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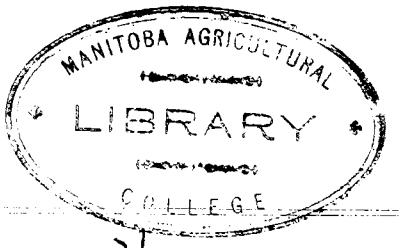
THE ACTION OF STRYCHNINE ON THE WYOMING GROUND SQUIRREL

[*Citellus elegans elegans*]

By W. L. BURNETT



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THE ACTION OF STRYCHNINE ON THE WYOMING GROUND SQUIRREL

[*Citellus elegans elegans*]

POISONING CAGED SQUIRRELS

By W. L. BURNETT

This study was not undertaken as a technical one to determine the lethal dose of strychnine for the Wyoming ground squirrel, but as an economic study concerned with the use of strychnine-poisoned grain, for squirrel control in the field, where it is necessary to use control measures for the protection of forage and cereal crops.

We are not in sympathy with total extermination methods, except where the squirrels enter into direct competition with the production of food for domestic animals, or for human consumption.

There are certain sections in the state, National Parks and other localities, where the squirrels have been so reduced in numbers they are no longer a serious menace to crops, and where they may remain unmolested since they, like other mammalian life, have a particular niche in the scheme of nature.

We were led to believe, by some work we carried on a few years ago with the Zuni prairie dog, that a tolerance for strychnine could be built up in these rodents, by using a weak strychnine mixture in preparing the poisoned grain, or by distributing the grain in small quantities in field operations. However, we now believe that to build a tolerance rapidly, the grain should be fed in rather large but less than lethal doses in the beginning.

There seems to be a vast difference in individual resistance to strychnine in the Wyoming ground squirrel. Concerning this point, however, I quote as follows:

"The action of strychnine is almost identical thruout the vertebrate kingdom.

"Man is more susceptible than other mammals, and young animals are more refractory than adults, perhaps owing to the less developed condition of the central nervous system." (Cushing Pharmacology and Therapeutics or the Action of Drugs, 1918.)

Schwartze states that

"Very young animals are comparatively resistant to asphyxia and recover their ability to breathe more easily than mature members of the same species. On this account they can endure more successfully a larger number of convulsions.

"The effective dose changes with the age of mammals of certain species. At birth the mouse, rabbit, cat, and dog possess a natal immunity against the fatal action of strychnine, in this respect resembling the lower forms of animal life. Upon further development, however, this resistance is lost. After the decline of this resistance in the mouse, a post-natal immunity, which reaches its limits about the same time of sexual maturity, develops. The guinea pig also develops such a post-natal immunity, but, owing to its relative mature state at birth, the decline of the natal immunity seen in other animals presumably is eclipsed by the period in utero. The cat, dog, and rabbit apparently develop no post-natal immunity, the adult lethal dose remaining at about the level to which the natal resistance declines." (U. S. D. A. Bulletin No. 1023 "The Relative Toxicity of Strychnine to the Rat.")

The poisoned grain we used in our experiments was prepared as follows:

Colorado Formula No. 46

Whole oats	16 quarts
Strychnine (alkaloid powdered)	1 ounce
Baking soda	1 ounce
Saccharin	⅛ ounce
Fine salt	½ pint
Petrolatum oil	¼ pint
Water	1 pint

Flour to thicken to a creamy paste.

The flour paste holds the insoluble strychnine in suspension while the grain is being coated. The coating was put on in a revolving barrel churn, which gives as even a coating of the poison on each kernel of the oats as is mechanically possible. However, there is bound to be a slight variation in the kernels. The poisoned oats with which the squirrels were fed was stirred each morning before feeding to eliminate, insofar as possible, the remote possibility of the more heavily coated oats collecting and causing the individual difference that appeared in the effect upon the different squirrels. The grain was fed each time in a small tin lid and the cage cleaned after each feeding, so that a check could be made on the oat hulls to see if any of the kernels were left.

One hundred seven squirrels were used in these experiments—95 were adults and 12 were young. There were 51 males and 56 females.

The first experiment, that of feeding the Wyoming ground squirrels poisoned grain, was with a caged female in the spring of 1926, designated as squirrel No. 1. This squirrel was trapped at Virginia Dale, Larimer County, in the spring of 1925, and it spent the winter of 1925-26 in partial hibernation.

We started the experiment by feeding poisoned oats prepared by using 1 ounce of strychnine to 48 quarts of oats. After

a few days, this was changed to 1 ounce of strychnine to 16 quarts of oats (our standard formula).

