The Veterinarian's Guide

to accidental rodenticide ingestion by dogs & cats

LIPHATECH®

Advanced technology. Effective control.

NOTE: The information in this brochure does not represent labeling and does not replace information on rodenticide labels relating to exposure of non-target species to anticoagulants.

Please read and follow all label directions on all rodenticide products.

LIPHATECH®

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Preface

This brochure addresses the problem of accidental rodenticide ingestion by dogs and cats. 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. This revision of the guide includes new brands in the marketplace and additional toxicity information.

Despite efforts by all parties concerned to reduce the risk of accidental poisonings by improving product labels, packaging and use patterns, such incidents continue to occur. The US Environmental Protection Agency now requires rodenticides marketed to consumers to be pre-packaged with tamper-resistant bait stations [54], which is expected to significantly reduce the potential for exposure to both children and pets. The new EPA rules also limit the types of rodenticide that may be sold to consumers, which is intended to further reduce the risks to children and pets, and also the potential risk to non-target wildlife from primary exposure (direct eating of bait) or secondary exposure (feeding on poisoned or dead rodents). Even with these precautions, veterinarians will continue to play a vital role in case diagnosis and saving animals exposed to rodenticides.

Recent work indicates that multiple exposures to anticoagulant rodenticides, over the course of multiple days, result in greater toxicity than is reflected by the standard single-dose acute oral toxicity LD_{50} test [55]. Veterinarians should consider this factor, especially for secondary exposure to dogs, cats and wildlife. Even though the amount of rodenticide contained in a poisoned rodent is small, repeated consumption over a prolonged period may result in toxicity to the predator or scavenger.

This brochure is intended to help veterinarians understand the differences in toxic action between the various active ingredients. Two 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 an exposed animal and of the role they can play in helping the animal recover. Tables 1 and 2 (pages 6 & 7) compare the acute toxicities of first- and second-generation anticoagulant rodenticides for dogs and cats. A table is also included outlining recommendations for treatment of rodenticide poisoning. This edition includes updated active ingredient trade names in the tables and corresponding footnotes to better reflect brands now found in the marketplace.

Preparation of the first edition of the 'Vet Guide' would not have been possible without special input from W. Jean Dodds, D.V.M. and Stephen C. Frantz, Ph.D. who served as Chief of Laboratory of Hematology and Rodent & Bat Specialist, Wadsworth Center for Laboratories and Research, New York State Department of Health (NYSDH) respectively at the time of these studies. Dr. Dodds 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. Frantz 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. Drs. Dodds and Frantz have also conducted 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 input. We'd also like to acknowledge Dr. Cheryl Roge for her expertise and assistance with the most recent updates to this guide.

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. By providing this information to veterinarians, we hope it will help maintain the good safety record, not only for our innovative rodenticides, but for all anticoagulants. While veterinary skills, if applied in time, can prevent most animal deaths, we recognize our responsibility to continue product improvements and user education aimed at minimizing exposure incidents. We thank everyone who, through their guidance and research efforts, made this brochure possible.

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 worldwide, rats destroy 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, 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 gas pipes or stripping insulation from electrical wires. Furthermore, the diseases carried by rodents in this country are numerous and include, dysentery, hantavirus pulmonary syndrome, leptospirosis, lymphocytic choriomeningitis, murine typhus, rabies, rickettsial pox, salmonellosis, trichinosis and tularemia. And each year, the several human deaths in the Western states resulting from rodent-borne sylvatic plague serve to remind us of the potential for disaster if we relax rodent control measures [42].

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 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 [42].

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. The addition of bittering agents and emetics to some acute baits offers added protection since rats and mice cannot vomit. However, the addition of emetics (to induce nausea and vomiting) or substances like Bitrex®, denatonium benzoate, which deter non-target species also reduce palatability of the bait to rodents.

Anticoagulant Rodenticides –
A Success Story

In the 1940's, with the development of warfarin, a new class of rodenticides became available which substantially improved chemical control of rodents while being 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 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 poisoning 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 K_1 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.

