

The Veterinarian's Guide

**To Managing Poisoning by
Anticoagulant Rodenticides**

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Preface

This brochure addresses the problem of poisoning of companion animals such as dogs and cats by anticoagulant rodenticides. It is intended to be of help to veterinarians faced with treating rodenticide-poisoned animals and is based on the research and experience of leading experts in the fields of rodent control and veterinary science.

Too often, rodenticides are relied upon as a cure-all instead of using rodenticides more judiciously as part of an integrated program of rodent management. Furthermore, there are too many occasions when rodenticides are placed in situations accessible to children, pets, domestic animals and wildlife. In addition, there are some incidents that reflect unexpected changes in human or animal use patterns, vandalism or accidents after proper bait placement.

Despite efforts by all parties concerned to reduce the risk of accidental poisonings by improving product labeling, packaging and use patterns, such incidents continue to occur. Recent attention has focused on encouraging users to place bait in tamper-resistant bait stations to minimize access to the bait by non-target species. In addition, the recent availability of more effective and toxic anticoagulant rodenticides enables a user to control rodents by using less bait at each bait point and exposing the rodents to bait for a shorter period. While these measures reduce the likelihood of non-target species exposure, when such exposure occurs, it has more serious consequences than when less toxic anticoagulants are involved.

Future efforts to reduce animal poisoning incidents are likely to focus on encouraging rodenticide users to be more careful and seeking ways to make rodenticide baits less attractive to non-target species. In the meantime, veterinarians must continue to play a vital role in case diagnosis and saving poisoned animals, whether from primary (direct eating of bait) or secondary poisonings (feeding on poisoned or dead rodents).

This brochure is intended to help veterinarians understand the differences in toxic action between the various anticoagulants. Three case histories are provided to describe the different courses of action and management of poisoning incidents involving

different anticoagulants. These case histories also

point out the potential importance of determining, whenever possible, the type and quantity of the anticoagulant consumed, the time of consumption and the health of an animal prior to anticoagulant ingestion. Based on these case histories, recommendations are made for treating animals exposed to various anticoagulants. In addition, guidelines are given for informing pet owners of the likely costs involved in treating a poisoned animal and of the role they can play in helping the animal recover.

Preparation of this brochure would not have been possible without the special inputs of W. Jean Dodds, D.V.M., Chief of Laboratory of Hematology, and Stephen C. Frantz, Ph.D., Rodent and Bat Specialist, Wadsworth Center for Laboratories and Research, New York State Department of Health (NYSDH). Dr. Dodds has received many awards for excellence in the field of veterinary medicine and has published more than 150 papers in the field of blood disorders. Dr. Dodds is also President of the Scientists' Center for Animal Welfare and was Chairman of the Committee on Veterinary Medical Sciences and Vice-Chairman of the Institute of Laboratory Animal Resources, National Academy of Sciences. Dr. Frantz has conducted research and taught rodent behavioral ecology and integrated pest management in the United States and abroad. He was technical consultant for Center for Disease Control's (CDC) Federal Rat Evaluation Laboratory. In recent years, Drs. Dodds and Frantz have been conducting research on poisoning of animals by anticoagulant rodenticides; the clinical data and recommendations reported here are drawn largely from their work.

We also wish to express our appreciation to those people who have reviewed this brochure and for their valuable comments, including R. O. Baker, R.A. Green, P.L. Hegdal, W.W. Jacobs, R.E. Marsh, M.E. Mount and V. Perman. Special credit is due Keith Story for his overall guidance and editorial inputs.

LiphaTech, Inc. has sponsored the production of this brochure as a service to veterinarians. As a leading developer and marketer of first- and second-generation anticoagulant rodenticides as well as

other rodent control products, we are committed to helping achieve effective and safe rodent control worldwide. Much of the information in this brochure has not been generally available outside the research community and, by bringing it to the attention of veterinarians, we hope it will help maintain the good safety record, not only of our chlorophacinone (Rozol[®]), bromadiolone (Boot Hill[®], Maki[®]), and difethialone (Hombre[™], Generation[™]) products, but of all anticoagulants. While veterinary skills, if applied in time, can prevent many animal deaths, we recognize our responsibility to continue product improvements and user education aimed at minimizing poisoning incidents. We thank everyone who, through their guidance and research efforts, made this brochure possible.