The poisoned grain was fed at intervals of 1 to 5 days. When we started feeding the poisoned grain to this squirrel, we were under the impression that, in order to build up a tolerance to the poison, it should be fed at first in small and slowly increased doses. We started February 19, by feeding this squirrel 3 kernels of oats at a time which were prepared by mixing 1 ounce of strychnine to 48 quarts of oats. We then increased from 2 to 5 kernels at a feeding at intervals of 2 to 5 days. On March 13 she ate 25 kernels for breakfast, making a total of 136 kernels in 22 days.

On March 16 this same squirrel was started with 3 kernels of oats prepared by mixing 1 ounce of strychnine to 16 quarts, and then was fed as before until April 17, when she ate 25 kernels and had eaten a total of 159. She was next offered the poisoned grain May 4, which she refused.

It was noticed on May 4, at the time she refused the poisoned grain, that there was a lessened activity and a partial paralysis of the hind quarters. Very little food was taken at this time and up to the latter part of May. About June 1, the paralytic condition showed decided improvement and feeding again became normal. However, in the early part of July we thought she was dying, as respiration was very slow. She revived and lived until October 28, when she died during the night.

She was, at time of death, very emanciated; weight 100 grams, teeth O. K., lungs light pink, some food in stomach, large intestine full of gas.

The poisoning experiments were not taken up again until the spring of 1928.

In 1928-29 and 30, the experiments were all carried on with our standard formula No. 46, 1 ounce of strychnine to 16 quarts of whole oats. In 1931, groats or hulled oats were used in place of whole oats.

Experimental squirrels were all taken where, to the best of our knowledge, they had never had access to poisoned grain in field operations, except the squirrels taken in 1930 and 31 at Redfeather Lakes, Larimer County. In this section there had been some poisoning of the squirrels for several years by individual land owners.

The following tables give records of individual squirrels fed the poisoned oats during the four seasons.

Condensed Data on Poisoned Oats Fed Wyoming Ground Squirrels, Season, 1928.
Whole Oats

Squirrel No.	Sex	Total number kernels fed to kill	Largest number kernels fed at one time	Number kernels fed at start	Age	How fed	Number times fed
2	♂	123	21	5	Adult	Every 2nd day	9
3	♀	187	30	4	"	Every day	11
4	♂	308	25	3	"	" 2nd day	22
5	♀	208	20	1	"	" " "	19
6	♀	12	5	3	"	" " "	3
7	♀	54	10	2	"	" " "	9
8	♂	344	26	4	"	" " "	23
9	♀	205	20	15	"	" " "	11
10	♂	18	8	4	"	" " "	3
11	♀	10	10	10	"	Every day	1
12	♀	49	10	5	"	" "	6
13	♀	65	12	3	"	" 2nd day	8

Condensed Data on Poisoned Oats Fed Wyoming Ground Squirrels, Season, 1929.
Whole Oats

Squirrel No.	Sex	Total number kernels fed to kill	time Largest number kernels fed at one	Number kernels fed to start	Age	How fed	Number times fed
14	♂	230	10	10	Adult	Every day	23
15	♂	50	10	10	"	Every 2d. day	5
16	♂	60	10	10	"	" 3rd "	6
17	♂	80	10	10	"	" 4th "	8
18	♀	90	10	10	"	" 5th "	9
19	♀	22	12	10	"	" 4th "	2
20	♂	275	10	10	"	Every day	28
21	♀	124	10	10	"	" "	13
22	♀	475	10	10	"	" "	48
23	♀	68	12	5	Young	" "	8
24	♀	50	10	10	Adult	" "	5
25	♀	26	8	5	Young *	" "	4
26	♀	11	6	5	" *	" "	2
27	♀	5	5	5	" *	" "	1
28	♀	11	6	5	" *	" "	2
29	♀	77	14	8	" *	" "	7
30	♀	408	40	8	Adult	" "	17
31	♀	8	8	8	Young *	" "	1
32	♀	17	9	8	" *	" "	2
33	♂	8	8	8	" *	" "	1
34	♂	17	9	8	" *	" "	2
35	♂	60	10	10	Adult	" "	6
36	♀	80	10	10	"	" "	8
37	♂	90	10	10	"	" "	9

*Two-thirds grown.

Condensed Data on Poisoned Oats Fed Wyoming Ground Squirrels, Season, 1930.