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 exposure to 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 [14, 15]. In 1983, the number of calls for all poisonings had increased, as did the percentage of anticoagulant-related calls, which were more than 10% [13]. 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 [51]. This represented about 8% of all their pesticide calls; 41% of all anticoagulant calls involved dogs, a fact also found in other countries [39].

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 slower 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 [8]. Similar results were noted in a 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 [20]. 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 [28, 43].

The anticoagulants first marketed in the 1950's could be described as multiple-dose or multiple-feeding anticoagulants. Warfarin, pindone and isovaleryl indandione 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 1950's and 1960's utilized more potent multi-feed anticoagulants: diphacinone (trade names include Ditrac®, Kaput®-D, Ramik®, TomCat®) and chlorophacinone (trade names include Borderline™, Rozol®).

Since the mid 1970's, we have seen the introduction of second-generation, single-feed anticoagulants, which are based on three toxicants which are many times more acutely toxic to rodents than warfarin [9, 22, 34]. These are, brodifacoum (trade names include Final®, Havoc®, Jaguar®, Weatherblok®XT and Talon®) bromadiolone (trade names include BootHill®, Hawk®, Just One Bite®, Maki®, Resolv®, Revolver™) and difethialone (trade names include BlueMax™, FastDraw®, FirstStrike®, Generation®, and Hombre™). 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).

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, 20, 31]. 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 [47]. These estimates may be biased because only a few rodenticide product labels include the HOTLINE number. Tables 1 and 2 compare the acute oral LD_{50} (where known) of first- and second-generation anticoagulants for dogs and cats.

In practical terms, these differences in acute oral LD_{50} 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 LD_{50} 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. [35] 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. Compounds other than warfarin have a longer residue half-life in tissues [49]. 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 [44]. 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 unfortunate that both amateur and professional users of rodenticides often use (and misuse) all anticoagulants as though they were as safe as first generation rodenticides such 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 [11, 17, 37, 38]. 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 case histories beginning on page 5 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 [18, 24]. Dog poisoning case histories have been chosen because these represent a substantial majority of the companion animal poisoning incidents which are reported [14, 20, 33, 39, 41, 43, 51]. 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.

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 K_1 and blood transfusion(s), if the latter are needed to control bleeding. Once laboratory data is available, vitamin K_1 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.

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.

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 and/or packaging, if available.

3. Collect blood samples for diagnostic tests (as described in Case Study I).

4. Initiate treatment (as described in Case Study I).

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 [29]. 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 [20]. Prompt treatment with vitamin K_1, 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.

Table 1

Acute Oral Toxicities (LD$_{50}$) of Anticoagulant Rodenticides to Dogs

Generic Name (Active Trade Name[a])	LD$_{50}$ of Active Ingredient (mg/kg)[b]	Usual % Active Ingredient in Bait	Quantity of Bait to Give LD$_{50}$ in 10 kg (22 lb) Dog	Source of Data for LD$_{50}$ Info (see Endnotes)
brodifacoum (d-Con®, Final®, Havoc®, Jaguar®, Ratak®, Talon®-G, Weatherblok® XT)	0.25-1.0 0.25-2.5 1.09-3.6	0.005[c]	50 g (1.8 oz) to 720 g (25.4 oz)	4, 5, 20 15 13
bromadiolone (BootHill®, Brigand™, Contrac®, Hawk®, Just One Bite®, Kaput®Doom, Maki®, Ratimor®, Ratoxin®, Resolv®, Revolver™)	11-15[d] 15-20 15-20 8.1	0.005	2,200 g (77.6 oz) to 4,000 g (141.1 oz)	14 2, 29 24 30
chlorophacinone (A-C Formula 90™, Borderline™, Rozol®)	50-100 50-100 50-100	0.005	10,000 g (352.7 oz) to 20,000 g (705.5 oz)	29 22 29
difenacoum (Di-Kill®, Multi-Kill®, Sorexa™)	50	0.005	10,000 g (352.7 oz)	19
difethialone (BlueMax™, d-Con®, FastDraw®, FirstStrike®, Generation®, Hombre™)	4 11.8	0.0025	1,600 g (56.4 oz) to 4,720 g (166.5 oz)	17 31
diphacinone (Ditrac®, Kaput®-D, Ramik®, TomCat®)	0.88 3.0-7.5 5-15	0.005	176 g (6.2 oz) to 3,000 g (105.8 oz)	21 18, 27, 29 6, 9, 23
warfarin (Kaput®, Rodex™)	20-50[e]	0.025	800 g (28.2 oz) to 2,000 g (70.5 oz)	7, 8, 20, 28