NOTE:

The information in this brochure is intended to supplement and not replace information on rodenticide labels relating to exposure of non-target species to anticoagulants. Please follow the label directions on all rodenticide products.

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Background on Rodents, Rodent Control and Anticoagulants

The Rodent Threat

Rodents are among the most important competitors with humans for food and other resources. It has been estimated that worldwide there is one rat for every human being. Both rats and mice constitute a major threat to mankind because of the disease organisms they harbor and damage they cause. The Food and Agricultural Organization of the United Nations reported that in 1982, worldwide, rats destroyed more than 42 million tons of food worth \$30 billion. Other reports indicate that one-fifth to one-third of all the world's food crops are consumed or contaminated by rats each year. Moreover, in the past century alone, more than 10 million people have died from rodent-borne diseases. Thus, rodent pest management is essential to achieving and maintaining an acceptable standard of living.

In the United States, the adoption of rodent control measures by homeowners and public health and professional pest control personnel has prevented the extreme losses seen in some developing countries. Nonetheless, each year an estimated 50,000 Americans, mostly children, are bitten by rats. Property losses include millions of dollars worth of food consumed or contaminated on farms and in warehouses. In addition, numerous building fires are attributed to rodents chewing lead gas pipes or stripping insulation from electrical wires. Furthermore, the diseases carried by rodents in this country are numerous and include murine typhus, rickettsial pox, lymphocytic choriomeningitis, tularemia, leptospirosis, trichinosis, salmonellosis and dysentery. And each year, the several human deaths in the Western states resulting from sylvatic rodent-borne plague serve to remind us of the potential for disaster if we relax rodent control measures [47].

In addition to spreading human diseases or causing damage to buildings and their contents, rodents can severely affect the health of farm and domestic animals. Rat attacks on animals such as newborn pigs and poultry cause death and mutilation, and numerous animals suffer illness or death from rodent-borne diseases.

Rodent Control

Against this background of rodent problems, commendable efforts have been seen in the development of more effective and more practical rodent control methods. While trapping rodents has been practiced for about 5,000 years, modern traps are easier to set and some feature a multiple catch capability. Other non-chemical methods of rodent control include public health education, physical exclusion of rodents, and sanitation measures, all of which are aimed at denying rodents food and shelter, measures that should form a primary part of any rodent control program. Unfortunately, non-chemical methods are time-consuming, may not always be practical or affordable, and used alone may not achieve acceptable short-term results. For these reasons, the use of rodenticides plays a vital role in most integrated rodent management programs.

Rodenticide use is not a new approach. Aristotle reported the use of strychnine for rodent control in 350 B.C. For the next 23 centuries, until 1950, the various rodenticides which were used could all be described as acute or single exposure toxicants. They included botanical extracts (e.g. red squill and strychnine), inorganic chemicals (e.g. arsenic, phosphorus and thallium sulfate) and, in the 20th century, various synthetic organic chemicals (e.g. ANTU, DDT and sodium fluoroacetate). In addition to the aforementioned chemicals which were used to make rodenticide baits, various fumigants, including hydrogen cyanide and carbon bisulfide, were used for many decades prior to 1945 [47].

Acute rodenticide baits and fumigants have the advantage of potentially producing a fast kill of rodents, sometimes within a few minutes. However, in the case of baits, the rodents often relate eating the bait to the onset of poisoning symptoms. This results in some rodents ceasing bait consumption before they have taken a lethal dose and, thereafter, becoming bait shy and virtually impossible to control with the same bait. Another important disadvantage of the acute rodenticides is that they are nearly all highly toxic to non-target species, including people, a drawback made worse by the absence of specific antidotes. However, some acute rodenticides, e.g.

zinc phosphide and red squill, do have a good safety record due to their taste, odor and color characteristics, which attract rodents while repelling most domestic animals. The addition of emetics to some acute baits offers added protection since rats and mice cannot regurgitate [35]. However, the addition of emetics or substances which repel non-target species may reduce palatability of the bait to rodents.

Anticoagulant Rodenticides – A Success Story

In the 1940s, with the development of warfarin and later pindone, a new class of rodenticides became available which substantially improved chemical control of rodents and was less hazardous than some older acute rodenticides. These new compounds are anticoagulants and their mode of action involves reducing the ability of blood to clot so that exposed animals bleed internally and die.

