CHAPTER

32

Anticoagulant Rodenticides

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- Anticoagulant rodenticides available in the United States may include brodifacoum, bromadiolone, chlorophacinone, coumafuryl, difenacoum, difethialone, diphenadione (diphacinone), pindone, valone, and warfarin.
- Dogs are intoxicated more commonly than cats or other domestic animals. Anticoagulant rodenticides act by inhibiting the "recycling" of vitamin K_1 to induce a coagulopathy. Animals with an anticoagulant rodenticide–induced coagulopathy may spontaneously bleed from any site.
- The site, volume, and rate of hemorrhage determine the clinical signs observed. The clinical signs observed in more than half of anticoagulant rodenticide–intoxicated animals are anorexia, weakness, coughing, epistaxis, or dyspnea caused by hemorrhage within the lung. However, hemorrhage can occur anywhere; ranging from petechiation and ecchymoses all the way to hematuria, hemoabdomen and even subdural hemorrhages of the central nervous system.
- Abnormalities observed in clinical laboratory tests may include a regenerative or nonregenerative anemia, hypoproteinemia, thrombocytopenia, slight elevation in alkaline phosphatase activity, hyperfibrinogenemia, elevated FDPs, low CO_2, low Po_2, and most important—elevated coagulation times (ACT, OSPT, and APTT). Although all these abnormalities are not present at all times in a given case, elevated coagulation times distinguish exposure from toxicity in all cases.
- Exposure can be confirmed by analysis of serum or whole blood or liver (postmortem) for the specific anticoagulant.
- Treatment options include blood or plasma transfusions, oral or SC vitamin K_1 (4-week duration), oxygen, antibiotics, thoracentesis or abdominal paracentesis, cage rest, and attention to caloric intake as indicated by the status of the animal.
- The prognosis is guarded to good, depending on the severity and location of the hemorrhage.

Pesticides are involved in more animal exposures and deaths than any other category of toxins. The term *pesticide* includes rodenticides, insecticides, herbicides, fungicides, avicides, and other miscellaneous compounds. Common rodenticide toxicoses involve anticoagulant rodenticides, bromethalin, cholecalciferol, strychnine, and zinc phosphide. This chapter is devoted to anticoagulant rodenticide toxicosis. It has been estimated that greater than 90% of all rodenticides used commercially are of the anticoagulant type.

Sources

The anticoagulant rodenticides were developed following investigations of moldy sweet clover poisoning in cattle. In this historical, well-known syndrome, the naturally occurring coumarin in the clover is converted by fungi to dicumarol, the toxic agent.[1] Warfarin was initially synthesized during these investigations of moldy sweet clover poisoning and was subsequently marketed as a rodenticide. Rodent species, however, have since developed resistance to it,[2] so compounds effective against warfarin-resistant rodents have been developed. The first-generation rodenticides, like warfarin and pindone, generally have shorter elimination half-lives and require higher concentrations and consecutive intake over days in order to deliver a lethal dose. Second-generation anticoagulant rodenticides were developed and are far more toxic than the first-generation anticoagulant compounds. Second-generation compounds are now more commonly encountered in veterinary exposures. They include brodifacoum, bromadiolone, chlorophacinone, coumafuryl, difenacoum, difethialone, and diphacinone. Coumachlor, coumatetralyl, and flocoumafen have not been marketed in the United States, and valone distribution in the United States was discontinued in 1993. The greater efficacy of these products against rodents is associated with a greater potential toxicity to nontarget species.