Table 1 Footnotes

a. See the inside of the front cover for additional information regarding trademark ownership and affiliation.

b. Underscored LD$_{50}$ range used in calculating 'Quantity of Bait to Give LD$_{50}$ in 10 kg Dog.'

c. This active ingredient is also available in .0025 (100 g to 1,440 g to reach LD$_{50}$ in 10 kg dog.)

d. This is derived from a study which was not designed to obtain an LD$_{50}$.

e. This LD$_{50}$ range was originally established by the U.S. Fish and Wildlife Service, 1949.

Table 2

Acute Oral Toxicities (LD_{50}) of Anticoagulant Rodenticides to Cats

Generic Name (Active Trade Name[a])	LD_{50} of Active Ingredient (mg/kg)[b]	Usual % Active Ingredient in Bait	Quantity of Bait to Give LD_{50} in 2 kg (4.4 lb) Cat	Source of Data for LD_{50} Info (see Endnotes)
brodifacoum (d-Con®, Final®, Havoc®, Jaguar®, Ratak®, Talon®-G, Weatherblok® XT)	25	0.005[c]	1,000 g (35.3 oz)	3, 5, 20
bromadiolone (BootHill®, Brigand™, Contrac®, Hawk®, Just One Bite®, Kaput® Doom, Maki®, Ratimor®, Ratoxin®, Resolv®, Revolver™)	25[d]	0.005	1,000 g (35.3 oz)	1
chlorophacinone (A-C Formula 90™, Borderline™, Rozol®)	unknown	0.005	--	--
difenacoum (Di-Kill®, Multi-Kill®, Sorexa™)	100	0.005	4,000 g (141.0 oz)	19
difethialone (BlueMax™, d-Con®, FastDraw®, FirstStrike®, Generation®, Hombre™)	>16	0.0025	1,280 g (45.2 oz)	25
diphacinone (Ditrac®, Kaput®-D, Ramik®, TomCat®)	5-15 15	0.005	200 g (7.1 oz) to 600 g (21.2 oz)	6, 9, 23 3
warfarin (Kaput®, Rodex™)	5-50[e] 6-40 200-300 2.5 - 20	0.025	20 g (0.71 oz) to 2,400 g (84.7 oz)	7, 10 20 9 16

Table 2 Footnotes

a. See the inside of the front cover for additional information regarding trademark ownership and affiliation.

b. Underscored LD_{50} range used in calculating 'Quantity of Bait to Give LD_{50} in 2 kg Cat.'

c. This active ingredient is also available in .0025 (2,000 g to reach LD_{50} in 2 kg cat.)

d. This figure is actually the maximum tolerated oral dosage (MTD).

e. Cats are generally regarded as being as susceptible as dogs to warfarin.
    The range of LD_{50} may be partly explained by increased susceptibility to poisoning during estrus (Spencer, 1950).

Recommendations for Treatment

The principles of treatment and management of anticoagulant rodenticide poisoning are summarized in Table 4 on page 10. Basically, once blood samples have been collected for the requisite diagnostic tests, the affected animal should receive a parenteral injection of vitamin K_1. This form of the vitamin is preferred because vitamin K_3 has little or no effect for the acute stages of poisoning [45]. Also, vitamin K_1 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 K_1. Treatment with vitamin K_1 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 K_1 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 K_1 given should generally not exceed 1 mg/lb/day, or at least should be given cautiously if higher doses are deemed necessary [17]. Doses exceeding 2 mg/lb/day may be dangerous and have been shown recently to induce Heinz body hemolytic anemia [19]. 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 K_1 for successful control of bleeding [17]. This regimen is about half the dosage recommended by Mount and Feldman [45, 46]. 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. As vitamin K_1 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.

