. These dogs tire quickly and lose their ability to do strenuous activities, such as running around or going up and down stairs. Veterinarians will note that lung sounds heard through a stethoscope are abnormal, and the heart will enlarge as the disease progresses. The part of the heart that pumps blood into the lungs, the right ventricle, enlarges the most. This occurs as that part of the heart works harder to pump blood into the increasingly resistant lungs. Because of dysfunction of their heart and blood vessels, affected dogs may also have blood become congested in the veins around their organs.

Hypersensitivity pneumonitis, a chronic condition in which a dog has an allergic reaction to inhaled organic dusts, results in symptoms that are very similar symptoms to those associated with pulmonary fibrosis and can lead to debilitating scarring of the lungs. If hypersensitivity pneumonitis is the cause of the problem, it can be prevented by eliminating exposure to the allergen. In some cases, skin testing may be used to identify the allergen responsible (see previous section on **Atopic Skin Disease).**

The diagnosis of idiopathic pulmonary fibrosis will be made based on the clinical signs, history, results of lung function tests and findings on radiographs (x-rays). Radiographs of the thorax typically reveal abnormalities in the lungs (e.g., loss of clear air space) and evidence of right ventricular enlargement. The veterinarian also may decide to measure the levels of oxygen and carbon dioxide in the patient's arterial blood.

In some cases, veterinarians may consider doing a lung biopsy, to collect tissue for microscopic examination and interpretation by a veterinary pathologist. In fact, biopsy of lung tissue is the gold standard used to make the diagnosis of idiopathic pulmonary fibrosis in humans.

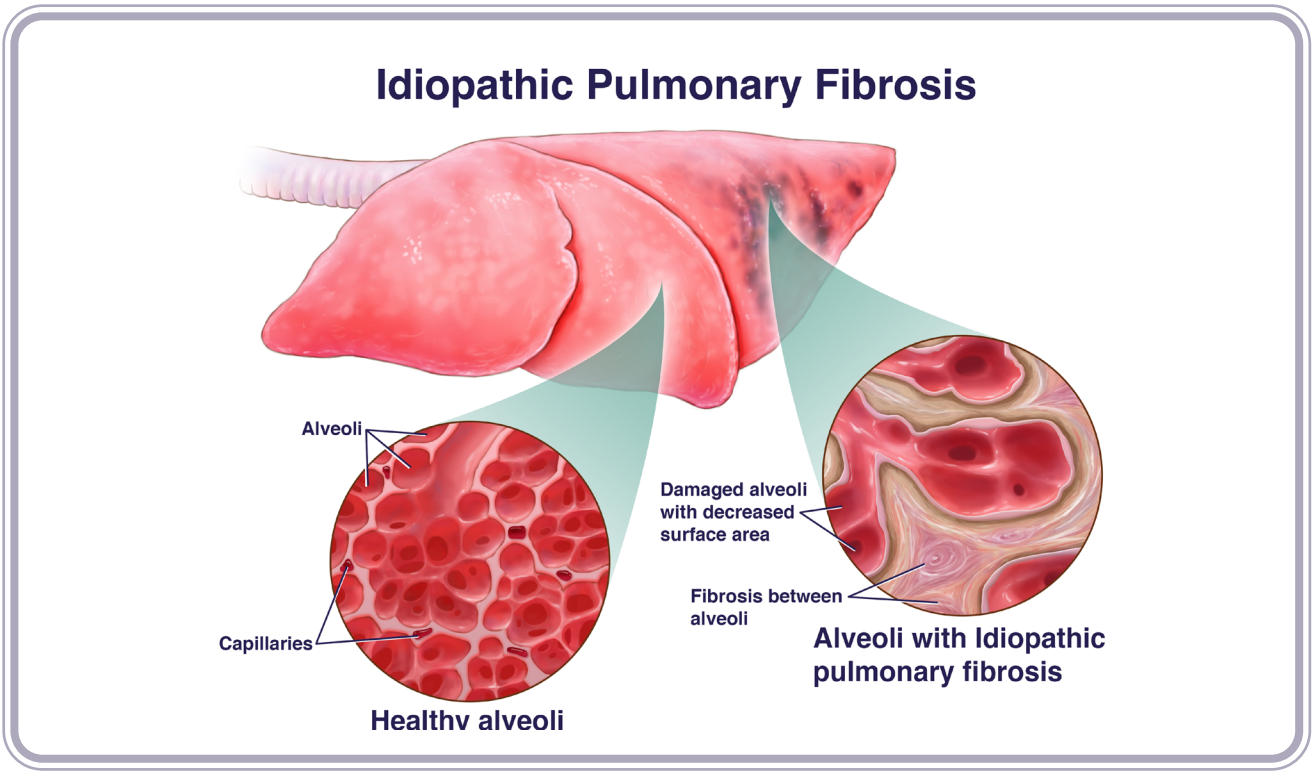

Figure 3.1 - In this illustration, differences between normal healthy alveoli within the lung are contrasted against those affected by idiopathic pulmonary fibrosis. The scar tissue between the alveoli and reduces alveolar surface area compromise the ability of the lungs to oxygenate the blood.