Anticoagulants are cumulative poisons and act relatively slowly compared to most acute rodenticides; rodents typically die several days after initial ingestion if anticoagulant consumption has been steady. The usually slow onset of undramatic toxic effects allows anticoagulant baits to be formulated with very low concentrations of active ingredient, which avoids their being repellent. Typically, rodents feed repeatedly on the rodenticide bait without becoming bait shy. In the case of warfarin and other so-called first-generation anticoagulant baits, multiple feeding over several days is usually necessary before a lethal dose accumulates in the rodent.

If the problem is identified or diagnosed early, the slow action of the first-generation anticoagulants allows more time for treatment of poisoned non-target species than with most non-anticoagulant materials. Most important, vitamin K₁ is an effective antidote for anticoagulant poisoning. For these reasons, and because of their effectiveness, anticoagulants have become the most widely used type of rodenticide. An estimated 95% of all chemical control of commensal rodents in the United States is now conducted with anticoagulants, and application of most acute rodenticides is restricted to professional use.

Anticoagulant Safety – A Complicated and Changing Issue

In general, anticoagulant rodenticides have had a good reputation for safety. This reputation is based on their widescale use by amateurs and professionals with relatively few serious incidents of poisoning of non-target species, despite numerous exposure incidents. Human poisoning records indicate that anticoagulant poisonings are substantially less than poisonings from medicines, alcohol and other household chemicals. Regarding animals, in the first three years (September 1978 to August 1981) of HOTLINE calls to the Animal Poison Control Center at the University of Illinois Urbana, 4.4% of total calls related to anticoagulants.

In 1982, anticoagulants accounted for 8% of HOTLINE calls and ranked fourth in concern, behind insecticides, toxic vegetation and certain household products [16, 17]. In 1983, the number of calls for all poisonings had increased, as did the percentage of anticoagulant-related calls, which were more than 10% [15]. For the year July 1982 to June 1983, about 0.8% of all calls to LAMARPIC (Los Angeles Medical Association Regional Poison Information Center) related to anticoagulant exposures of all species [57]. This represented about 8% of all their pesticide calls; 41% of all anticoagulant calls involved dogs, a fact also found in other countries [45].

Considering that more than 25 million pounds of anticoagulant bait are estimated to be used each year in the United States, the safety record is impressive but hardly surprising. After all, such baits contain low concentrations of toxicant and their mode of toxic action and the availability of an antidote make death of non-target domestic animals unlikely, particularly when veterinary intervention is available. A survey of 483 dogs treated by veterinarians for warfarin poisoning in England showed that the majority (81%) recovered, although the number that succumbed was significant and the costs incurred for veterinary care were considerable [9]. Similar results were noted in a recent survey of United States veterinary institutions: 35 dogs (22%) died of the 158 poisoned with warfarin (or associated anticoagulants generically termed as such), where the outcome was known [26]. Fortunately, permanent effects from sublethal intoxication with anticoagulants are rare.

The past good safety record of anticoagulants is no reason for complacency. Recent events indicate that more care in their use by both professional and non-professional applicators is essential because a wider variety of anticoagulant rodenticides is now available, some of which are widely used and differ markedly from warfarin in toxicity and effects on rodents and non-target species [33, 48].

The anticoagulants first marketed in the 1950s could be described as multiple-dose or multiple-feeding anticoagulants. Warfarin, pindone and isovaleryl indandione (PMP) are examples of such first-generation anticoagulants. These products, as formulated into baits, are only moderately toxic to rodents and most non-target species, and normally achieve their lethal effects only when repeated feedings over several days produce an accumulation of the compound within the body. A single feeding by a rodent or non-target animal is usually sublethal.

The challenge is to place these baits where they will be frequently consumed by rodents and not by non-target species.

Two baits introduced later in the 1950s and 1960s utilized more potent anticoagulants: diphacinone (trade names include Ditrac[®], Promar[®], Ramik[®]) and chlorophacinone (trade names include Rozol[®]). These products also tend to be more toxic to certain non-target species, although chlorophacinone is about as toxic as warfarin to dogs and cats and is apparently less toxic to humans and swine than warfarin.