Table 3

Checklist of Treatment Actions
Based on Poisoning Category / Case Study of Exposure

Category / Case Study	Checklist of Actions Taken by Veterinarians
I. Clinical signs of bleeding; no history of exposure.	• Collection of blood samples for routine blood counts and coagulation profile.* • Treatment with vitamin K_1 plus blood transfusion(s), if needed.
II. Known exposure to anticoagulant rodenticide; no obvious clinical signs of bleeding at time of admission.	• Induce vomiting. • Obtain sample of product and/or packaging 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 K_1 as a prophylactic measure if lab data are abnormal.

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

Table 4

Treatment of Rodenticide Poisoning

Therapy	Dosage	Comments
Vitamin K$_1$	Parenteral initial dose*, not to exceed 1 mg/lb/day, and followed by the same parenteral or oral dosage for another six days. Reduce to ½ mg/lb/day for the second week and then reduce by ½ for another two weeks. After 1 month of treatment dosage is continued 2-3 times a week for another 2 weeks.	Six weeks of therapy needed to correct long-term effects of the more potent products. 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.
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 on previous pages).

Endnotes

1. ANONYMOUS. (Undated). Maki bromadiolone. Rodenticide technical bulletin. Chempar Chemical Co. Inc., New York, NY. 9pp.

2. ANONYMOUS. (Undated). Rozol and Maki, Chempar Rodent Control Products. Chempar Chemical Co. Inc., New York, NY. 11pp.

3. ANONYMOUS. (Undated). Klerat, ICI Public Health Products. ICI Surrey, England. 39pp.

4. ANONYMOUS. (Undated). Talon technical information: for experimental use only. ICI Americas Inc., Goldsboro, NC. 4pp.

5. ANONYMOUS. 1978. Talon rodenticide technical information: for experimental use only. ICI Americas Inc., Wilmington, DE. 4pp.

6. ANONYMOUS. 1977. Rodent eradication and poisoning programs. U.S. Dept. H.E.W., P.H.S., CDC, Atlanta, GA. 83pp.

7. ANONYMOUS. 1949. U.S.D.I. Fish and Wildlife Service, Denver, CO. Special report, 58.

8. ASHWORTH, B. 1973. The frequency of animal poisoning by warfarin. The Veterinary Record, 93:50.

9. BARLOW, A.M., A.L. GAY and B.K. PARK. 1982. Difenacoum (Neosorexa) poisoning. British Medical Journal, 285:541.

10. BENTLEY, E.W. and Y. LARTHE. 1959. The comparative rodenticidal efficiency of five anticoagulants. Journal of Hygiene, 57(2):135-149.

11. BRAITHWAITE, G.B. 1982. Vitamin K and brodifacoum. Journal of American Veterinary Medical Association, 181:531-532.

12. BROOKS, J.E. 1970. Properties, uses and hazards of common rodenticides. NYS Dept. Health, Albany, NY, 10pp.

13. BUCK, W.B. 1983a. Personal communication (Dec. 16, 1983). Director, Animal Poisoning Control Center, Univ. IL, Urbana, IL.

14. BUCK, W.B. 1983b. A report of poisonings in the dog and cat in 1982. Presented at 75th Annual Conference for Veterinarians, NYS College of Veterinary Medicine, Ithaca, NY, 18-20 Jan., 1983.

15. BUCK, W.B. 1983c. Causes of poisoning in dogs and cats. Pest Management, 2(7):11-13.

16. BUCK, W.B., G. D. OSWEILER and G.A. VAN GELDER. 1976. Clinical and diagnostic veterinary toxicology, 2nd Edition. Kendall/Hunt Publishing Co., Dubuque, IA. pp. 253-256.

17. DODDS, W.J. and S.C. FRANTZ. 1984. Dog and cat poisonings. Pest Control Technology, 12(3):14.

18. FELDMAN, B.F. 1981. Coagulopathies in small animals. Journal of American Veterinary Medical Association, 179:559-563.

19. FERNANDEZ, F.R., A.P. DAVIES, D.J. TEACHOUT, A. KRAKE, M.M. CHRISTOPHER and V. PERMAN. 1984. Vitamin K-induced Heinz body formation in dogs. Journal of American Animal Hospital Association, 20:711-720.

