

HYPER-INFLAMMATORY DISEASE IN THE WEIMARANER

Overview

Several significant disease syndromes affect the Weimaraner breed (Table 1). Many of these diseases are part of a broader hyper-inflammatory syndrome seen in Weimaraners of similar bloodlines. A common underlying cause has been postulated, and the most appropriate treatment will be determined by the age of onset, clinical signs and overall prognosis.

Hypertrophic osteodystrophy (HOD) is a major manifestation of the hyper-inflammatory syndrome, and causes high fever, pain and lameness associated with swelling of the growth plates in the femur and humerus. This is typically seen in one or two puppies in a genetically susceptible litter, soon after they receive multivalent vaccination, although it also can occur after monovalent vaccination. Other recognized disease syndromes include a post-vaccinal reaction with high fever and nodular skin disease; humoral antibody immunodeficiency syndrome with recurrent infections involving the bowel, skin, and urinary tract; and aseptic meningitis.

Table 1. Prevalence of immune-mediated disease in the Weimaraner.

Disease	Prevalence
Hypertrophic osteodystrophy	5.4%
Vaccine reactions	1.3%
Chronic diarrhea/IBD	1.2%
Steroid-responsive meningitis	0.6%
Immunodeficiency (IgA, IgM, IgG)	0.5%

**Weimaraner DNA-disease database at University College, Dublin, Ireland, July 2000*

Hypertrophic Osteodystrophy (HOD)

Diagnosis of HOD relies not only on the typical history and clinical signs, but also on the characteristic radiographic findings of changes at the growth plate of long bones. Clinical signs include swollen, painful metaphyses, fever, lameness and reduced appetite. Many dogs have self-limiting small bowel diarrhea prior to onset of the fever and joint pain. Males and females are equally affected, and the age of onset is typically 8-16 weeks.

The cause of HOD remains unknown, as earlier speculations of vitamin C deficiency or over nutrition have not been substantiated. A link between HOD and humoral antibody immunodeficiency disease has not been established. Low levels of serum IgA, IgM, or IgG are found inconsistently in HOD-affected dogs. The high heritability of HOD within certain families suggests a significant genetic effect, and a DNA marker analysis is ongoing at the Veterinary Genetics Laboratory at UC-Davis.

Treatment of HOD in breeds other than the Weimaraner has traditionally relied on rest, non-steroidal anti-inflammatory drugs (such as carprofen or meloxicam), and opiate analgesics (such as butorphanol, tramadol, or fentanyl) as needed. In most cases, the disease is self-limiting, and most dogs recover in several weeks. However, the disease in Weimaraners is different, as these dogs are prone to a severe multi-organ inflammatory form of the disease, which commonly becomes fatal without appropriate treatment. Prompt recognition of the disease, and treatment with high doses of corticosteroids are key to a good outcome in this disease.

While the mode of inheritance of HOD has not been determined, an obvious breed predisposition exists such that genetic factors play an important role. Research from the Dublin group has found a high heritability for Weimaraner HOD (0.68 ; 95% confidence interval of 0.65 – 0.71). This is important both for genetic counseling and for potential development of a genetic marker test. Until then, the only way to detect dogs carrying HOD-susceptibility genes has been by test matings.

Humoral Antibody Immunodeficiency

Immunodeficiency in the Weimaraner is well established, although the cause is poorly understood. Low immunoglobulin levels are the consistent feature, and have been associated with chronic, recurrent disease involving a variety of tissues including the bowel, skin, and central nervous system.

Steroid-Responsive (Aseptic) Meningitis

Steroid-responsive aseptic meningitis is another relatively rare disease syndrome in Weimaraners. At least 15 cases have been documented. All of these dogs were presented to veterinarians for fever and neck/back pain. The age of onset is typically between 16 – 30 weeks of life, older than for puppies with HOD. Males are more frequently affected than females. The diagnosis is confirmed by spinal tap and analysis of cerebrospinal fluid. Many of these dogs require long term treatment with corticosteroids and azathioprine to control the disease, with recurrence seen when doses of these immuno-suppressive drugs are lowered.