In the past 15 years, we have seen the introduction of second-generation anticoagulants, which are based on three toxicants which are many times more acutely toxic to rodents than warfarin [10, 28, 40]. These are brodifacoum (trade names include Ratak[®], Talon[®], Havoc[®], Klerat[®]); bromadiolone (trade names include Boot Hill[®], Maki[®], Super-Caid[®], Just One Bite[®] brand, Bromone[™], Contrac[®]); and difethialone (trade names include Hombre[™], Generation[™], and D-Cease[™]). Even low concentration (0.005%) baits based on brodifacoum and bromadiolone toxicants and even lower concentration (0.0025%) baits with difethialone are capable of producing rodent kill after a single feeding; hence they are commonly referred to as single-feeding anticoagulants (although in practice rodents feed repeatedly and can accumulate much more than a lethal dose).

Unfortunately, these three toxicants and diphacinone, mentioned above, are much more acutely toxic to non-target species like dogs and cats than the older anticoagulants such as warfarin. Of these, brodifacoum has appeared to be the most toxic to dogs and swine [5, 26, 38]. Indeed, in 1984, HOTLINE calls to the Animal Poison Control Center showed that the number of rodenticide-related calls had risen to first place, with 17% of total calls, ahead of calls related to insecticides and toxic vegetation. More than 92% of these rodenticide-related calls were due to anticoagulants and, of those calls where toxicosis or suspected toxicosis was assessed, 57% were due to brodifacoum [52]. These estimates may be biased because only a few rodenticide product labels include the HOTLINE number. Tables 1 and 2 compare the acute oral LD₅₀ (where known) of first- and second-generation anticoagulants for dogs and cats.

In practical terms, these differences in acute oral LD₅₀ potentially mean that, in the case of the most toxic products, a single bait station or consumer packet contains enough product (a few to several ounces) to kill an otherwise healthy 22-pound dog which consumes the entire contents at one time. In contrast, the same dog may need to eat the contents of 15 or more bait stations or consumer packets containing more than 35 ounces of 0.05% warfarin bait before consuming a lethal dose. However, the differences between anticoagulants go far beyond differences in acute oral LD₅₀ values. Some of the newer anticoagulants have longer or much longer biological half-lives than warfarin and may remain in the body at a toxic level for many months [41]. The prolonged turnover may reflect differences in metabolic rates, tissue and blood release of compounds, binding to blood or other cells and plasma proteins, and genetic susceptibility or resistance. By contrast, compounds other than warfarin have a longer residue half-life in tissues [55]. The residue half-life is clearly of importance both from the viewpoint of treating poisoned animals and in the potential for secondary poisoning when companion animals or wildlife consume poisoned rodents [49]. A long biological half-life also increases the possibility of primary intoxication in non-target species such as dogs, which may repeatedly consume sublethal doses with an additive lethal outcome.

Considering these differences among anticoagulants, it is indeed unfortunate, whether from ignorance or apathy, that both amateur and professional users of rodenticides often use (and misuse) all anticoagulants as though they were as safe as warfarin. The result is an increasing number of severe or fatal poisoning incidents involving non-warfarin toxicants. The problem is exacerbated when, in the absence of information to the contrary, veterinarians treat the animals for generically-assigned warfarin poisoning when, in the case of more toxic anticoagulants, the animal may require much more extensive antidotal therapy and supportive treatment [13, 20, 43, 44]. For instance, in many cases involving brodifacoum poisoning of dogs, the animals died after being sent home following veterinarian examination and treatment for anticoagulant poisoning. The majority of these animals could have been saved by extending antidotal therapy.

The following case histories are representative of the range of dog poisoning incidents involving anticoagulants now being encountered and thus may be of use to veterinarians when designing treatment programs. While the focus in this brochure is on anticoagulant poisoning, it is important that veterinarians understand that acquired or inherited hemostatic defects (e.g. disseminated intravascular coagulation, liver disease, quantitative and qualitative platelet defects, von Willebrand's disease, and the hemophilias) may produce symptoms that can be confused or concomitant with anticoagulant poisoning. The various coagulation tests and their limitations should also be borne in mind when making differential diagnoses [23, 30]. Dog poisoning case histories have been chosen because these represent a substantial majority of the companion animal poisoning incidents which are reported [16, 26, 39, 45, 46, 48, 57]. However, poisoning of cats, birds, horses and other animals are also reported and their treatment would similarly vary according to the type of anticoagulant to which they had been exposed.

