Bait Shyness to ANTU In Wild Norway Rats

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In spite of the fact that certain deficiencies limit the usefulness of alpha-naphthyl thiourea (ANTU) as a rodenticide under operational conditions, it is safe and, when used infrequently, effective in controlling populations of Norway rats.

No controlled study appears to have been made on the persistence of tolerance and/or bait shyness to ANTU under field conditions. Therefore, the present study was conducted to determine what effect ingestion of a sublethal dose of ANTU would have on the subsequent acceptance of the poison by Norway rats and their intoxication by it. Laboratory and simulated field studies were made. In each instance, the rats had available a supply of wholesome food, so that they were not limited to the dilemma of poison or starvation.

The use of ANTU as a rodenticide was developed by Richter (*1*) during World War II. The compound differs from other common rodenticides in its relative specificity for Norway rats; it is essentially ineffective against roof rats, and impractical for their control. However, its use has been advocated on the basis of effectiveness and safety (*2*). Although the compound is highly toxic to pigs, to cats, and especially to dogs, it is significantly less toxic to many other species of domestic animals, and it is estimated that man also is highly resistant to the poison (*1*, *3*, *4*). Before the introduction of warfarin, ANTU was considered the safest rodenticide, with the exception of red squill (*5*).

Richter (*6*) demonstrated in the laboratory that Norway rats with no choice of wholesome food developed a tolerance and refusal response for ANTU-poisoned bait which persisted, in general, less than a month. The persistence of tolerance and/or bait shyness for a month under field conditions would present a distinct but minimal disadvantage. Actual field experience (*2*) has shown that this disadvantage of ANTU may be important if the compound is used more often than once a year on the same premises.

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Materials and Methods

The technique used for collecting and maintaining wild Norway rats was the same as that described in an earlier article (*7*). The procedure for the laboratory, as well as for simulated field studies, was to give the rats a sublethal dose of ANTU in bait and, after an interval, to test the reaction of the rats to the same poison in the same bait (group I). Two kinds of control groups were used: group II, those which were sublethally poisoned and later were offered ANTU in a different bait from that used for the sublethal dose; and group III, those which had had no previous experience with the poison whatever.

In giving the sublethal dose, it was considered highly important to have the rats take it voluntarily so that the conditions of the experiment would resemble those of the field as closely as possible. To accomplish this, ANTU was mixed in yellow corn meal (maize) at the rate of 0.1 percent by weight (1 mg./gm.). This bait was then weighed out individually for each rat used in laboratory experiments, in such a way that if the rat ate its entire portion it would consume 6 mg. of ANTU per kilogram of body weight (rats tested after 1 or 2 weeks) or 5 mg./kg. (rats tested after 1, 2, and 3 months). Rats which failed to take the entire portion within a 2-day period, as well as those which died as a result of the dose, were discarded. Rats which ate the poisoned corn meal properly were placed in stock cages and held on a diet of Purina Laboratory Chow for the appropriate number of weeks or months before testing.

All poison bait used either for the "sensitizing" dose or for the final tests in the laboratory or in the field was thoroughly mixed for 15 minutes with an electric food mixer. In the laboratory, all bait was fed in nonspillable food cups to rats individually caged in Army Medical School-type cages. During the actual tests, each rat was offered a choice of a weighed ANTU-poisoned bait and another bait which was identical except for the omission of ANTU. The baits were exposed for 2 days, after which they were reweighed and the consumption was computed. Surviving rats remained under observation for a week after the poison was removed; they were not reused for a second test.

The simulated field tests were conducted in a manner basically similar to that used in the laboratory. Rats were housed in wooden, barracks-type buildings, measuring about 20 by 100 feet. These buildings were ratproofed and supplied with ample harborage, consisting of boxes, paper, and other rubbish. Each building was artificially infested with rats at least 6 weeks before the tests were started. Before and during the test periods the rats were maintained with liberal supplies of corn meal and wheat shorts as well as water.

The ANTU-poisoned bait was distributed in the buildings in patches of approximately a heaping teaspoonful each near the harborage and along the runways. It was left exposed to the rats for 2 days and then was removed by sweeping. No attempt was made to determine the amount of bait consumed in the buildings. Two to three days later, the harborage was removed piece by piece; the dead rats were picked up and all the survivors were caught by hand in the empty room. Rats which survived the poisoning were then returned to the building, and the harborage was returned each time until the study was completed. The original sensitizing dose was given by offering ANTU in ground laboratory chow at a concentration of 0.1 percent by weight.

The simulated field tests differed from those in the laboratory in the following ways:

1. There was no assurance that every rat which survived the sensitizing dose of ANTU actually took any of the compound.

2. The sensitizing dosage of ANTU consumed by rats in the barracks-type buildings undoubtedly varied considerably on a milligram-per-kilogram basis. It was considered more valuable to simulate field conditions closely than to use an exact dosage.