Domestic animals are sometimes inadvertently, and occasionally maliciously, exposed to anticoagulant rodenticide baits. In fact, anticoagulant rodenticides are second only to cholinesterase inhibitors as a cause of death in dogs and cats. Dogs are more commonly poisoned than cats. Some reports have indicated no seasonal predilection; however, in the Pacific Northwest, the majority of confirmed anticoagulant cases occurs in the late fall and early spring when rodent activity is high. This apparent discrepancy may be associated with the source of the samples received—such as urban versus rural and national versus regional. Nevertheless, brodifacoum is the active ingredient most commonly identified in cases of anticoagulant rodenticide–induced coagulopathies diagnosed in the Washington State University (WSU) Veterinary Teaching Hospital. Diphacinone (diphenadione), bromadiolone, and chlorophacinone come in as distant second, third, and fourth. Warfarin and other compounds account for less than 5% of diagnoses. A partial list of the many anticoagulant rodenticide products on the market is presented in Table 32-1. Anticoagulant rodenticide products come in grain-based pellets, minipellets, wax-paraffin blocks, meal baits, dry concentrates, water bait, tracking powder, ground spray, whole and broken grains, nylon pouches, coated talc, and dust. Concentrations of the active ingredient vary from 0.05% to 0.25% between products, but are generally consistent for a given product. To decrease the incidence of exposure of these compounds to children, pets, and wildlife, the U.S. Environmental Protection Agency has instituted measures that require over-the-counter sales of some products for residential use be available in tamper-resistant bait stations and that some compounds be classified for restricted use.

Toxic Dose

At least 10 anticoagulant rodenticide active ingredients are distributed in the United States. They may be obtained over the counter or through pest control operators. They are categorized as first- or second-generation anticoagulant rodenticides on the basis of their efficacy against warfarin-resistant rats. Anticoagulant rodenticide compounds that are effective against warfarin-resistant rats are termed second-generation anticoagulant rodenticides by definition.

The second-generation anticoagulant rodenticides are more potent, longer acting, or both when compared with first-generation compounds. The dose is higher, and the length of vitamin K_1 treatment is longer when treating nontarget species with toxicoses from second-generation compounds compared with the first-generation compounds (Table 32-2).

The likelihood of secondary toxicity occurring in a rodent-eating pet is of interest when anticoagulant rodenticides are used. Although secondary poisoning is theoretically more likely with the second-generation compounds, it is extremely uncommon to confirm field

Table 32-1 Trade Names and Names of the Active Ingredient for Some Anticoagulant Rodenticide Products*

Trade Name	Chemical Name
Acilone	Bromadiolone
Actosin C	Chlorophacinone
Banarat	Bromadiolone
Bar Bait	Warfarin
Boot Hill	Bromadiolone
Bromacal	Bromadiolone
Bromalone	Bromadiolone
Bromapoint	Bromadiolone
Bromone	Bromadiolone
Caid	Chlorophacinone
Castrix D	Difenacoum
Cekurat	Bromadiolone
Chlorocal	Chlorophacinone
Contracts	Bromadiolone
Contrax-W	Warfarin
Contrax-D	Diphenadione
Co-Rax	Warfarin
Coumafene	Warfarin
Cov-R-Tox	Warfarin
D-Cease	Difethialone
D-Con	Brodifacoum
D-Con Mouse-Prufe II	Brodifacoum
Denkarin	Warfarin
Dethmor	Warfarin
Dicusat M	Chlorophacinone
Dicusat E	Warfarin
Diphacin	Diphenadione
Ditrac	Diphenadione
Drat	Chlorophacinone
Enforcer Mouse Kill	Brodifacoum
Famarin	Coumachlor
Final	Warfarin
Forwarat	Brodifacoum
Frunax-DS	Difenacoum
Fumarin	Coumafuryl
Havoc	Brodifacoum
Hawk	Bromadiolone
Jaquar 50 Rodenticide Place Pac	Brodifacoum
Just One Bite	Bromadiolone
Killrat	Bromadiolone
Kill-Ko Rat and Mouse Blues	Coumafuryl
Kill-Ko Rat Killer	Diphenadione
Klerat	Brodifacoum
Kukbo Rat KO	Bromadiolone
Kukbo Stunt	Coumatetralyl
Kukbo Yaong	Brodifacoum
Kypfarin	Warfarin
Lafar	Bromadiolone
Lepit	Chlorophacinone
Lightning	Bromadiolone