Table 1

Acute Oral Toxicities (LD₅₀) of Anticoagulant Rodenticides to Dogs

I	II	III	IV	V
Generic Name (Trade Name*)	LD ₅₀ of Active Ingredient (mg/kg)†(a)	Usual % Active Ingredient in Bait	Quantity of Bait to Give LD ₅₀ in 10 kg (22 lb) Dog	Source of Data for Column II (see Bibliography)
brodifacoum (Havoc, Talon, d-CON)	<u>0.25</u> -1.0 0.25-2.5 <u>1.09-3.6</u>	0.005	50 g (1.8 oz) to 720 g (25.4 oz)	4, 5, 38 31 27
bromadiolone (Boot Hill, Maki, Confrac)	<u>11-15</u> (b) 15- <u>20</u> 15-20	0.005	2,200 g (77.6 oz) to 4,000 g (141.2 oz)	29 2, 56 43
chlorophacinone (Rozol)	<u>50-100</u> 50-100 50-100	0.005	10 kg (352.7 oz) to 20 kg (705.4 oz)	56 39 56
coumafuryl (Fumarin)	equal to warfarin	0.025	--	7
diphacinone (Diphacin, Ditrac, Promar, Ramik)	<u>0.88</u> 3.0-7.5 <u>5.15</u>	0.005	176 g (6.2 oz) to 3,000 g (105.8 oz)	37 34, 51, 56 7, 14, 42
isovaleryl indandione (PMP, Valone)	unknown (c)	0.055	--	22
pindone (Pival)	<u>4</u> 75- <u>100</u>	0.025	160 g (5.6 oz) to 4,000 g (141.1 oz)	25 11
warfarin (Coumafene)	<u>20-50</u> (d) 200 <u>200-300</u>	0.025 or 0.05 (e)	400 g (14.1 oz) to 6,000 g (211.6 oz)	8, 12, 38, 53 51 14, 32
difethialone (Hombre, Generation, Generation BlueMax, D-Cease)	<u>4</u>	0.0025	1600 g (57.1 oz)	59

* Common examples of trade names. This does not imply endorsement of these products by either the authors or their respective affiliations.

Table 1 Footnotes

† Key to Column II and III

- Underscored LD₅₀ range used in calculating Column IV.
- This is derived from a study which was not designed to obtain an LD₅₀.
- Secondary poisoning studies suggest that isovaleryl indandione baits are more hazardous to dogs than warfarin baits (Evans and Lorin, 1967). It is now mostly used in the form of a 2% tracking powder.
- This LD₅₀ range was originally established by the U.S. Fish and Wildlife Service, 1949.
- This bait concentration used for calculating Column IV.

Table 2

Acute Oral Toxicities (LD₅₀) of Anticoagulant Rodenticides to Cats

I	II	III	IV	V
Generic Name (Trade Name*)	LD ₅₀ of Active Ingredient (mg/kg)†(a)	Usual % Active Ingredient in Bait	Quantity of Bait to Give LD ₅₀ in 2 kg (4.4 lb) Cat	Source of Data for Column II (see Bibliography)
brodifacoum (Havoc, Talon, d-CON)	<u>25</u> (approx.)	0.005	1,000 g (35.3 oz)	3, 5, 38
bromadiolone (Boot Hill, Maki, Confrac)	<u>25</u> (approx.) (b)	0.005	1,000 g (35.3 oz)	1
chlorophacinone (Rozol)	unknown	0.005	---	--
coumafuryl (Fumarin)	unknown	0.025	--	--
diphacinone (Diphacin, Ditrac, Promar, Ramik)	<u>5-15</u> 15	0.005	200 g (7.0 oz) to 600 g (21.2 oz)	7, 14, 42 3
isovaleryl indandione (PMP, Valone)	unknown	0.055	--	--
pindone (Pival)	unknown (c)	0.025	--	--
warfarin (Coumafene)	<u>5-50</u> (d) 6-40 <u>200-300</u>	0.025 or 0.05 (e)	100 g (3.5 oz) to 6,000 g (211.6 oz)	8, 18 38 14
difethialone (Hombre, Generation, Generation BlueMax, D-Cease)	> <u>16</u>	0.0025	1,280 g (45.7 oz)	60

* Common examples of trade names. This does not imply endorsement of these products by either the authors or their respective affiliations.