3. In the 2-, 3-, and 4-month tests, some immature rats never had an opportunity to encounter a sensitizing dose of ANTU before they received the final dose.

4. Certain adult rats in the later simulated tests had more than one opportunity to take a small sensitizing dose. (The duration of bait shyness was measured from the last sensitizing exposure.)

After the sensitizing dose had been given, all rats in laboratory or simulated field experiments, except those tested in the laboratory after only 1 week, were offered ANTU at a concentration of 2.0 percent by weight. The latter animals received 1.0 percent ANTU, but the mortality of the controls was considered too low. Consequently, the higher concentration of poison was adopted for the remainder of the experiment. Concentrations of 1.0 to 5.0 percent are commonly recommended for field use.

Results

Laboratory Tests

The results of the laboratory studies are presented in table 1. Test animals had previously ingested ANTU in corn meal at a dosage of 5 mg./kg., except those held 1 and 2 weeks, which ingested ANTU at a dosage of 6 mg./kg. Group III rats were previously untreated. The

Table 1. Effect of the voluntary ingestion of a sublethal dose of ANTU in bait by wild Norway rats upon their subsequent acceptance of and intoxication by ANTU in bait

Concentration of ANTU (percent)	Time since ANTU last ingested	Group No.	Bait	Number rats	Body weight (gm.)		Percent mortality	Bait consumed per rat (gm.)				Ratio mean p/p-f [1]	Rats refusing bait (percent)	
								Poisoned		Poison-free				
					Range	Mean		Range	Mean	Range	Mean		Poisoned	Poison-free
1.0	1 wk	I	C. M.[2]	12	----------	-----	33	0. 2–1. 1	0. 5	0. 5– 5. 7	2. 5	0. 20	42	33
	1 wk	II	L. C.[3]	12	----------	-----	33	. 2–1. 5	. 6	. 3– 5. 0	2. 6	. 23	8	58
	-------	III	C. M.	13	----------	-----	62	. 3–0. 8	. 5	1. 0– 2. 7	1. 6	. 31	15	38
	-------	III	L. C.	16	----------	-----	69	. 2–0. 5	. 4	. 4– 2. 6	1. 1	. 37	19	44
2.0	2 wks	I	C. M.	14	170–394	246	14	. 2–0. 5	. 3	. 5– 5. 4	1. 4	. 21	36	50
	2 wks	II	L. C.	15	166–440	264	67	. 2–0. 8	. 4	. 5– 5. 5	2. 9	. 14	13	27
	-------	III	L. C.	20	170–388	254	85	. 2–1. 1	. 6	. 6– 6. 0	4. 1	. 15	5	45
	1 mo	I	C. M.	17	166–332	251	6	. 4–0. 8	. 7	. 9– 8. 0	3. 6	. 20	76	71
	1 mo	II	B. C.[4]	17	163–362	236	71	. 3–1. 5	. 8	. 8– 9. 1	2. 4	. 33	12	29
	-------	III	L. C.	16	156–440	277	94	. 5–2. 8	1. 2	. 5– 7. 1	1. 5	. 80	6	25
	2 mos	I	C. M.	12	221–351	274	25	. 2–0. 8	. 5	. 9– 4. 3	2. 0	. 25	50	25
	2 mos	II	L. C.	15	190–375	282	33	. 2–1. 3	. 6	1. 0–10. 0	4. 5	. 13	33	40
	-------	III	L. C.	15	152–297	207	73	. 3–1. 1	. 6	1. 0– 2. 0	1. 4	. 43	7	40
	3 mos	I	C. M.	13	197–377	306	23	. 2–1. 5	. 6	1. 0–10. 0	3. 0	. 20	38	38
	3 mos	II	L. C.	12	213–495	333	67	. 3–1. 1	. 9	. 5– 8. 5	3. 5	. 26	17	25
	-------	III	C. M.	13	187–515	330	54	. 2–1. 4	. 7	. 5– 2. 3	1. 7	. 42	23	50

[1] Poisoned/poison-free. [2] Corn meal. [3] Laboratory chow. [4] Bread crumbs.

mortality (6 to 33 percent) among group I rats previously poisoned by ANTU in the same bait is significantly different from the mortality (54 to 94 percent) among group III rats used as untreated controls. The fact that the previously treated rats which were offered ANTU in corn meal in these tests generally took a larger proportion of their total food from the poison-free bait than did rats in group III indicates that the specific ANTU-bait combination was detected by the group I rats. Furthermore, among the same previously poisoned rats there was not much difference in the percentage of those which refused poisoned bait and those which refused poison-free bait, suggesting that the refusal response was partially directed at the corn meal as such, although the possibility that the refusal of unpoisoned bait may have been caused by illness induced by eating the poison must be considered, as shown by Richter (*6*).