Continued

Table 32-1 Trade Names and Names of the Active Ingredient for Some Anticoagulant Rodenticide Products*—*cont'd*

Trade Name	Chemical Name
Lim-N8	Brodifacoum
Liphadione	Chlorophacinone
Kill-Ko Rat and Mouse Blues	Difenacoum/Brodifacoum
LM 91	Chlorophacinone
Luxarin	Warfarin
Maki	Bromadiolone
Matikus	Brodifacoum
Matrak	Difenacoum
Microzul	Chlorophacinone
Mole Patrol	Chlorophacinone
Mouse Maze	Diphenadione
Mouse Out	Chlorophacinone
Neosorexa	Brodifacoum/Difenacoum
Nofar	Brodifacoum
Parakakes	Diphenadione
PCQ	Diphenadione
Pivacin	Pindone
Pival	Pindone
Pivaldione	Pindone
Pival Parakakes	Pindone
Pivalyn	Pindone
Place-Pax	Warfarin
PMP tracking powder	Valone
Prolin	Warfarin
Promar	Diphenadione
Prozap	Diphenadione
Racumin	Coumatetralyl
Ramik	Diphenadione
Ramik Mouse Pack	Diphenadione
Ramik Mouser	Diphenadione
Ramorin	Warfarin
Ramucide	Chlorophacinone
Ratak	Difenacoum
Ratak Plus	Brodifacoum
Rat & Mouse Blues II	Diphenadione
Rat and Mouse Killer	Warfarin
Raterex	Bromadiolone
Ratilan	Coumachlor
Ratimus	Bromadiolone
Ratomet	Chlorophacinone
Ratox	Bromadiolone
Ratoxin	Warfarin
Ratimus	Bromadiolone
Rat Zap rodent bar	Diphenadione
Raviac	Chlorophacinone
RAX	Warfarin
Redentin	Chlorophacinone
Rodent Cake	Diphenadione
Rodex	Warfarin
Rodex Blox	Warfarin

Table 32-1 Trade Names and Names of the Active Ingredient for Some Anticoagulant Rodenticide Products*—*cont'd*

Trade Name	Chemical Name
Ropax	Brodifacoum
Rosex	Bromadiolone
Rozol	Chlorophacinone
Salsbury Ropax Bars	Warfarin
Sorexa	Difenacoum/Brodifacoum
Storm	Flocoumafen
Stratagem	Flocoumafen
Super Caid	Bromadiolone
Talon	Brodifacoum
Tomcat	Bromadiolone
Tomorin	Coumachlor
Topitox	Chlorophacinone
Tox-Hid	Warfarin
Trap-NA-Sak	Diphenadione
Tri-ban	Pindone
Trokat Bait	Chlorophacinone
Volid	Brodifacoum
Warf 42	Bromadiolone
Warfarin Concentrate	Warfarin
Warfarin Plus	Warfarin
Warfarin Q	Warfarin
Warficide	Bromadiolone
Warfotox	Warfarin
WeatherBlok	Brodifacoum
Woprodenticide	Warfarin
Zoocoumarin	Warfarin

*Some products may be discontinued and unavailable for purchase.

cases of toxicosis in domestic species caused by secondary poisoning. This may be related to the "dilution effect" of the rodent species ingesting the bait. For example, a brodifacoum-poisoned rodent may have a liver concentration of brodifacoum of 2 to 5 ppm, whereas the bait is typically 50 ppm. Secondary poisonings are commonly seen in raptors or any animals whose diet consists mostly of rodents and who stay in areas where there is high use of the anticoagulant rodenticide baits.

Toxicokinetics

Plasma, liver, milk, and fetus are the tissues of most interest in a veterinary setting, although anticoagulant rodenticides may travel to a number of other tissues. Peak plasma concentrations of anticoagulant rodenticides occur within minutes to hours of oral exposure. However, the onset of clinical signs (accompanied with abnormal clotting times) is normally at least 36 hours after exposure for the reasons discussed in the mechanism section below. Plasma elimination half-lives in the dog are about 14 hours for warfarin, 4½ days for diphenadione, and about 6 days for brodifacoum. Consequently, whole blood is the specimen of choice by some laboratories for anticoagulant rodenticide analysis in a live animal.