Table 2 Footnotes

† Key to Column II and III

- Underscored LD₅₀ range used in calculating Column IV.
- This figure is actually the maximum tolerated oral dosage (MTD).
- Secondary poisoning studies suggest that pindone has low toxicity to cats (Beauregard et al., 1955).
- Cats are generally regarded as being as susceptible as dogs to warfarin. The range of LD₅₀ may be partly explained by increased susceptibility to poisoning during estrus (Spencer, 1950).
- This bait concentration used for calculating Column IV.

The following case studies taken from the files of the Laboratory of Hematology of NYSDH exemplify three common scenarios with respect to anticoagulant rodenticide poisonings and have been summarized in Table 3. Diagnostic and therapeutic regimes reflect a composite of inputs including foreign sources [19, 20, 36, 44, 50].

Case Study I

History:

A three-year-old, spayed female terrier was admitted to a veterinarian's office because of recent clinical signs of occasional bleeding from the gums accompanied by the presence of black, tarry stools. On questioning the owner, there had been no previous history of a bleeding tendency and no known exposure to anticoagulant rodenticides or other toxicants.

Course of Action:

The referring veterinarian in considering the history rules out the likelihood of a congenital coagulation defect because the animal was spayed uneventfully and had no previous history of excessive bleeding. Suspecting rodenticide toxicosis, the veterinarian has two courses of action to recommend:

1. The **preferred option** involves collection of blood samples to perform routine hemograms and coagulation profiles, plus immediate treatment with vitamin K₁ and blood transfusion(s), if the latter are needed to control bleeding. Once laboratory data are available, vitamin K₁ treatment can cease if results rule out anticoagulant rodenticide exposure. As the time from ingestion of rodenticide to sampling is unknown in many confirmed cases, treatment should continue for 4-6 weeks to control the long-term effects of the more toxic first- or second-generation anticoagulants. The alternative is to serially monitor coagulation weekly or biweekly until values return to normal limits, although costs may be substantial here.
2. The **alternative option**, when costs are a factor for the client, is to initiate and maintain treatment without confirmatory laboratory data. This is less desirable because the suspected diagnosis cannot be confirmed, thus failing to provide adequate documentation should it be needed, and treatment must be maintained for 4-6 weeks in the absence of serial monitoring for the reasons stated above.

Note that induction of vomiting is not recommended in such cases because the animal is already bleeding, and retching may aggravate the situation. Also, if rodenticide exposure is the cause, the toxicant has already been absorbed as clinical signs are evident and vomiting is unwarranted.

Case Study II

History:

A six-month-old intact Doberman pinscher female was admitted to a veterinarian's office with a swollen stifle. X-rays revealed only a soft tissue swelling. However, epistaxis began the next day and continued until the hematocrit had dropped to 13%. The owner indicated that on searching the area where the dog usually exercised, small amounts of material like warfarin were found. A local rancher admitted to placing the toxicant in the surrounding area to control rodents in the past few days, and the dog's owner failed to keep the dog confined to his own property.

Course of Action:

Upon admission but prior to the onset of clinical signs obviously referable to bleeding, the veterinarian should:

1. **Induce vomiting**, as toxicant exposure is known and one needs to eliminate any remaining, unabsorbed stomach contents.
2. **Examine and identify** sample of poison, if available.
3. **Collect blood samples** for diagnostic tests (as described in Case Study I above).
4. **Initiate treatment** (as described in Case Study I above).

As toxicant exposures may need to be proven to establish responsibility for the incident, it is especially important that properly collected blood samples (anticoagulated with citrate or "blue-top" Vacutainer® tubes, and not with EDTA or "purple-top" Vacutainers) be obtained. Coagulation profiles and preferably specific clotting factor assays should be performed as soon as possible on the plasma prepared from the patient's whole blood. Ideally, the blood should be immediately spun to remove

plasma, and this should be put on ice if testing is delayed. These tests are usually run only at commercial clinical reference laboratories or by veterinary teaching institutions or specialized laboratories such as the NYSDH Laboratory of Hematology in Albany, New York.