Whole Oats

Squirrel No.	Sex	Weight at death Grams	Total number kernels poisoned oats eaten to kill	Largest number eaten at one time	Number kernels fed to start	Age	How fed	Times fed
38	♀	241	30	15	15	Adult	Every day	2
39	♂	204	195	15	15	Adult	" "	13
40	♀	151	15	15	15	"	" "	1
41	♀	179	15	15	15	"	" "	1
42	♀	232	465	150	15	"	Irregular	7
43	♂	344	1065	225	15	"	"	10
44	♂	399	40	20	20	"	Every day	2
45	♂	348	700	100	20	"	" "	31
46	♂	329	220	20	20	"	" "	11
47	♂	355	60	20	20	"	" "	3
48	♀	270	250	100	25	"	" "	4
49	♀	270	700	175	25	"	" "	7
50	♀	236	250	100	25	"	" "	4
51	♂	346	1640	170	20	"	" "	21
52	♂	252	170	35	20	"	" "	7
53	♀	376	3475	250	20	"	" "	30
54	♂	385	1310	150	20	"	" "	19
55	♀	227	175	100	25	"	Irregular	3
56	♀	99	25	25	25	Young	Every day	1
57	♀	185	75	50	25	"	Every 3rd day	2
58	♀	319	90	90	100	Adult	Every day	1
59	♀	246	95	95	100	"	" "	1
60	♂	252	89	89	100	"	" "	1
61	♀	289*	X**	192	100	"	" "	10
62	♂	287	96	96	100	"	" "	1
63	♂	259	41	41	100	"	" "	1
64	♀	233	68	68	100	"	" "	1
65	♂	211	75	75	100	"	" "	1

* Live weight.

** Unable to kill, ate a total of 1591 kernels in the 10 times fed.

Twenty-five of the 28 squirrels fed the poisoned oats, season of 1930, were divided into three groups, A, B and C. Group A of 15 squirrels was subdivided into four lots. Lot 1, squirrels 38, 39, 40, 41; Lot 2, squirrels 44, 45, 46, 47; Lot 3, squirrels 48, 49, 50; Lot 4, squirrels 51, 52, 53, 54.

The squirrels in Lot 1 were started with 15 kernels of the poisoned oats and fed thereafter 15 kernels each day until killed. The ones in Lot 2 were started with 20 kernels each and fed thereafter 20 kernels a day until killed. The ones in Lot 3 were started with 25 kernels each and this number was increased 25 kernels each day until killed. The ones in Lot 4 were started with 20 kernels each and fed the same number for 4 days, then increased by 5 kernels each for 4 days, then increased by 10 kernels each day until killed.

Condensed Data on Poisoned Oats Fed Wyoming Ground Squirrels, Season, 1931.
Hulled Oats

Squirrel No.	Sex	Weight at death Grams	Total number kernels poisoned oats eaten to kill	Largest number eaten at one time	Number kernels fed to start	Age	How fed	Times fed
66	♂	340	275	50	5	Adult	Every day	10
67	♂	290	275	50	5	"	" "	10
68	♂	309	765	85	5	"	" "	17
69	♂	259	50	20	5	"	" "	4
70	♂	289	225	45	5	"	" "	9
71	♂	289	140	35	5	"	" "	7
72	♂	288	275	50	5	"	" "	10
73	♂	270	180	40	5	"	" "	8
74	♂	272	330	55	5	"	" "	11
75	♀	252	105	45	25	"	" "	3
76	♀	225	25	25	25	"	" "	1
77	♀	232	278	65	25	"	" "	6
78	♀	227	225	65	25	"	" "	5
79	♀	264	160	55	25	"	" "	4
80	♂	259	60	35	25	"	" "	2
81	♀	204	425	85	25	"	" "	8
82	♀	227	1105	145	25	"	" "	13
83	♂	270	700	115	25	"	" "	10
84	♀	270	38	38	50	"	" "	1
85	♀	227	200	50	50	"	" "	4
86	♂	289	200	50	50	"	" "	4
87	♀	232	50	50	50	"	" "	1
88	♂	275	50	50	50	"	" "	1
89	♂	252	30	30	50	"	" "	1
90	♂	204	44	44	50	"	" "	1
91	♀	227	31	31	50	"	" "	1
92	♀	289	50	50	50	"	" "	1
93	♀	233	146	96	50	"	" 7 "	2
94	♂	344	250	100	50	"	" 7 "	2
95	♂	399	283	133	50	"	" 7 "	3
96	♂	289	50	50	50	"	" "	1
97	♂	241	250	100	50	"	" 7 "	2
98	♀	289	300	150	50	"	" " "	3
99	♂	290	300	150	50	"	" " "	3
100	♀	227	250	100	50	"	" " "	2
101	♀	234	144	94	50	"	" " "	2
102	♀	227	50	50	50	"	" " "	1
103	♀	204	50	50	50	"	" " "	1
104	♀	290	98	98	100	"	" " "	1
105	♂	319	300	150	50	"	" " "	3
106	♀	200	75	75	100	"	" " "	1
107	♀	204	132	132	100	"	" " "	2