While this procedure is invasive (i.e., it requires sedation / anesthesia and surgical preparation, at a minimum), it is the only way to examine the lung itself for abnormal changes indicating disease. Veterinarians may also use a technique called bronchiolar lavage to collect cells from inside the bronchioles and alveoli. This diagnostic procedure involves sedating the dog, instilling dilute physiologic sterile saline solution into the patient's lungs, and then suctioning it out with a syringe. When the fluid sample is then retrieved, it contains cells and debris from the lungs and airways. Experienced veterinary clinical pathologists can then examine the cellular makeup of this fluid to learn more about the types of disease that may be present. In many dogs with idiopathic pulmonary fibrosis, this fluid contains an increased total number of white blood cells, principally macrophages, neutrophils and mas cells. Typically bacteria are not isolated from the fluid.

Prevention and Treatment

Idiopathic pulmonary fibrosis is a serious and progressive disease that primarily affects older Westies. Because of the strong breed predisposition for this disease, prevention of this devastating disease starts with careful decisions regarding breeding. Current research studies are being performed to identify which of a particular dog's offspring are at risk for developing the condition. While in most affected dogs pulmonary fibrosis remains idiopathic, smoking is a common cause of the disease in humans. The hot gases from cigarette smoke damage lung tissues and this leads to scarring, lung remodeling and emphysema. Living with a human who smokes will dramatically increase any dog's risk of developing pulmonary fibrosis and other lung diseases.

> "The body's natural response to injury is to replace damaged cells and fibers with fibrous connective (scar) tissue."

There is no cure for pulmonary fibrosis, and treatment is difficult. Currently, affected dogs can be helped by the use of corticosteroids, which reduce inflammation, suppress the immune system and help interrupt the cycle that leads to fibrosis. Non-steroidal anti-inflammatory drugs, such as aspirin or ibuprofen, have not been shown to be particularly effective in reducing the signs of disease or arresting the progressive scarring associated with the disease. Without a good understanding of the cause of this disease, therapies are not specific to the disease and do not completely alleviate symptoms. Bronchodilators, such as theophylline, and cough suppressants may help make some patients more comfortable, but there is evidence that different dogs respond differently to therapy. In recent years, pirfenidone, a drug that has antifibrotic, antioxidant and anti-inflammatory effects, has been used in human patients with the disease. The results of a small number of clinical trials with this drug suggest that it slows, but does not prevent, disease progression in these patients. Dogs diagnosed in earlier stages of the disease can often be managed more successfully than those that have progressed significantly by the time the diagnosis is made. Dogs with longstanding disease may be at risk for developing heart problems and these, too, will need to be identified and managed.

Current Research About Canine Idiopathic Pulmonary Fibrosis

Niinikoskio I, Kouki S, Koho N, Aromaa M et al. Evaluation of VEGF-A and CCL2 in dogs with brachycephalic obstructive airway syndrome or canine idiopathic pulmonary fibrosis and in normocephalic dogs. Res Vet Sci 2022 Dec 20:152:557-563.

Brachycephalic obstructive airway syndrome and canine idiopathic pulmonary fibrosis of West Highland White Terriers often cause intermittent or chronic hypoxemia. The objective of this study was to evaluate serum and bronchoalveolar lavage fluid concentrations of hypoxemia-related proinflammatory mediators, vascular endothelial growth factor A (VEGF-A) and chemokine ligand 2 (CCL2) in brachycephalic dogs and West Highland White Terriers with and without pulmonary fibrosis. The results of this study confirmed earlier findings of CCL2 as an important biomarker for canine idiopathic pulmonary fibrosis.

Soliveres E, McEntee K, Couvreur T, et al. Utility of Computed Tomographic Angiography for Pulmonary Hypertension Assessment in a Cohort of West Highland White Terriers With or Without Canine Idiopathic Pulmonary Fibrosis. Front Vet Sci 2021 Sep 23:8:732133.

West Highland white terriers affected with canine idiopathic pulmonary fibrosis are at risk of developing precapillary pulmonary hypertension. The primary aim of this study was to evaluate the use of various computed tomographic angiography parameters to diagnose pulmonary hypertension in West Highland white terriers. The results of this study suggest that the diameter of the pulmonary trunk measured by computed tomographic angiography can be used to diagnose pulmonary hypertension in West Highland white terriers with canine idiopathic pulmonary fibrosis.

Laurila HP, Rajamaki MM. Update on Canine Idiopathic Pulmonary Fibrosis in West Highland White Terriers. Vet Clin North Am Small Anim Pract. 2020 Mar;50(2):431-446.

Canine idiopathic pulmonary fibrosis is a chronic, progressive, interstitial lung disease affecting older West Highland white terriers. According to one classification, canine idiopathic pulmonary fibrosis is a familial fibrotic interstitial lung disease in the group of idiopathic interstitial pneumonias. Etiology is unknown but likely arises from interplay between genetic and environmental factors. Canine idiopathic pulmonary fibrosis shares features with human idiopathic pulmonary fibrosis and human nonspecific interstitial pneumonia. This article describes clinical signs, findings in physical examination, arterial oxygenation, diagnostic imaging, bronchoscopy, bronchoalveolar lavage, histopathology, disease course, and outcome of West Highland white terriers with canine idiopathic pulmonary fibrosis; compares canine and human diseases; summarizes biomarker research; and gives an overview of potential treatment.

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