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ANTICOAGULANT TOXICITY IN
THE CANINE

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ABSTRACT: Anticoagulant poisoning is only one of several causes of hemorrhage in dogs. Hemophilia, von Willebrand's disease, liver diseases, and infections are cited as additional causes of hemorrhage. The duration of anticoagulant activity determines the treatment protocol. The half-life of warfarin is 19 hours; diphacinone, 30 days; brodifacoum, 180 days. The treatment of anticoagulant poisoning requires doses of vitamin K₁, at the rate of 5 mg/kg, initially intramuscularly, then orally. Warfarin intoxication is treated for 4 days; diphacinone and brodifacoum for 30 days. Where hemorrhage is present, the prognosis is guarded, and fresh whole blood transfusions are indicated.

The emotional values that are associated with companion animals are not measured in statistical or monetary terms.

There are 55 million dogs (Wise 1984a) and 52 million cats (Wise 1984b) in the United States, which has 84 million households. One in every two households owns a companion animal. The health care of these animals occupies 80 percent of the capacity of veterinary practices at an annual cost of \$3,616,000,000 (Wise 1984a).

The companion animal is just that; frequently acquired at the birth of the first child and, subsequently, a surrogate for the child who has left the home. It is a true and trusted companion of the aged, and this bond is beyond value. This is a relationship that is valued by its presence and devastated by its loss.

Consequently, hazards and life-threatening situations to the companion animal are not to be lightly regarded. Accidental anticoagulant poisoning of the pet animal does occur. Anticoagulants act by interfering with the vitamin K economy of the mammal. This economy is very strict. The small amounts of vitamin K in the body are constantly reclaimed and reused by the liver to manufacture clotting factors.

Warfarin is mistaken for vitamin K epoxide--that is, used vitamin K--by the enzyme vitamin K epoxide reductase. This is an irrevocable mistake (Fasco et al. 1982). The linkage is permanent, and the enzyme is out of business until new enzymes are made to replace it (Ren et al. 1974). With the vitamin K recovery system inoperative, the small amounts of vitamin K present are rapidly used up. The production of clotting factors comes to a halt, and in four to five days, when these are depleted, hemorrhage occurs.

There is another factor which is of critical importance in the treatment of anticoagulant poisoning. How long will the anticoagulant be present? Less than 10 percent of a dose of warfarin goes to the liver to exert its effect. More than 90 percent of the warfarin is tied to albumin. This is gradually released over the period of 24 hours and so defines the period of direct action of warfarin.

The treatment of warfarin exposure is based on the flooding of the liver sites with large amounts of vitamin K over a three-to-four-day period. Vitamin K will diffuse to the sites of clotting factor production when present in concentrations 40 times greater than normal (Lowenthal and MacFarlane 1964).

Treatment utilizes injections of vitamin K₁, at doses of 5 mg/kg intramuscularly to rapidly obtain a high level of vitamin K in the liver. This is followed by the oral administration of a similar dosage for four to five days. This is a highly successful treatment with excellent prognosis for avoidance of hemorrhages.

The treatment of diphacinone exposure is more difficult. The vitamin K therapy described has often proved to be ineffective and, in some cases, nerve damage has also been reported.

Diphacinone is not the equivalent of warfarin. It belongs to another class of compounds, acts at a different site in the vitamin K utilization, and also in a different manner from warfarin.

Diphacinone is an indandione and competes with vitamin K at the point of utilization. To further compound the problem, diphacinone remains bound to body proteins for 30 days and so not only blocks the utilization of vitamin K, but does so for a very much longer period than warfarin. Therapy is again with massive doses of vitamin K, initially by intramuscular injection and followed with oral therapy at the rate of 5 mg/kg for 30 days. Relapses and hemorrhage can occur at any time during this 30-day period if vitamin K therapy is stopped (Mount and Feldman 1983). Brodifacoum is believed to act in a manner similar to warfarin by blocking the recovery of used vitamin K₁. Similarly, therapy is based on large doses of vitamin K and continued for 30 days. Brodifacoum is present in the body for up to 180 days.

The presence of hemorrhage is a very serious sign and reduces the likelihood of successful treatment. When hemorrhages are observed, internal hemorrhages may have already damaged vital organs, and the rate at which vascular accidents occur is very fast in contrast to the previous three to four

days, when few, if any, symptoms are observed. Fresh blood transfusions are the therapy of choice, supported with vitamin K₁. The clotting factors in the blood are rapidly lost; some have a half-life of a day. Hence, the blood for such transfusions must be freshly drawn from a donor.

Warfarin exposure is readily treatable, with an excellent prognosis for recovery. Diphacinone requires prolonged therapy, and there may be nerve damage as a complicating factor. Brodifacoum will also require prolonged vitamin K₁ therapy.

The presence of hemorrhage is not diagnostic of anticoagulant poisoning. There are many other causes of hemorrhage. A diagnostic rule-out approach is necessary to validate the cause of the hemorrhage and to plan an appropriate therapy.

Hemorrhages are associated with genetic disorders of blood coagulation. Hemophilia occurs in dogs and is seen in Irish setters, poodles, and other breeds, von Willebrand's disease is seen in Doberman pinschers, Weimaraners, and Scottish terriers. Liver diseases, particularly in their severe and advanced forms, can result in disorders of blood clotting. This is seen in dogs that have developed scavenging habits. The potential to scavenge rodenticide baits, and their effect on an impaired liver function, almost constitutes a "high risk" type of canine behavior.

How frequently does anticoagulant poisoning of dogs occur? A survey of the major veterinary clinics did not indicate other than a sporadic incidence. However, it occurs frequently enough that it is encountered in most large clinics. The National Animal Poison Control Center recorded 200 enquiries in 1983 related to warfarin (Buck 1984). Only 10 of these enquiries were related to the symptoms and illness; five of these resulted in death. During a similar period, and facilitated by a listed telephone number, brodifacoum baits generated 881 enquiries (Buck 1984). One hundred seventy of these enquiries were for information; 68 enquiries described illness or symptoms associated with possible exposure to brodifacoum; and 13 were associated with mortality.

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