However, we stopped feeding squirrel No. 53 when she had reached 250 kernels of the poisoned oats at a feeding. She was then given a rest for 7 days, which should allow for the elimination of the strychnine from her system. She was then fed 150 kernels, of which she ate 105, which killed her. Group B of two

squirrels, Nos. 42 and 43, were started with 15 kernels each of the poisoned oats June 19. We fed them 20 kernels each June 25, 25 kernels each July 1, and 30 kernels each July 6. On July 11 we fed them 100 kernels each, on July 12, 125 kernels each, and on July 13, 150 kernels each. This number killed squirrel No. 42, but squirrel No. 43 lived 3 days longer and ate an increase of 25 kernels each day, when he was killed after eating 225 kernels at one time, or a total of 1065 kernels.

The eight squirrels in group C were fed 100 kernels each the first feeding of the poisoned oats, and 7 were killed. Squirrel No. 58 was killed with 90 kernels, No. 59 with 95 kernels, No. 60 with 89 kernels, No. 62 with 96 kernels, No. 63 with 41 kernels, No. 64 with 68 kernels, No. 65 with 75 kernels.

We were unable to kill squirrel No. 61 with the poisoned oats. We fed her 100 kernels each day for 3 days and she ate them all. Then for 5 days we fed her 200 kernels each day. She ate, of these, from 172 to 192 kernels at a feeding. We then kept all food from her for 3 days, then again fed her 200 kernels on an empty stomach. She ate 173 of these. We then let her rest for 7 days, the same as squirrel No. 53, and again fed her 200 kernels, of which she ate 185, or a total of 1591 kernels for the 10 times fed. Several weeks later she died a natural (?) death while in a state of semi-hibernation.

The number of kernels of the poisoned oats eaten by squirrels 51, 53 and 54, might suggest that the grain was not properly poisoned. All the squirrels fed this season were fed from the same bag of poisoned oats, picked at random from a pile of the grain prepared for sale for the control of rodents. Oats from the same bag killed squirrels 40 and 41 at the first feeding of 15 kernels each, and squirrel No. 38 at the second feeding of 15 kernels. Squirrel No. 44 was the largest squirrel by body weight in group A, and was killed with 40 kernels at two feedings of 20 kernels each.

Squirrels 51, 53 and 54, a half hour after they had eaten about 90 kernels of the poisoned oats, were unable to whistle. They would shake their sides the same as when they gave their whistle, but a hissing was the only sound they could make. The following morning their whistle was normal; however, squirrel No. 53 finally lost her voice entirely when she had eaten about 200 kernels at a feeding. She regained her voice after we stopped feeding her the poisoned oats July 21, and until we started feeding her July 28.

Group of 12 Young Wyoming Ground Squirrels Fed the Poisoned Grain.

Squirrel No.	Sex	Total kernels poisoned oats fed to kill	Largest number kernels fed at one time	Number kernels fed to start	Age	How fed	Times fed
23	♀	68	12	5	⅔ grown	Every day	8
25	♀	26	8	5	"	"	4
26	♂	11	6	5	"	"	2
27	♂	5	5	5	"	"	1
28	♂	11	6	5	"	"	2
29	♀	77	14	8	"	"	7
31	♀	8	8	8	"	"	1
32	♀	17	9	8	"	"	2
33	♂	8	8	8	"	"	1
34	♂	17	9	8	"	"	2
56	♀	25	25	25	½ grown	"	1
57	♀	75	50	25	⅔ grown	Every 3rd day	2

These 12 young squirrels were past the weaning stage, but probably had not reached sexual maturity. They showed less resistance to the poison than adult squirrels. However, they showed about the same individual variation of tolerance to the poison as did the adults.

POISONING THE WYOMING GROUND SQUIRREL

Our experimental work shows that the Wyoming ground squirrel does not, at any time, refuse the strychnine-poisoned oats prepared by Colorado Formula No. 46.

The statement is often made that, in poisoning operations in the field, ground squirrels that survive the first eating of the poisoned grain "get wise" to the poison and then refuse to eat it. *We have no data that even suggest that the squirrels under field or cage conditions refuse to eat freely of the poisoned oats prepared according to Colorado Formula No.* 46, *either in single or repeated doses. Practically all our caged squirrels have shown a decided preference for the poisoned oats over the unpoisoned.*

Our caged squirrels were fed dandelion and poisoned oats at the same time in the morning, the dandelion every morning, the poisoned oats in some cases every morning, in others irregularly.