In the specific case described here, the animal's clinical signs were more severe than would be expected by exposure to a standard warfarin product. The clue comes from the fact that the patient is a Doberman pinscher, a breed known to have a high prevalence (50%) of von Willebrand's disease (VWD), an inherited bleeding disorder, as well as hypothyroidism, which also produces a bleeding tendency [19]. Thus the animal should be blood tested for both VWD and thyroid function. As it turns out, many of the recently studied rodenticide poisoning cases involving Dobermans kept as guard dogs and allowed to roam free also had VWD, which aggravated their clinical course upon rodenticide ingestion [26]. Prompt treatment with vitamin K₁, whole blood transfusions and thyroid supplementation if needed, is especially important in such cases.

The above situations emphasize certain breed susceptibilities to complications arising from poisonings or low-dosage exposures which might otherwise be of little consequence. Another example is with whippets and greyhounds, two breeds known to have an overall lower tolerance to toxicants. The physiological and health status of the animal (e.g. estrous, pregnant, pseudo-pregnant, hypothyroid, debilitated, geriatric, etc.) at the time of exposure can also contribute significantly to the severity of signs and outcome of the case.

The size of the exposed animal is important as well, because smaller animals can go into shock and become moribund more rapidly from blood loss. Massive bleeding into the gastrointestinal tract can produce ileus with delayed emptying of the bowel. In such cases, there may be no overt signs of hemoptysis or melana, but just progressive weakness or collapse. It is critical to monitor the hematocrit here, for if it continues to drop precipitously, internal bleeding should be suspected. Prompt treatment with whole blood transfusions and vitamin K₁ should reverse the situation. Usually within the next 12-24 hours, black, tarry stools will begin to be passed as the ileus relaxes.

Case Study III

History:

An eight-year-old, intact golden retriever male was found by the owner lying in the backyard with blood running from the nose; black, tarry feces were noticed nearby. The owner immediately rushed the animal to the nearest veterinary clinic where rodenticide toxicosis was the presumptive diagnosis. The dog was treated with a fresh whole blood transfusion (300 cc) and vitamin K₁.

On questioning the owner, he related that a pest control operator (PCO) had placed a second-generation rodenticide product in the neighborhood for rodent control, but had assured the local residents that the product was "entirely safe around pets." Nevertheless, the animal made a dramatic and uneventful recovery and was sent home three days later with oral vitamin K₁ supplementation prescribed for five days' duration. Two weeks after the initial hemorrhagic crisis, the dog became lethargic and refused to eat; the following day he collapsed and was readmitted to the veterinary clinic. At this time blood samples were collected for routine hemograms and coagulation tests, and the toenail bleeding time exceeded 15 minutes (normal range up to 6 minutes), at which point the nail was cauterized and bleeding ceased. The animal was treated again with vitamin K₁ pending laboratory results, which confirmed the persistence of anticoagulant poisoning.

Course of Action:

In cases such as this one it is important to:

1. **Obtain a sample** of the product or discuss the matter with the PCO involved, and thereby identify the suspected causative toxicant.
2. **Collect blood samples** for coagulation tests to confirm the diagnosis, as it was suspected that a more toxic rodenticide, having a prolonged in vivo metabolic half-life, was involved.

This case serves to emphasize the importance of treating poisoned animals for several weeks to control the long-lasting effects of newer, more toxic products and the need for education of professional pest control operators, homeowners and veterinarians about the enhanced toxicity and dangers of such products to non-target species. All

too often, poisonings are generically referred to as warfarin to include any type of anticoagulant rodenticide. Such mistakes can be costly to the animal and the client.

Table 3**Case Studies***

Category/Case Study	Checklist of Actions Taken by Veterinarians
I. Clinical signs of bleeding; no history of exposure.	<ul style="list-style-type: none"> · Collection of blood samples for routine blood counts and coagulation profile.† · Treatment with vitamin K₁ plus blood transfusion(s), if needed.
II. Known exposure to anticoagulant rodenticide; no obvious clinical signs of bleeding at time of admission.	<ul style="list-style-type: none"> · Induce vomiting. · Obtain sample of product and identify it, whenever possible. · Collection of blood samples, as above, to confirm diagnosis and provide data in the event of legal action. · Treatment with vitamin K₁ as a prophylactic measure if lab data are abnormal.
III. Known exposure to a new second-generation or a more toxic first-generation anticoagulant rodenticide along with clinical signs of bleeding.	<ul style="list-style-type: none"> · Obtain sample of product and identify it whenever possible. · Collections of initial blood samples, as above, plus serial monitoring once weekly or biweekly until lab values return to normal range. · Treatment with extended regimen of vitamin K₁ plus blood transfusion, if needed.