20. FRANTZ, S.C., W.J. DODDS and S. KIM. 1984. A study of accidents, illnesses and deaths resulting from the use of commensal rodenticides. EPA Public Hearings on Rodenticide Bait Stations, Sacramento, CA, March 5, 1984.

21. GODFREY, M.E.R., T.C. REID and H.J.F. McALLUM. 1981. The oral toxicity of brodifacoum to rabbits. N.Z. Journal of Experimental Agriculture, 9:23-25.

22. GODFREY, M.E.R., T.C. REID and H.J.F. McALLUM. 1981. The acute oral toxicity of the anticoagulant brodifacoum to dogs. N.Z. Journal of Experimental Agriculture, 9:147-149.

23. GRAND, M. 1976. Experimental data on a new anticoagulant raticide: bromadiolone. Phytiatrie-Phytopharmacie, 25:69-88.

24. GREEN, R.A., P. ROUDEBUSH, and C.L. BARTON. 1979. Laboratory evaluation of coagulopathies due to vitamin K antagonism in the dog: three case reports. Journal of the American Animal Hospital Association 15:691-697.

25. HADLER, M.R. 1979. Brodifacoum a potent new rodenticide. Proceedings Fifth British Pest Control Conference, Stratford-upon-Avon, England. September 26-29, 1979. pp.1-8.

26. HAGAN, E.C. and J.L. RADOMSKI. 1953. The toxicity of 3-(acetonylbenzyl)-4-hydroxycoumarin (warfarin) to laboratory animals. Journal of American Pharmaceutical Association. 52(6):379-382.

27. HARLING, R., P. BUFORD, and S. FREYER. 1986. LM2219 (difethialone) oral toxicity study in beagle dogs (13 weeks). Huntindon Research Center, UK. Unpublished study.

28. HAYES, W. 1982. Pesticides studied in man. Williams and Wilkins, Baltimore, 672pp.

29. HAZELTON LABORATORIES Inc. 1957. Report on diphacinone (2-diphenylacetyl-1,3-indandione). Hazelton Laboratories Inc., Falls Church, VA, April 19, 1957.

30. I.N.D.I.A. Industrie Chimiche Technical Data Sheet for NOCURAT WAX BLOCKS undated.

31. KAUKEINEN, D.E. 1979. Experimental rodenticide (Talon) passes lab tests; moving to field trials in pest control industry. Pest Control 46(1):19-21.

32. KOSMIN, M. and J.N. BARLOW. 1976. Rodent control using a novel formulation of diphacinone, Ramik®. Proceedings First Afro-Asian Vertebrate Pest Congress. Nov. 8-11, 1976. Cairo, Egypt. 7pp.

33. LABE, J. and G. LORGUE. 1977. Intoxication des carnivores domestiques par les raticides anticoagulants. pp128-140. Notes de Toxicologie Veterinaire, No. 3. Centre d'Informations Toxicologiques Veterinaire, Ecole Nationale Veterinaire, Marcy L'Etoile, France.

34. LECK, J.B. and B.K. PARK. 1981. A comparative study of the effects of warfarin and brodifacoum on the relationship between vitamin K_1 metabolism and clotting factor activity in warfarin-susceptible and warfarin-resistant rats. Biochemical Pharmacology, 30:123-128.

35. LIPTON, R.A. and E.M. KLASS. 1984. Human ingestion of a "Superwarfarin" rodenticide resulting in a prolonged anticoagulant effect. Journal of American Medical Association, 252:3004-3005.

36. LISELLA, F.S., K.R. LONG and H.G. SCOTT. 1971. Toxicology of rodenticides and their relationship to human health. Part II, Journal of Environmental Health, 33(4):361-365.

37. LORGUE, G. 1980. Bromadiolone toxicity in the dog: an antidotal therapy in the intoxicated dog. Laboratory of Toxicology, Ecole National Veterinaire de Lyon and Lyonnaise Industrielle Pharmaceutique, Lyon, France.

38. LORGUE, G. 1984. Domestic animal poisonings by rodenticides. Pratique Medicale et Chirurgicale de l'Animale de Compagnie. Ecole National Veterinaire de Lyon, Charbonnieres-les-Bains, France. 19(2):133-135.