On mornings that the poisoned oats were fed, they always ate the oats first, altho dandelion was their favorite green food. After eating the oats, they would go back into their nests and remain quiet for an hour or two before eating the green food. So the poisoned oats were always taken on an empty stomach.

As soon as the poisoned oats were put in the cage and we were out of sight, the squirrels would come out of their nests and eat the oats at once. Several of the squirrels had repeated slight convulsions several days before they were killed, but the next mornings they were as eager as ever for their feed of the poisoned oats.

Our experiments with caged squirrels suggest that the difficulty which arises in poisoning the few remaining squirrels in field operations is not due to their refusing to eat the poisoned grain, but to a resistance to the poison that they already have, and an additional tolerance which may be built up, both of which vary greatly with the different individuals.

Poisoned whole oats are used in field operations for the control of this squirrel. The same was used with our caged squirrels in 1928-29 and 30.

A thin flour paste is used as a carrier for the strychnine, and the poison is all on the hulls of the oats. The squirrels get sufficient poison in the process of hulling the oats to kill them.

In 1928-29 and 30, when our caged squirrels were fed the whole oats, they hulled them so deftly that the only way one could determine that the kernel had been removed, was to press the hulls between the fingers. In hulling the oats much of the poison would be lost with the hulls and might vary with individual squirrels, as they might not all hull alike. This might account for the wide variation in the number of kernels required to kill in different squirrels.

To determine whether or not this variation could, in part, be explained in this manner, we fed the 1931 caged squirrels poisoned groats (hulled oats). The groats were fully eaten and, as there were no hulls to be discarded, there was no loss of poison. As would be expected, the variation in the number of kernels required to kill was not so great and the number of kernels required for a lethal dose was less. However, the variation did show that the squirrels do have widely varying individual resistance to the poison and that a greatly increased resistance may be built up by feeding it in daily increased doses.

The statement has been made that one or two kernels of the poisoned oats are sufficient to kill a squirrel (Reference No. 11), but this is not borne out in our experiments with Colorado Formula No. 46. Rarely have less than 10 kernels proved fatal and the average number at first feeding has been far more than this.

In poisoning operations it seems very essential, on account of the varying tolerance, that the amount of grain used in the field be large enough to insure a kill of the most resistant

squirrels at first eating. Less than a lethal dose will build a tolerance that is hard to overcome.

STRYCHNINE—ITS ACCUMULATION, TOLERANCE AND ELIMINATION

(References 1-2-3-4-5-6-7-8*)*

Winslow states (7) that a tolerance for strychnine can be acquired in man and with difficulty in dogs, but that the drug is not cumulative, in the sense of producing sudden and violent action following its continual use in increasing doses.

In our work of feeding strychnine-poisoned grain to Wyoming ground squirrels, we find that a tolerance may be built up for the drug by these rodents, and that there must be some accumulation of the strychnine in the squirrel's system, at least, for a few days.

This accumulation is seemingly built up rather rapidly, and is rather slowly eliminated, but if several days (about 7) are allowed to elapse after the feeding of the poison, elimination seems to be complete, as indicated by loss of tolerance.

It seems to be generally accepted that the elimination of strychnine from the system is accomplished by the kidneys, but there seems to be some difference of opinion concerning the rapidity with which elimination takes place.

From our observations on caged squirrels, there is a considerable individual difference in the amount of water excreted. Our caged squirrels were kept in individual compartments. The squirrels were all fed the same green food and in about equal amounts. Some of the compartments were always comparatively dry, while in others, the waste from the food was thoroly soaked and had to be removed each morning with a scraper.

This variation in individual excretion may be a factor that controls, to some extent, the toxicity of the strychnine, by more rapid elimination of the drug. We failed to check on these points until it was too late.

Our data suggest accumulative action. If tolerance was developed as suggested by the experiments, and there was no accumulative action, the feeding in constant non-lethal doses, should have been possible indefinitely without fatal results.

For example, squirrels No. 77 and 81 were each started with 25 kernels of the poisoned oats at a feeding, and were both fed the poison every day, with an increase of 10 kernels at each feeding, until killed. Squirrel No. 77 ate 65 kernels and survived to

May 22, but on May 23 she ate 53 of the 75 kernels fed and was killed.

Squirrel No. 81 ate 85 kernels on May 24, and survived, but 40 kernels of the 95 fed on May 25 killed her. Squirrel No. 53 was started with 20 kernels of the poisoned oats and the number was increased in 29 days to 250 kernels at a feeding, or a total of 3370 in the 29 days, which did not kill. We then stopped feeding her the poison for 7 days and then fed her 150 kernels of which she ate 105, which caused death.