Liver is the tissue of choice for analysis in a dead animal because it has the highest concentration of most anticoagulant rodenticides. Conclusive studies on the passage of the anticoagulant rodenticides into milk or into the fetus have not been reported in dogs or cats. Warfarin is known to pass in the milk of lactating humans. A few field cases indicate

Table 32-2 Toxicity of Some Anticoagulant Rodenticides

Active Ingredient	Bait Concentration (ppm or mg/kg bait)	Acute oral LD_{50} Compound (mg/kg BW) Dog	Compound (mg/kg BW) Cat	Bait* (oz/# BW) Dog
Short Acting				
Warfarin	250	20-50	5-30	1.3
Fumarin	250	NA	NA	NA
Pindone	250	5-75	NA	0.3
Valone	250	NA	NA	NA
Long Acting				
Chlorophacinone	50 (0.005%)	50-100	NA	NA
Brodifacoum	50 (0.005%)	0.2-4	25†	0.06
Bromadiolone	50 (0.005%)	11-15	>25‡	3.5
Difethialone	25 (0.0025%)	4	>16	2.6
Diphacinone	50 (0.005%)	3-7.5	14.7	1

*Ounces of finished bait per pound of body weight required to achieve the lowest LD_{50} value reported in the dog.
†Animals should be closely observed and reexamined at the end of therapy.
‡Limited data.
NA, Data not available.

that intramammary and transplacental distribution of anticoagulant rodenticides should be considered in lactating or pregnant pets exposed to these products.

Mechanism of Toxicity

The clinically relevant toxic event in anticoagulant rodenticide poisoning is a coagulopathy. The coagulopathy occurs because of reduction in activatable forms of clotting factors II, VII, IX, and X. The reduction in activatable forms of these clotting factors occurs because of insufficient amounts of vitamin K_1 at the site of posttranslational modification of these clotting factors.

Vitamin K_1 is required for synthesis of the forms of clotting factors II, VII, IX, and X that are active in fibrin formation. To be active in fibrin formation, these factors need to be able to bind calcium. To bind calcium, there need to be dicarboxylic acid groups on several locations on each clotting factor. Initial synthesis of each of these clotting factors provides only a single carboxylic acid on these locations. Vitamin K_1 is required for the addition of the second carboxylic acid group—this is termed a posttranslational modification of the clotting factor protein. Vitamin K_1 becomes oxidized to vitamin K_1-epoxide during the process of adding the second carboxylic acid group. Vitamin K_1-epoxide is normally reduced back to vitamin K_1 by one or more enzymes. This reduction is sometimes referred to as the *recycling* of vitamin K_1. The activity of recycling enzymes is inhibited by the anticoagulant rodenticide compounds. This inhibition results in a decrease in vitamin K_1 and an increase in vitamin K_1-epoxide concentrations in hepatocytes and plasma.[3]

Synthesis of activatable clotting factors II, VII, IX, and X is subsequently impaired. Factors VII, IX, and X have plasma half-lives of 6.2, 13.9, and 16.5 hours, respectively, in the dog, so they become somewhat reduced in circulation 24 to 64 hours after exposure of the animal to the anticoagulant rodenticide. Clinical coagulopathy occurs after depletion of vitamin K_1 in the liver and then depletion of activatable factors VII, IX, and X in plasma. This indirect mechanism of action is responsible for the lag time commonly observed between the ingestion of bait and the onset of clinical signs. This lag time is normally 3 to 5 days. These proteins are ineffective in clot formation because they do not have sufficient

dicarboxylic acid groups to bind calcium. The vitamin K_1–dependent clotting factors are involved in both the intrinsic and extrinsic clotting cascades, so one-stage prothrombin time (OSPT), activated partial thromboplastin time (APTT), and activated clotting time (ACT) become prolonged.