Vaccination

An important finding has been the association of HOD disease with recent vaccination. About 70% of Weimaraners diagnosed with HOD have received a multivalent vaccine within 1 – 2 weeks of the disease onset. There has been no association with a particular brand or type of vaccine, and most brands have been implicated. An important point is the occasional case of a Weimaraner puppy with HOD that had *not* received vaccines within the previous 3 weeks. This indicates that vaccination is but one trigger for HOD in dogs with a susceptible genetic background.

Vaccination Recommendations

Core vaccine components including parvovirus, distemper, and adenovirus-2 are recommended for all Weimaraner puppies. Killed rabies vaccination is recommended as per regulatory requirements, usually at 16 – 24 weeks of age.

Non-core vaccines should remain at the discretion of the local veterinarian, and vaccination for Lyme disease or leptospirosis should be considered in endemic regions. However, these non-core vaccines should be avoided or delayed in bloodlines known to be at high risk for vaccine reactions. Coronavirus and Giardia vaccination are not recommended.

References: Couto, Krakowka, Johnson et al, *Vet Immunol Immunopathol*, 23: 103 – 112, 1989; Hansen, Clercx, Henroteaux et al, *J Sm An Pract*, 36: 128 – 131, 1995; Day, Power, Oleshenko et al, *J Sm An Pract*, 38: 311- 315, 1997; Abeles, Harrus, Angles JM et al, *Vet Rec*, 145:130-134, 1999; Dodds, *JAAHA* 38: 1-4, 2001; Harrus, Waner, Aizenberg et al, *J Sm An Pract*, 43: 27-31, 2002; Foale, Herrtage, Day, *Vet Rec*, 153:553-8, 2003.

(Excerpted from Dr. John Angles in “the Weimaraner Manual” – Weimaraner Club of America, June 2004)

Hypersensitivity to Sulfonamides

The Weimaraner is among those breeds documented to be hypersensitive to sulfonamides. Other affected breeds include: Doberman pinschers, Samoyeds and other white-coated breeds, miniature schnauzers, and breeds having a dilute coat color.

Sulfonamides are known to cause thrombocytopenia, and do so by either increasing platelet destruction or by bone marrow suppression. They also inhibit platelet function. Other documented side-effects of sulfonamides include fever, hepatopathy, neutropenia, keratoconjunctivitis sicca (KCS), hemolytic anemia, arthropathy, uveitis, skin and mucocutaneous lesions, proteinuria, facial palsy, suspected meningitis, hypothyroidism, pancreatitis, facial edema, and pneumonitis. Dogs with sulfonamide-induced hepatopathy have a generally poor prognosis.

References: Cribb, *JAVMA* 195:1612-1614, 1989; Dodds, *JAVMA* 196: 681-682, 1990; Cribb, Lee, Trepanier et al, *Adv Drug React Toxicol Rev* 15: 9-50, 1996; Trepanier, *Vet Dermatol*, 10: 421-248, 1999; Trepanier, *JVIM* 17: 647-652, 2003; Trepanier, *J Vet Phamacol Ther* 27: 129-138, 2004.

LAB TIPS: Influence of age, breed type, and athletic conditioning on thyroid function testing: Previous studies have established that thyroid hormone concentrations are higher in healthy young and adolescent animals, and lower in geriatric animals. Similarly, healthy toy and small breed dogs have higher metabolic rates and higher basal thyroid concentrations than large or giant breed dogs. Sighthounds as a group have lower resting thyroid hormone concentrations, and values in healthy sighthounds often fall just below the laboratory reference ranges. Athletic conditioning or endurance exercise is another variable that affects thyroid hormone concentrations in healthy dogs. Significant decreases in T4 and free T4 concentrations (<established references ranges in 11 or 19 and 8 or 19 dogs, respectively), and significant

increases in TSH concentrations were consistently found for dogs in the peak training state for athletic events (sled dog racing) as compared with concentrations in the untrained state. Thus, endurance training has a profound impact on thyroid hormone concentrations in competitive sled dogs. Similar findings have been observed for greyhounds during racing season, and dogs conditioned for competition lure coursing.