Squirrel No. 61 was started with 100 kernels of the poisoned oats, which dose was increased in 9 days to 200 kernels at a feeding, or a total of 1406 kernels, from which she survived. We then stopped feeding her the poison for 7 days, the same as we did No. 53, then fed her 200 kernels, of which she ate 185; and lived.

Squirrel No. 53 suggests practical elimination of the poison in the 7 days and a breaking down of the tolerance. Squirrel No. 61 suggests slower elimination and a greater tolerance to the poison. The weight of squirrel No. 53 was 376 grams, and of No. 61, 289 grams.

Body weight of squirrels does not seem to be an important factor in the action of strychnine.

The variation in the lethal dosage of the poisoned grain is as great when the squirrels are fed a small number of kernels every day. For example, squirrels No. 14, 20, 21, 22, 24, 25, 36 and 37 were all fed, every day 10 kernels each until killed. The total numbers of kernels eaten to kill varied from 50 to 475.

Squirrels No. 44, 45, 46 and 47 were fed every day 20 kernels each until killed. The variation in number of kernels eaten was from 40 to 700.

SUMMARY

Our experimental work with caged Wyoming ground squirrels shows that many squirrels possess great inherent resistance to strychnine fed to them on poisoned grain, and that this resistance varies greatly in different individuals. The experiments also show that additional tolerance may be built up by daily feeding the poisoned grain in less than lethal doses.

The amount of the poisoned grain necessary to kill varies so much with individual squirrels that we are unable to decide what should be considered a lethal dose.

Our data indicate both a progressive tolerance to strychnine, when fed in less than lethal doses, and a gradual accumulation of the poison when fed in quantities exceeding daily elimination, which, if taken too rapidly, may overtake the increased

resistance and finally cause death. In one case at least, the resistance was gradually built up to a point where the squirrel was able to withstand the total of 250 kernels at a feeding. But when 105 kernels were eaten after a 7-day cessation of feeding and elimination of the poison, death resulted.

TANNIN AND STRYCHNINE

"It has been found by Mr. Garlough that where ground squirrels are eating green Alfilaria in quantity, poison grain, tho eaten, has little or no effect. This is explained by the fact that this plant contains Tannin, which is an antidote for strychnine, to neutralize the poison. In certain localities acorns are said to have a similar effect."—(Dixon, Circular No. 296, University of California Exp. Sta., p. 2.)

Insofar as rodents are concerned, we question correctness of the tannic-acid theory as given above.

We quote the following medical authorities on the subject of tannin and strychnine.

"Chemic Antidotes.—Potassium Permanganate is probably the most effective, if it is given sufficiently early, since it destroys the strychnine. One gram (¼ teaspoonful) should be dissolved in a quart of warm water carefully decantered, and administered in tumbler doses at short intervals.

"Iodine (15 drops of tincture in ½ glass of hot water) or tannin (teaspoonful in ½ glass of hot water) merely delay absorption, but this is distinctly useful. Tea or coffee should be avoided, since the caffein is synergistic. Charcoal, or better caramel or Fuller's earth, are useful for absorbing the strychnine, and delaying its absorption, (Sabbatani, 1914; Fautus, 1, 1915); but their efficiency is limited."—(A manual of Pharmacology and its Application to Therapeutics and Toxicoloty. Thorald Sollmann 1917, p. 197.)

"In cases of strychnine poisoning, the first treatment consists in the evacuation of the stomach by means of emetics, or better, by the stomach tube. It may be necessary to give chloroform, as the attempt to pass the tube is often followed by violent convulsions. Preparations of tannic acids, such as strong tea, may be given in order to form insoluble tannate, which, however, must be removed as quickly as possible, as it is broken up by acid gastric juice and the strychnine is rapidly absorbed.

"Tannic acid then does not exist in the tissues as such, but only in the form of traces of gallate or tannate of sodium, which are devoid of stringent properties. The effects of tannic acid are therefore limited to the point of application and there is no evidence of any weight that it exercises any action after absorption.

"In cases of poisoning with metals and alkaloids, tannic acid is often used to cause precipitation in the stomach, but the tannate formed must be removed at once, as it is gradually dissolved in the digestive fluids. The administration of tannic acid is therefore only a temporary expedient to al-

low of active measures being taken to empty the stomach."—(Pharmacology and Therapeutics, on the Action of Drugs, Cushing.)

"Tannic acid is an antidote to alkaloids, metallic salts, and tartar emetic, forming insoluble tannates, which should be removed if possible by evacuation of the stomach."—(Veterinary Materia Medica and Therapeutics, Winslow.)