Clinical Signs

Following depletion of active clotting factors, animals may hemorrhage from virtually any site. It is the authors' experience that approximately half of anticoagulant exposed companion animals will hemorrhage into their lungs; therefore, bilateral epistaxis, hemoptysis, weakness, lethargy, pallor, exercise intolerance, and dyspnea are commonly reported clinical signs.[4] Unfortunately, since the other half of exposed animals can bleed anywhere, presenting signs are quite varied: melena, hematochezia, hematuria, lameness (joint hemorrhage), paresis or paralysis (epidural or subdural hemorrhage), ecchymoses, gingival bleeding, acute collapse (hemorrhage into a major body cavity), seizures (cerebral hemorrhage), acute upper airway obstruction (laryngeal or thymic hemorrhage), abdominal distention and pain, and shaking.[5] Extensive bruising of the skin can occur, depending on how the patient was handled at the time the coagulopathy was present. Occasionally a diagnosis of anticoagulant rodenticide poisoning is made after surgical procedures have been performed on patients when uncontrolled hemorrhage occurs at the incision site after surgery. Checking an ACT time before surgery is wise if there is a suspicion of a rodenticide being consumed.

Minimum Database

The minimum database should include collection of blood before treatment for a complete blood count, serum chemistry panel, hemostasis screen, and major and minor cross matches. Red cell counts, total protein, platelet count, and prothrombin time (PT)/partial thromboplastin time (PTT) are parameters that should be frequently monitored throughout the progression of the disease. Mild to severe anemia, thrombocytopenia (rarely do they fall to <35,000/μL), and hypoproteinemia are observed in most patients. These abnormalities are not seen all the time and depend on the site and severity of hemorrhage. Lack of these abnormalities should not rule out the possibility that problems might occur in the future, particularly when exposure is well documented. Depending on how soon the patient is examined, the anemia may or may not be regenerative. A mild elevation in alkaline phosphatase level is considered nonspecific and is most likely related to the degree of hypoxia present. Notable elevations in liver enzymes are probably an indicator of severe liver damage from other causes and should be considered an important predisposing factor for the development of clinical illness. We are aware of a case of a dog suffering from both brodifacoum poisoning and liver failure secondary to metastasis of a mammary adenocarcinoma. This dog did not respond to vitamin K_1 therapy, most likely because of the liver's inability to produce the necessary coagulation proteins.

Evaluation of clotting times is crucial in confirming a coagulopathy. An ACT can be rapidly performed in house while awaiting OSPT or APTT results. The OSPT is prolonged first in poisoned patients, but prolongation of both OSPT and APTT is normally present before the onset of clinical signs. Fibrin degradation products and hyperfibrinogenemia have also been documented in approximately 50% of anticoagulant-poisoned patients.[5] A reduction in elevated coagulation parameters 12 to 24 hours after adequate vitamin K_1 treatment supports a diagnosis of vitamin K_1–responsive coagulopathy, which is virtually always an anticoagulant rodenticide–induced coagulopathy.

Blood gas analysis can be useful in guiding supportive treatment if it is readily available. A mild acidosis with low CO_2 levels, PO_2 values of less than 50 mm Hg, and an anion gap that is normal to slightly elevated are common observations.

Thoracic or abdominal radiographs or ultrasound can be very useful in identifying the site of hemorrhage—such as a pericardial, thoracic, or pulmonary hemorrhage. The most commonly reported abnormalities include pleural effusion with increases in lung

opacification, hemothorax, air bronchogram signs, interlobar fissure lines, extraluminal compression of the trachea, and loss of abdominal or retroperitoneal detail.[5] Thoracentesis or abdominal paracentesis may yield a bloody effusion with a high packed-cell volume that does not clot in a serum tube.[6]

Confirmatory Tests

Identifying the specific compound involved may influence the dose or duration of vitamin K_1 treatment. It is reasonable to assume that an exposure would be to a long-acting, anticoagulant compound until proved otherwise, given how easily available these products are to pets.