* For details, see text.

† To establish responsibility for the incident now or at a later date (N.B. cost factors need to be considered and interpretation may be complicated when the time from exposure to sampling is unknown).

Recommendations for Treatment

The principles of treatment and management of anticoagulant rodenticide poisoning are summarized in Table 4. Basically, once blood samples have been collected for the requisite diagnostic tests, the affected animal should receive a parenteral injection of vitamin K₁. This form of the vitamin is preferred because vitamin K₃ has little or no effect for the acute stages of poisoning [50]. Also, vitamin K₁ should not be given intravenously, as the manufacturer's insert clearly recognizes the hazard of anaphylaxis from intravenous use of this product.

On numerous occasions, the authors have been informed of situations where anaphylaxis was associated with intravenous vitamin K₁, a circumstance which may not be defensible in subsequent litigation. Treatment with vitamin K₁ should continue for up to 4-6 weeks unless

laboratory monitoring of coagulation shows that values have returned to normal limits sooner. In cases where the toxicant is known to be warfarin rather than generically referred to as such, vitamin K₁ supplementation is usually needed for up to 5-7 days. However, when identity of the toxicant is unknown, it is prudent to assume that one of the more toxic, longer-lasting products is involved.

The dosage of vitamin K₁ given should generally not exceed 1 mg/lb/day, or at least should be given cautiously if higher doses are deemed necessary [20]. Doses exceeding 2 mg/lb/day may be dangerous and have been shown recently to induce Heinz body hemolytic anemia [24]. In our extensive experience with the monitoring and treatment of rodenticide poisoning cases, we have not had to exceed 1 mg/lb/day of vitamin K₁ for successful control of bleeding [20]. This regimen is about half

the dosage recommended recently by Mount and Feldman [50, 51]. Regardless of the anticoagulant involved, it is important to initiate therapy promptly. When the product has not been identified, as frequently occurs, it is necessary to follow the regimen of prolonged treatment outlined in Table 4 to avoid relapse and to reduce the overall cost to the client.

For severely poisoned cases, bleeding may have caused serious anemia and therefore also necessitates one or more transfusions with fresh compatible whole blood. In addition to transfusions, where animals have bled in the pulmonary, pleural or pericardial cavities, surgical intervention may be necessary to remove blood to give space for lung or cardiac function. Once the poisoned animals are under treatment and are recovering, it is important to

keep them quiet, confined and on a softened diet, for another 2-7 days (depending on the toxicant involved) to minimize hemorrhage in locations such as the central nervous system. Foods rich in vitamin K are green, leafy vegetables (especially broccoli, green beans and lettuce). As vitamin K replenishes circulating clotting factors in a time course consonant with their respective synthetic half-lives, it takes several days for severely depleted animals to resynthesize these factors and no longer be at risk for bleeding complications.

Finally, in cases of acute emergencies related to poisonings, call Chemtrec at 1-800-424-9300.

Table 4

Treatment of Rodenticide Poisoning

Therapy	Dosage	Comments
Vitamin K ₁	<p>Parenteral initial dose*, not to exceed 1 mg/lb/day, and followed by the same parenteral or oral dosage for another six days.</p> <p>Reduce to ½ mg/lb/day for the second week and then reduce by ½ for another two weeks.</p> <p>After 1 month of treatment dosage is continued 2-3 times a week for another 2 weeks.</p>	<p>Six weeks of therapy needed to correct long-term effects of the more potent products.</p> <p>If less toxic anticoagulants are known to be involved or monitoring of coagulation tests shows return to normal values sooner, the length of treatment can be reduced accordingly.</p>
Whole blood transfusions	Compatible fresh blood given at 5-7 cc/lb body weight, if needed in severe cases.	The blood should be fresh to ensure the activity of clotting factors, which are labile on storage.

* Given subcutaneously and not intravenously (see text).

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