There was some advantage in using an alternate bait against previously poisoned rats, although the mortality (group II, 33 to 71 percent) was generally less than among rats used as untreated controls (group III, 54 to 94 percent). These results suggest that Norway rats detect ANTU as such and are not entirely dependent for their protection on an association between previous illness and a particular kind of food (in this instance, corn meal).

In the laboratory tests, bait shyness did not appear to increase or decrease when tested at intervals of 1 and 2 weeks and 1, 2, and 3 months. Under the conditions of the experiment, bait shyness lasted for an undetermined period greater than 3 months.

The actual consumption of ANTU was computed individually for each rat on a milligram-per-kilogram basis. A review of these figures showed that, on the average, rats previously exposed to ANTU were killed by the same small dosage which killed the previously unexposed controls. There was, then, no evidence for the presence of tolerance. It should be recalled, however, that the experiment was not designed for the study of tolerance, and its presence, as a minor factor, is not excluded.

Simulated Field Tests

The experimental design and summary of tests conducted with ANTU-poisoned bait against wild Norway rats living under simulated field conditions from March 31, 1949, to February 6, 1950, are presented in table 2. All rats had been in their respective buildings at least 6 weeks before they were exposed to ANTU. A breakdown of the same data for adult and immature rats is given in table 3. The mortality among all rats previously offered ANTU in the same bait was very low (group I: 0.0 to 47.7; average 15.3 percent) as compared with the mortality among rats used as untreated controls (group III: 50.7 to 80.0; average 68.1 percent). The use of different bait against rats of group II previously exposed to ANTU gave a mortality of 2.9 to 23.4 percent (average, 16.2 percent). This result confirms the presence of bait shyness to ANTU, but it fails to support the idea that this bait shyness is augmented when the poison is presented a second time in the same bait. Although the figures differ, the result is the same whether one considers the entire populations or only the adult rats which were tested.

Bait refusal among rats previously exposed to ANTU persisted unchanged for at least 4 months from the time they were last exposed.

As expected, the percentage mortality was much greater among adult rats than among immature rats (table 3). Richter (*6*) has estimated that young rats are six to seven times more resistant than adults.

It may also be noted that, although the present experiments were not designed to test the importance, which has been noted by others, of

Table 2. Experimental design and summary of results of simulated field tests with ANTU

Date	Item	Building No. 5021	5022	5023	5024	5026
Mar. 31, 1949	Group No.	S [1]	S [1]	--------	--------	--------
	Bait	L. C. [2]	L. C. [2]	--------	--------	--------
	ANTU (percent)	0.1	0.1	--------	--------	--------
	Total population	33	71	--------	--------	--------
	Number surviving	26	66	--------	--------	--------
	Mortality (percent)	21.2	7.0	--------	--------	--------
May 2, 1949	Group No.	II	I	III	--------	--------
	Bait	B. C. [3]	L. C. [2]	L. C. [2]	--------	--------
	ANTU (percent)	2.0	2.0	2.0	--------	--------
	Total population	25	52	69	--------	--------
	Number surviving	20 [4]	48	34	--------	--------
	Mortality (percent)	20.0	7.7	50.7	--------	--------
July 5, 1949	Group No.	--------	II	I	--------	III
	Bait	--------	B. C. [3,5]	L. C. [2]	--------	L. C.
	ANTU (percent)	--------	2.0	2.0	--------	2.0
	Total population	--------	47	51 [4]	--------	30
	Number surviving	--------	36	48	--------	6
	Mortality (percent)	--------	23.4	5.9	--------	80.0
Oct. 5, 1949	Group No.	--------	II	I	III	--------
	Bait	--------	C. M. [6]	L. C. [2]	L. C. [2]	--------
	ANTU (percent)	--------	2.0	2.0	2.0	--------
	Total population	--------	102	44	53	--------
	Number surviving	--------	99	23	14	--------
	Mortality (percent)	--------	2.9	47.7	73.6	--------
Feb. 6, 1950	Group No.	--------	II	I	--------	--------
	Bait	--------	L. C.	L. C.	--------	--------
	ANTU (percent)	--------	2.0	2.0	--------	--------
	Total population	--------	92	76	--------	--------
	Number surviving	--------	75	76	--------	--------
	Mortality (percent)	--------	18.5	0.0	--------	--------

[1] Rats receiving sensitizing dose.
[2] Laboratory chow.
[3] Bread crumbs.
[4] Rats in building 5021 combined with those in 5023 on May 6, 1949.
[5] Containing 10 percent peanut butter.
[6] Corn meal containing 5 percent bacon grease.