Analytical methods are available to identify specific anticoagulant rodenticides in blood, serum, plasma, liver, gastrointestinal contents, and suspect bait. High-performance liquid chromatography and gas chromatography–mass spectrometry methods are available in several veterinary diagnostic laboratories in the United States. These methods are most commonly used when the specific agent must be identified. However, analytical results are often not available for several days, and clinicians should not delay initiating treatment waiting on confirmation of the specific chemical involved. The concentration of the specific anticoagulant rodenticide detected in blood or liver is not related to the severity of the disease because of the toxicokinetics of the various compounds and the fact that the exposure dose is rarely known with certainty in field cases. Detecting the presence of an anticoagulant rodenticide chemical in an animal with a coagulopathy supports a diagnosis of an anticoagulant rodenticide–induced coagulopathy. In a clinical setting, the main reason for needing to know the specific anticoagulant rodenticide is to help establish the dose and duration of vitamin K_1 therapy. The easiest way to make this decision is to evaluate the ingredient listing on the box of bait used at the home if available.

Treatment

Treatment regimens vary depending on when the exposed patient is presented to the clinic and whether there is evidence of a coagulopathy. Traditional decontamination procedures of inducing emesis, then administering activated charcoal, followed by a cathartic may be performed in patients that come in within a few hours of exposure. These procedures are not generally indicated if coagulation abnormalities are already present. The dilemma that most clinicians face at this point is whether or not to initiate vitamin K_1 therapy or have the patient return 36 hours later to check PT and PTT times. This decision should be based on an estimate of the exposure dose, the success of decontamination procedures, and the time interval between exposure and presentation of the patient.

Determining the risk to the patient can be done by either estimating the exposure dose and then comparing with a known toxic dose (if amount consumed and percentage of active ingredient of the anticoagulant in the bait are both known), or determining how much of the bait the patient would have had to ingest in order to receive a toxic/lethal dose and determining whether this scenario is feasible or not, based on history. Regardless of how the risk assessment is done, one must use available toxicity data for the known compounds (see Table 32-2). It is important to note that most toxicity data for the anticoagulants are reported as LD_{50}s—the dose that will induce lethality in 50% of the exposed patients. It is the authors' suggestion that when using the data to assess risk, you should reduce the LD_{50} by a factor of 10 when performing your mathematical computations for risk. This will provide a margin of safety in an attempt to make a safer prediction of risk.

When vitamin K_1 therapy is not initiated, a clotting parameter, such as OSPT, PTT, and ACT, can be checked at 36 hours and perhaps again at 96 hours after exposure. Additional treatment is not warranted if the clotting times are not prolonged at this time. If the clotting times are prolonged, aggressive vitamin K_1 treatment and plasma transfusion are warranted.

Primary treatment aims for the bleeding patient are to replace the inactive clotting factors by transfusion(s) and vitamin K_1, to maintain adequate cardiovascular support, and to

administer basic appropriate supportive care and exercise restriction. All patients in this category that are admitted to the WSU Veterinary Teaching Hospital are transferred immediately to the intensive care unit where they can be continuously monitored for at least the first 24 hours. The length of stay can range from 24 hours to several days. Clotting factors can be immediately restored with one or more transfusions of either plasma or whole blood once blood samples have been collected for clinical evaluation. The choice of fluid therapy depends on the degree of anemia present. Plasma should be administered at 6 to 10 mL/kg or whole blood at 12 to 20 mL/kg depending on whether clotting factors or red cells, respectively, are indicated. An estimate of the total volume of whole blood transfused should be based on the packed-cell volume. Autotransfusion with thoracentesis or abdominal paracentesis fluid may be used in emergency situations to replace red cells and plasma fluid volume, but not clotting factors. Consultation with a clinical pathologist may be necessary in some cases.