39. LORGUE, G. and A. NAHAS. 1984. Les intoxications des carnivores domestiques: generalites. Pratique Medicale et Chirurgicale de l'Animal de Compagnie. Ecole National Veterinaire de Lyon, Charbonnieres-les-Bains, France. 19(2):125-127.

40. LORGUE, G. 1986. Acute oral toxicity study of LM2219 (difethialone) in cats. Ectoxicology Laboratory (INRA-ENVL), National Veterinary School, Lyon, France. Unpublished study.

41. MADDY, K.T. and J. WINTER. 1980. Poisoning of animals in the Los Angeles area with pesticides during 1977. Veterinary and Human Toxicology, 22:409-412.

42. MALLIS, A. 1982. The handbook of pest control. Franzak and Foster, Cleveland OH. 1101pp.

43. MARSH, R.E. 1985 (in press). The susceptibility of dogs to anticoagulant rodenticides.

44. MENDENHALL, V.M. and L.F. PANK. 1980. Secondary poisoning of owls by anticoagulant rodenticides. Wildlife Society Bulletin, 8:311-315.

45. MOUNT, M.E. and B.F. FELDMAN. 1982. Vitamin K and its therapeutic importance. Journal of American Veterinary Medical Association, 180:1354-1356.

46. MOUNT, M.E. and B.F. FELDMAN. 1983. Mechanism of diphacinone rodenticide toxicosis in the dog and its therapeutic implications. American Journal of Veterinary Research, 44:2009-2017.

47. NATIONAL ANIMAL POISON CONTROL CENTER. 1985. Annual progress report, 1984. College of Veterinary Medicine, Urbana, Illinois.

48. PAPWORTH, D.S. 1958. A review of the dangers of warfarin poisoning to animals other than rodents. Royal Society of Health Journal, 78:52-60.

49. POCHE, R.M. Personal communication (Nov. 30, 1984). Director of Technical Services, Lipha Chemicals Inc.

50. RAMPAUD, M. 1981. Toxicologie des raticides. Conference Prononcee en Novembre 1981 au Collogue de Moulins (Allier) 53-59.

51. SMITH, C.R. 1984. Survey of rodenticide bait-related exposures reported by the Los Angeles Medical Association Regional Poison Information Center - July 1, 1982, to June 30, 1983. EPA Public Hearings on Rodenticide Bait Stations, Sacramento, CA, March 5, 1984.

52. POCHE, R.M. 1988. Rodent tissue residue and secondary hazard studies with bromadiolone. Bull. OEPP/EPPO Bull. 18: 323-330.

53. U.S. ENVIRONMENTAL PROTECTION AGENCY. 2004. Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: a Comparative Approach. 23pp.

54. U.S. ENVIRONMENTAL PROTECTION AGENCY. 2008. Risk Mitigation Decision for Ten Rodenticides. Dated May 28, 2008. 60pp.

55. VYAS, N.B., AND RATTNER, B.A. 2012. Critique on the use of the standardized avian acute oral toxicity test for first generation anticoagulant rodenticides. Human and Ecological Risk Assessment 18: 1069–1077.

Additional Sources

ANONYMOUS. (Undated). Technical report on chlorophacinone (approved name). Lipha Laboratories, Lyon, France. 72pp.

DODDS, W.J. 1984. Von Willebrand's disease in dogs. Modern Veterinary Practice, 95:681-686.

EBELING, W. 1978. Urban entomology. University of California Press, Berkeley. 695pp.

HOUPT, K., J.C. ZGODA and C.C. STAHLBAUM. 1984. Use of taste repellents and emetics to prevent accidental poisoning of dogs. American Journal of Veterinary Research, 45:1501-1503.

KECK, P. 1984. Diagnostic analytique et traitement des intoxications des carnivores. Department of Pharmacology and Toxicology, National Veterinary School, Lyon, France. 19(2):129-131.

PLESTINA, R. 1984. Prevention, diagnosis and treatment of insecticide poisoning. WHO/VBC/84.889.

SPENCER, H. J. 1950. U.S.D.I. Report of Activities, Wildlife Research Laboratory, Denver, CO. 1st Quarter, 12.