Table 3. Mortality among adult and immature wild Norway rats poisoned with ANTU under simulated field conditions

Date of test	Months since last exposure	Group No.	Building No.	Adult rats: Number in building	Adult rats: Number dead	Adult rats: Percent mortality	Immature rats: Number in building	Immature rats: Number dead	Immature rats: Percent mortality
Mar. 31, 1949	--------	---------	5021	26	7	26. 2	7	0	0
	--------	---------	5022	28	5	17. 9	43	0	0
May 2, 1949	1	I	5022	22	4	18. 2	30	0	0
	1	II	5021	18	4	22. 1	7	1	14. 3
	--------	III	5023	32	28	87. 5	37	7	18. 5
July 5, 1949	2	I	5023	35	3	8. 6	16	0	0
	2	II	5022	47	11	23. 4	0	---------	---------
	--------	III	5026	30	24	80. 0	0	---------	---------
Oct. 5, 1949	3	I	5023	32	21	65. 6	12	0	0
	3	II	5022	46	3	6. 5	56	0	0
	--------	III	5024	38	37	97. 4	15	2	13. 3
Feb. 6, 1950	4	I	5023	43	0	0. 0	33	0	0
	4	II	5022	71	17	23. 9	21	0	0

season (*8*) or temperature (*9*) on the susceptibility of Norway rats, no effects correlated with season or temperature were noted.

Discussion

In the use of ANTU as a rodenticide one encounters the problem of bait shyness (secondary bait refusal). This study has shown that such shyness lasts at least 4 months under simulated field conditions. As already mentioned, Emlen reported that poor control may result if ANTU is used more than once a year on the same premises. Following control estimated at 85 to 90 percent, essentially isolated populations recover in 15 to 44 months, or at a rate of 2 to 6 percent per month (*2*, *10*). Under these circumstances, a large proportion of the rats present 1 year after the use of ANTU would be young adults which had never been exposed to the compound. Present field and laboratory experience cannot, therefore, rule out the possibility that bait shyness to ANTU in the Norway rat lasts more than a year, or even for the lifetime of the individual rat.

Regardless of the method by which ANTU is used, it must be recognized that there is a wide variation in its effectiveness against immature and against adult Norway rats (*1*, *4*). Its unsuitability for roof rats has already been mentioned.

What, then, is the status of ANTU in rat control? Its various deficiencies should not mask the facts that (*a*) when properly used for the first time against populations of Norway rats it gives rapid and acceptable control, and (*b*) among quick-acting rodenticides it has a good record of safety under conditions of actual use.

The use of ANTU or any other rodenticide should be accompanied by appropriate ratproofing and sanitation. Destruction of the remnant of population left after the use of any quick-acting rodenticide may best be accomplished by using a different poison. However, like ANTU, other quick-acting rodenticides induce bait shyness to some extent, and their value for repeated use is thus limited. Except for red squill, which is a relatively ineffective compound, none of the quick-acting materials offer the same degree of safety as does ANTU. The advantages of warfarin for eliminating the remnants of larger populations, or for maintaining what has been called chemical ratproofing, have recently been pointed out (*7*).

The failure of this study to demonstrate the presence of tolerance does not constitute any contradiction of earlier work on this phenomenon. It does suggest that, under actual field conditions, bait shyness is a much more important factor than is tolerance in determining the outcome of control operations with ANTU. The study thus establishes a clear reason for the failure of ANTU to control Norway rats when used at too-frequent intervals.

Summary and Conclusions

1. Under laboratory conditions and with a free choice of food, Norway rats retained bait shyness to ANTU for 3 months following a single dose of it at the rate of 5 mg./kg.

2. Under simulated field conditions, bait shyness was demonstrated 4 months after the last exposure to ANTU. The time at which this reaction might eventually decrease was not determined.

3. Tolerance was not demonstrated, but, because of the nature of the tests, this result was not considered to rule out the presence of tolerance as a minor factor.

4. Bait shyness was considered a major factor limiting the usefulness of ANTU under operational conditions.

5. In spite of its deficiencies, ANTU presents the advantage of safety and, when used for the first time against populations of Norway rats, the advantage of effectiveness.

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Renewed Efforts To Uncover Scrap Metal Urged

Defense Mobilization Director Charles E. Wilson has urged increased efforts to uncover supplies of metal scrap urgently needed by the Nation's mills and foundries so that maximum steel production might be maintained. Industry, business institutions, government agencies, and other organizations are requested to redouble their efforts to increase the flow of dormant scrap to the mills.

The Public Health Service, as that agency of the Federal Government most closely associated with health departments and hospitals of the country, has been asked to bring to the attention of these organizations the pressing need for scrap metal and to request an intensification of the effort to increase supplies.

Hospitals, health departments, and other agencies and institutions can aid materially in the drive by continually surveying their installations for obsolete and worn-out machinery and equipment and disposing of such items to local scrap dealers.

Public Health Service hospitals and installations have been directed to cooperate to the fullest extent possible in the drive.