Vitamin K_1—but not vitamin K_3—should always be administered to patients with an anticoagulant rodenticide coagulopathy or to patients where the risk is high of developing a coagulopathy. This form of the vitamin is immediately available for synthesis of new clotting factors. Other chemical forms of vitamin K are not. In fact, vitamin K_3 is ineffective in the treatment of warfarin[7] or dicoumarol toxicosis, so it is contraindicated for the treatment of anticoagulant rodenticide toxicosis. Dogs dosed with 25 mg/kg of vitamin K_3 may develop Heinz body anemias, hemoglobinuria, urobilinuria and urobilinogenuria, methemoglobinemia, cyanosis, and hepatic damage.[7] Production and marketing of injectable vitamin K_3 was suspended in 1985 for safety and efficacy reasons by the Center for Veterinary Medicine of the Food and Drug Administration.

However, vitamin K_1 has no direct effect on coagulation, and clinically significant synthesis of new clotting factors commonly requires approximately 6 to 12 hours. Thus, emergency need for replacement of circulating clotting factors can only be met with a transfusion.

Oral or subcutaneous are the most commonly used routes of administering vitamin K_1. Vitamin K_1 may be administered by the intravenous (IV), intramuscular (IM), subcutaneous (SC), or oral routes. Differences of minutes in the absorption of vitamin K_1 are not clinically significant between the administration routes, so patient factors determine the preferred route of administration. The IV route is not recommended for reasons of safety—the potential for anaphylaxis is always present with IV vitamin K_1 administration.[8] Similarly the IM route is not recommended for reasons of safety because of the pain and hemorrhage that may result. In general, the clinician is often faced with deciding whether to use the oral or SQ route; the oral route should be chosen unless the patient parameters indicate otherwise. Animals with severe hypovolemia may have poorly perfused peripheral tissue, thus reducing vitamin K_1 absorption from a SC site. Oral administration of vitamin K_1 should be reconsidered in animals known to have a fat malabsorption problem, those that are vomiting, or those that were given oral activated charcoal.

Nevertheless, the two most commonly recommended routes of vitamin K_1 administration are oral and SC. The bioavailability of oral vitamin K_1 is increased four to five times when given with canned food.[9] Feeding is likely to stimulate the availability of bile salts and formation of chylomicrons necessary for vitamin K_1 absorption.[10]

Daily dosage recommendations of vitamin K_1 range from 0.25 to 2.5 mg/kg in animals exposed to warfarin; however, these warfarin compounds are rarely encountered by pets because of limited use. A commonly utilized dosage recommendation for most exposures in pets is 1.25 to 2.5 mg/kg every 12 hours (twice daily). The author recommends twice daily dosing; however, there are others who advocate one-time daily dosages of 2.5 to 5 mg/kg. Loading doses are sometimes given at the same dose recommended for daily treatment. The exact dose chosen depends on an estimate of the amount of the exposure and the severity of the coagulopathy. Be aggressive! Adverse effects from proper administration of vitamin K_1 are not known to occur.

Vitamin K_1 treatment must be maintained until toxic amounts of the compound are no longer present in the animal, because vitamin K_1 does not appear to affect the metabolism or elimination of the rodenticide. The length of vitamin K_1 treatment depends on the dose

and kinetics of the specific anticoagulant rodenticide. Abnormal coagulation may last for 7 days after warfarin exposure or 4 weeks after exposure to second-generation anticoagulant rodenticides (see Table 32-2). The times necessary for therapy in this table are based on dogs that were experimentally dosed with an oral LD_{50} dose of the respective rodenticide. In a given case, the length of therapy required is directly related to the amount of anticoagulant ingested. Most field cases of anticoagulant rodenticide toxicosis receive a 3- to 4-week treatment protocol with good success.