Milks has the following to say under tannic acid:

"Antedote to poison.—It is the chemical antidote to various metallic and alkaloidal poisons, since it precipitates these as the insoluble tannates. The precipitate should be immediately removed, however, as it is gradually dissolved by the fluids of the intestinal tract."—(Veterinary Pharmacology and Therapeutics.)

If we interpret the above quotations correctly, the action of the tannic acid on the strychnine is of short duration, and if the stomach is not quickly evacuated by artificial means, the strychnine is still dangerous to the patient.

The use of tannic-acid treatment, no doubt, is very applicable for humans and domestic animals, where medical service is quickly available, but rodents do not regurgitate their food.

Alfilaria, as mentioned by Dixon and Garlough in connection with tannic and strychnine, is scientifically known as *Erodium cicutarium*, and belongs to the Geranium family *Geraniceae*.

Erodium is a plant introduced from Europe. It is common in California, but rare in Colorado. In Colorado, to the best of our knowledge, it does not occur in the territory inhabited by *Citellus elegans elegans*.

We fed a number of Wyoming ground squirrels Alfilaria, which we raised in our back yard from seed secured from California. The squirrels were fed nothing but the Alfilaria for 7 days and then were fed the poisoned oats. The same number of check squirrels were fed nothing but dandelion for the same length of time, and then were fed the poisoned oats.

Our experimental work feeding the Wyoming ground squirrel Alfilaria has shown that, insofar as this squirrel is concerned, this tannin-bearing plant has no effect on the action of the strychnine-poisoned oats when the squirrels are fed the Alfilaria for a period of 7 days before feeding the poison.

The squirrels fed the Alfilaria and dandelion showed no difference in poisoning results, and had the same individual resistance to the drug whether they had been fed dandelion or Alfilaria.

Our experimental work does not indicate that tannin-bearing plants neutralize strychnine on poisoned grain to an appreciable extent when fed to the Wyoming ground squirrels.

We would advance the following theory as to why the poisoned grain has little or no effect on the squirrels: It is possible that they have been repeatedly poisoned until a resistance to strychnine has been built up almost to the point of immunity, or that they have a high individual resistance for the poison, or a combination of the two.

We have found no reason to think that rodents "get wise" to poison when fed oats poisoned by Colorado Formula No. 46, nor that tannin-bearing plants neutralize or counteract the toxic effect of strychnine eaten by the Wyoming ground squirrel.

We have so far been unable to find a good published chemical analysis of the two plants fed, dandelion and Alfilaria. However, in "Practice of Pharmacy," Remington, 1896, we find the following under dandelion:

"Taraxacum owes its bitterness to taraxacin, C_8 H_{16} O. It also contains pectin, sugar, resin, gum."

In Bulletin 91, Delaware College Agricultural Experiment Station, "Toxicity of Tannin," 20 different plant families are listed as containing the greatest amount of tannin. The family that the dandelion belongs to is not among those listed.

In the California Board of Forestry Bulletin No. 2, Schneider, "Pharmacae Plants" is stated that geranium species is rich in tannin. The family to which the geranium species belongs *(Geraniaceae)* is among the 20 listed in the Delaware Bulletin. Alfilaria *(Erodium)* belongs to the geranium family.

REFERENCES

TOLERANCE

1.—"The continuous use of strychnine does not lead to tolerance, on the contrary, the repetition of its action 'educates' the nervous system to respond more readily, so that the effects are apparently slightly increased." —(A manual of Pharmacology and its Application to Therapeutics and Toxicology. Thorald Sollmann. 1917, p. 196.)

2.—"A rat can eat without apparent injury an amount of strychnine which would be quickly fatal to a prairie dog or ground squirrel.

"The extraordinary resistance of the rat to strychnine will likely be found to be true for organic poisons in general, and this resistance is seemingly correlated with the semi-parasitic habits of the animal. Its ability to subsist on partially decomposed food and garbage, containing many organic poisons, must be one of the greatest factors in its success in an urban environment."—(Dice Journal of Mammalogy, Vol. 4, No. 3, 1923.)

3.—"When considering the question of the production of tolerance of the living body to certain poisons two drugs may be pointed out as representing entirely different types. On one hand is nicotine, against which the body is popularly supposed to gain a very easy resistance, at the opposite extremity stands strychnine, for which no tolerance seems to be gained.

Such experiments as have been carried out with this drug seems to indicate an increased susceptibility when it is administered at short intervals. The question naturally arises as to whether such an apparent increase in sensitiveness was really due to an increased susceptibility or whether it might not be due to the too frequent administration of the drug.

"It is so slowly excreted that it might tend to accumulate in the body and the symptoms produced might be explained as those of cumulative action.

Conclusions

"In dogs a tolerance for strychnine may be gained, but it is very slowly acquired and at best is very imperfect.