In clinical situations the exposure dose and the specific anticoagulant may not be known, so some practitioners elect to evaluate patients periodically. In this approach patients should receive vitamin K_1 therapy for 3 to 4 weeks. Then OSPT or ACT evaluations are performed 36 to 48 hours after cessation of vitamin K_1 treatment. If the clotting time is prolonged, therapy is continued for another week. If the clotting time is normal, the rodenticide may be adequately eliminated and treatment can be discontinued. Remember that even though clotting times are normal, individual clotting factors may still be greatly reduced.[11]

Animals recovering from second-generation anticoagulant rodenticide toxicosis appear to be more sensitive to reexposure to anticoagulant rodenticides. The fact that the clotting times have returned to normal does not mean that the animal has completely eliminated the second-generation anticoagulant rodenticide compound. Animals may develop a coagulopathy after exposure to a dose of a second-generation compound that is less than that listed in Table 32-2. Owners should be strongly urged to remove all bait before reintroducing their pet to the environment.

Additional nonspecific supportive care measures include cage rest to prevent self-induced trauma, oxygen therapy (e.g., nasal catheter, oxygen cage, and tracheotomy), IV fluid therapy to maintain cardiovascular support, and broad-spectrum antibiotics (e.g., enrofloxacin, ciprofloxacin, and cephalosporins), particularly in patients with pleural effusions. Thoracentesis may be necessary to alleviate severe dyspnea, and pericardiocentesis may be necessary to alleviate cardiac tamponade. Approximately 50% of blood in the thorax or abdomen will be reabsorbed in 48 hours, so many patients will undergo some degree of auto-transfusion. A multitude of drugs has been either documented or theorized to interact with anticoagulant rodenticides; clinicians should refer to hospital formularies or veterinary drug handbooks for a comprehensive list. Paretic patients require intensive care to prevent pressure sores. Because most patients may remain anorexic for a few days, attention should be paid to meeting their nutritional needs.

Lactating and pregnant animals present a special problem. The most conservative approach to treating exposed lactating animals is to wean the pups or kittens early and provide them with oral vitamin K_1 for 2 to 3 weeks. The bitch or queen can also be treated with vitamin K_1 depending on the evaluation of exposure dose and evidence of coagulopathy. Another option is not to wean the pups or kittens but treat the bitch or queen directly while monitoring the coagulation status of the pups or kittens and/or treating the pups and kittens. Bitches and queens exposed to anticoagulant rodenticides while pregnant should be treated with vitamin K_1 until whelping or queening occurs.

Prognosis

The prognosis in patients with anticoagulant rodenticide poisoning is generally guarded to good, depending on the site and severity of hemorrhage. Predisposing liver disease or other complications may of course interfere with the animal's ability to respond to therapy or to control life-threatening hemorrhage.

Gross and Histologic Lesions

It is important to emphasize that anticoagulant rodenticide–poisoned animals may hemorrhage at any site. Approximately 50% of anticoagulant rodenticide–poisoned patients coming to either the WSU Veterinary Teaching Hospital or presenting to the Washington Animal Disease Diagnostic Laboratory experience pulmonary hemorrhage. Other reported

sites include cerebral, thymic, laryngeal, intramedullary, renal, perirenal, thoracic, abdominal, hepatic, pericardial, gastrointestinal, and mediastinal hemorrhages. Petechiation and ecchymosis are sometimes seen on the skin and within the mesentery and gastrointestinal tract. The author is aware of a case involving a pregnant dog that died from an anticoagulant rodenticide. The bitch was necropsied, and the pups showed gross evidence of internal bleeding. This provides further evidence that anticoagulants can pose a risk to developing pups and kittens in utero.

Differential Diagnoses

Anticoagulant rodenticide poisoning (prolonged ACT, PT, PTT) in the dog and cat must be differentiated clinically from other causes of coagulopathy, such as disseminated intravascular coagulopathy, congenital factor deficiencies (e.g., von Willebrand's disease), liver disease, chronic gastrointestinal malabsorption, and exposure to sulfaquinoxaline. Response to appropriate vitamin K_1 treatment distinguishes the anticoagulant rodenticides from many of these differentials.

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