"The results for guinea-pigs are much less conclusive, as they seem to vary a great deal in their response to the same dose."—Journal of Pharmacology 1909 (Hale.)

Strychnine Tolerance

4.—"Total amounts of strychnine equal to several times the single fatal dose may be administered to cats, dogs and guinea-pigs in fractional doses on each of several successive days, without causing permanent injury, and we must suppose that the poison is eliminated, insofar as its presence in an active state is concerned, as rapidly as it is given in those cases.

"The mechanism of the elimination, be it by fixation in certain tissues, excretion or decomposition, remains to be considered.

"The results already recorded point conclusively to the destruction of strychnine in the animal's body, and since total instantaneous destruction of such an alkaloid as strychnine is hardly to be expected, it seems probable that it is stored in some of the tissues or organs in which it is destroyed, or which gives it up slowly to be decomposed.

"Experiments on cats, dogs and guinea-pigs show that toxic doses of strychnine may be administered at short intervals during periods up to 12 days, the total amount so admisitered being equal 25 times the single fatal dose without causing perceptible lasting effect."—Journal of Pharmacology 1917 (Hatcher and Eggleston.)

5.—"The extremely high tolerance of the rat (as well as of other animals) to consecutive injections of strychnine would seem to be significant in respect to the possibility of correlating this with the failure to demonstrate as yet an habituation to this drug."—Journal of Pharmacology (Schwartze.)

6.—"Sufficient has been here demonstrated in the rat as well as by other investigators in the other animals to make feasible the beginning of an interesting investigation of the factors underlying species tolerance to strychnine."—Journal of Pharmacology 1922 (Schwartze)

Elimination

7.—"Strychnine escapes to some extent unchanged, in the urine. It appears within half an hour of ingestion and a part is delayed in the tissues and may be discovered in the urine from 3 to 8 days thereafter. The greater part of strychnine is probably oxidized in the body. The drug is not cumulative, in the sense of producing sudden and violent action following its continual use in increasing doses, yet a tolerance for it can be acquired.

in man and with difficulty in dogs."—Veterinary Materia Medica and Therapeutics, 8th Edition, Winslow.)

Elimination of Strychnine

"Elimination of strychnine in the urine of man."

8.—"There is a diversity of opinion concerning the length of time during which the administration of strychnine is followed by its elimination in the urine."—Studies on Strychnine. Grace Newman—Journ. Pharm. vol. 30-1926, p. 3.

Weiss and Hatcher found that elimination was virtually completed within 72 hours following its oral administration.

Cushing states that strychnine continues to be excreted in the urine of man for from 3 to 8 days.

Newman states the results of her experiments as follows:

"The results of these experiments are in harmony with those reports by Weiss and Hatcher, and they show that only traces of strychnine are present in the urine after 4 days."

Toxicity of Strychnine

9.—"To the Editor—Please inform me as to the average minimum lethal dose of strychnine sulphate. A young man of this town took one-eighth ounce of strychnine sulphate with suicidal intent. The undertaker was called in less than an hour, and I understand that death occurred within 20 minutes of the time the strychnine was swallowed.

"A physician who was called as soon as possible after the ingestion of the strychnine shocked me by stating that he thought that as he had taken so much it would not kill him anyway. I was called by the undertaker about an hour after the patient died, to investigate the death, as I happen to be the coroner for this county.

"My understanding of the matter is that only such drugs as act as emetics when taken in large quantities. Strychnine not being an emetic, my judgment is that the larger the dose taken the shorter the time required by the dose to cause death. If I am wrong in my reasoning, please correct me."

Answer.—"A dose of 30 mg. of strychnine has been fatal, tho the ordinary fatal dose has been about 100 mg. by mouth. The idea is perfectly correct that the larger the dose of poison, the greater its toxic effect, unless the substance has emetic action."—(The Journal of American Medical Association, June 15, 1929, p. 2044.)

Large Versus Small Doses of Poison for Building up a Resistance to Same

10.—"The more morphine you take the first time, the less effect a second dose is likely to have. This summary is the result of the researches of Dr. Carl F. Schmidt and Dr. A. E. Livingston, of the University of Pennsylvania. The idea of building up resistance to the effect of poisons by taking.

small but gradually increasing doses, is erroneous. Working with dogs they found that a tolerance to morphine developed much more slowly when minute doses were given than when larger quantities were administered. And when very large doses were given at the outset the resistance to subsequent doses were still more accentuated."—(Science Aug. 23, 1929.)

11.—Leo Laythe's report on rodent control work by the U. S. Biological Survey in Colorado, dated June 22, 1929.